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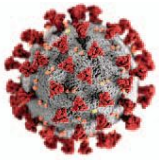
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The Journal of the Missouri State Medical Association - Since 1904

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With a large and respected editorial board and regular participation by Missouri's six medical schools on eight campuses, *Missouri Medicine* is among the nation's foremost state medical journals.

Articles are frequently cited in impact factor journals and regularly featured in the national media including: *Wall Street Journal*, CSPAN-2, KevinMD, *Outside Magazine*, *Runner's World*, *NBC News*, *General Surgery News, Ophthalmology Times*, and many others. Issues of *Missouri Medicine* are printed on acid-free paper with open access to digital issues available at www.msma.org/missouri-medicine-library.

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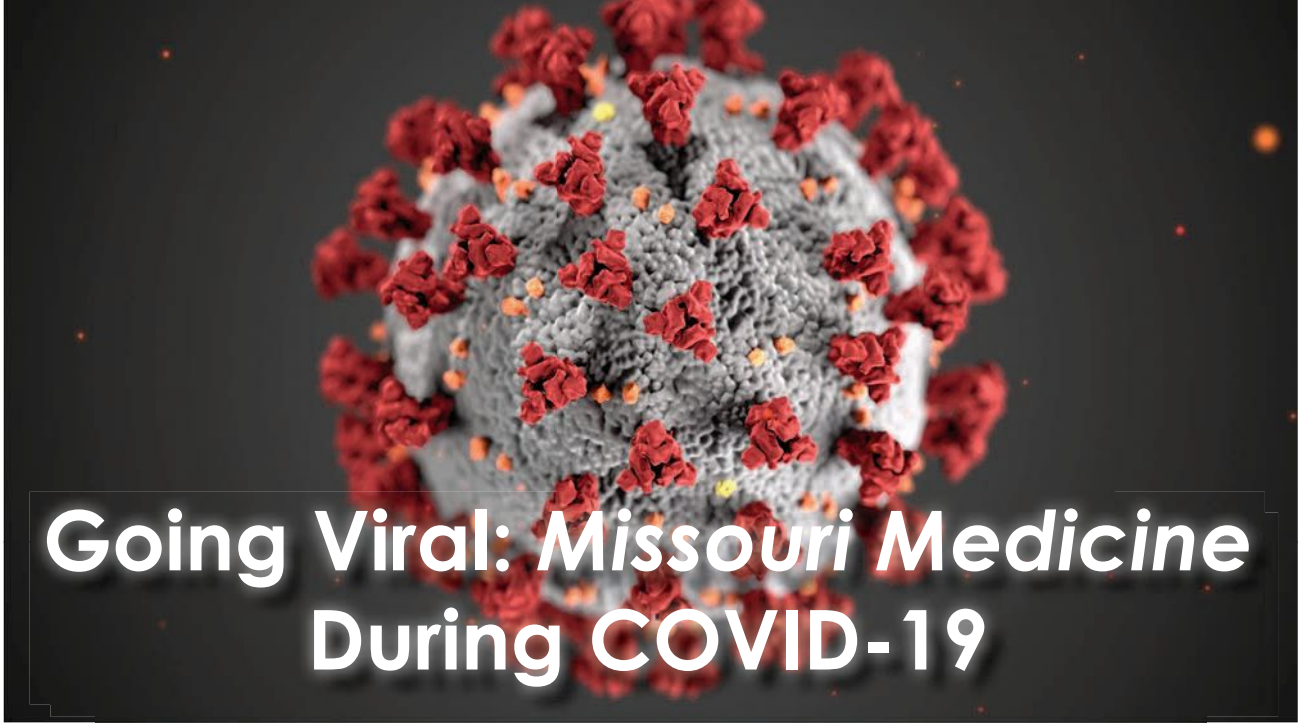


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Going Viral: *Missouri Medicine* During COVID-19

by John C. Hagan, III, MD

The much-lauded March/April 2020 Special Report "COVID-19: A Worldwide Pandemic" was produced almost from scratch over three exhausting weeks.

Is there anything about COVID-19 ("COVID") and our century's devastating pandemic that hasn't been said or that would hold your interest for about 1,200 words? I hope so, and in that frame of mind, I plunge ahead with this editorial.

Adapting *Missouri Medicine* to the COVID Pandemic, March 2020

Missouri Medicine plans ahead more than a year for its acclaimed theme issues. In early March 2020, as COVID brutally struck in full force, already in publication pre-production were themes on telemedicine (MU May/June 2020) and infectious disease (UMKC July/August 2020). How fortuitous! Given these were then among the most relevant and critical areas in all of Medicine, we contacted the respective departments and asked that manuscripts be made as inclusive as possible with any pandemic interface. We asked authors to do last minute revisions or add epilogs to give our readership the timeliest COVID information. We were greeted with enthusiasm, professionalism, and scores of timely, well-written articles. Heartfelt thanks to these authors and coordinators.

The in-production March/April 2020 Journal theme of Frontiers of Surgery, (SLU) had to be temporarily set aside as we button-holed, called, texted, emailed and otherwise cajoled various national COVID experts to ask they write 'on the fly' articles for our upcoming issue. This was while they were dealing with burgeoning clinical loads of very ill patients. The ranks of authors that stepped forward are too numerous to individually thank here but their names can be found in the table of contents page 77, volume 117, 2020. Visit http://www.omagdigital.com/publication/?m=11307&i=656017&p=2&pre=1.



John C. Hagan, III, MD, FACS, FAAO, is a Kansas City, Missouri, ophthalmologist and *Missouri Medicine* Editor since 2000. He is a multi-year Diamond Contributor to MMPAC. Shown here with long-time ophthalmic assistants Brandy and Lanette on Veterans' Day 2020.

In the face of long hours and crushing clinical loads, to a person they graciously submitted timely and authoritative newly minted articles. The much-lauded issue of March/April 2020 COVID-19: A Worldwide Pandemic with its quickly produced but authoritative *Special Report: COVID-19*, was put together in slightly more than three frantic weeks (Figure 1).

The telemedicine and infectious disease themes were given a COVID-19 orientation. In April 2020, a deluge of COVID-related perspective and scientific articles began to be received. So many, it was the proverbial 'drinking from a firehose.' The scientific articles needed peer-review; the perspectives needed sorting and editing. Our Editorial Board reviewers were quickly overwhelmed with submitted manuscripts. We turned to non-board reviewers who, similarly over-worked, found time to judge which manuscripts merited publishing. Peer reviews included detailed and extensive recommendations to elevate the article quality. These 'invited peer-reviewers' were listed in our November/December 2020 issue on page 535. Thanks, one and all, including those presently reviewing 2021 submissions.

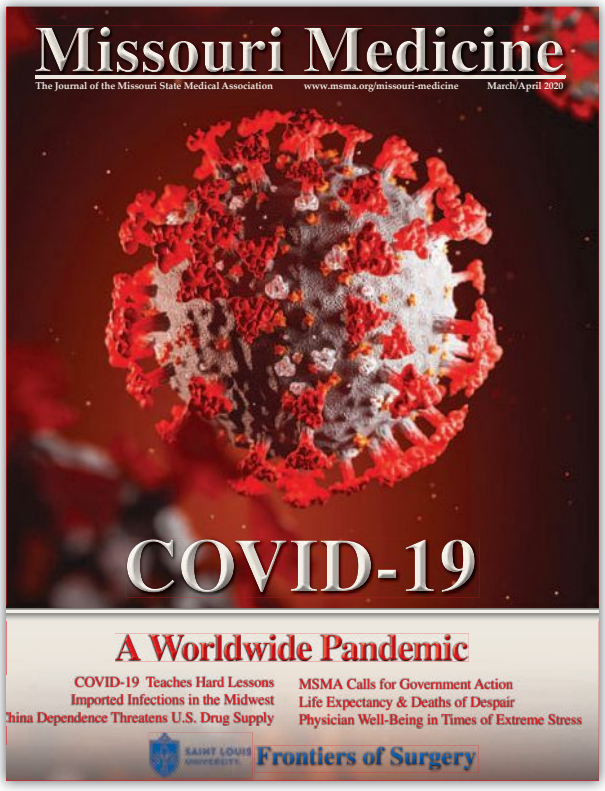


Figure 1. March/April 2020 *Missouri Medicine*

Non-COVID articles in our publication queue had to be 'bumped' as pandemic material 'went to the front of the line.' We thank these bumped authors, some of whom are still waiting for their works to be published, for their infinite patience. Even with prioritization and lengthening our queue, we had to obtain permission from MSMA to generate several issues that were the largest page counts in our Journal's 116-year history. Kudos to Patrick Mills and Jeff Howell of MSMA staff for these authorizations and absorbing the extra expense. A great example of MSMA's unsurpassed service to all physicians.

For all its professional success and national reputation, our Journal singularly owes much to its ultra-competent, dedicated Managing Editor Liz Fleenor. For 19 years, Liz has worked with me on compilation and production of our Journal. During COVID, she worked at times at MSMA headquarters, at times from home. She had to use two different computers with no complete set of files. Hardware and software problems occurred. As throughout her tenure, she worked tirelessly and competently to get each issue composed and timely uploaded to PubMed/PubMed Central and Ovid Bell Press. The content was outstanding and had a polished, appealing appearance. I greatly enjoy working with Liz; she is a huge asset for *Missouri Medicine* and MSMA. She also serves as Director of Communications. Thank you, Liz, on behalf of a grateful Editor and MSMA.

Personal Musings on COVID

It is a matter of conjecture who first recognized the potential for a COVID pandemic. Some say Bill Gates, some Nostradamus, some a careless viral researcher at the Wuhan BSL-4 Viral Laboratory. My nod goes to an ophthalmologist in our Discover Vision Centers office who predicted in early January 2020 that this would be a pandemic. He warned all who would listen to prepare for something akin to the 1918 Influenza Pandemic. Me, being me, thought I had seen in all; Asian Flu, Hong Kong Flu, Swine Flu, SARS, MERS, Avian Flu. While serious, none had lived up to their predictions as the next 1918 Influenza Pandemic. Our staff would ask me if our ophthalmologist was a Casandra or on to something. I would shake my head knowingly and say, "None of the other flu epidemics in the last 60 years have been as bad as predicted; I think this will be more fizzle than sizzle." I have apologized several times to my colleague.



Figure 2. The Hagan's COVID Art Gallery

I've asked him if he has any thoughts about winning Power Ball numbers or stocks that will soar in 2021 to let me know.

My wife Becky and I moved frequently during training from Missouri to medical school (Chicago), internship (Milwaukee), USAF medical corps (North Dakota), and residency (Atlanta). We have endured blizzards, tornados, forest fires, widespread riots, floods, ice, and snow storms of Biblical proportions. Long ago we learned to stock our home with emergency provisions, something I wrote about in *Missouri Medicine* previously.[1] Visit http://www.omagdigital.com/publication/?m=11307&i=117278&p=24. Our current emergency amenities include natural gas-powered electricity generator, more stored water than a small swimming pool, and enough freeze dry food to feed two people and a voracious over-weight cat for a year. Yes, we even had an adequate supply of toilet paper and Lysol wipes. Consider reading the article and laying in your own emergency provisions.

Becky and I live in a lovely subdivision of Kansas City North called Briarcliff Estates. It was developed about 1982-83. We are the last of the original home owners. It is now populated with young and middle-aged families. We are among the oldest people in the neighborhood. Early in COVID, our younger neighbors came to check on us almost daily to see how we were doing. They brought us cookies and baked goods. Their children made us colored drawings with inspirational messages which we displayed in our window. We called this collection the "COVID Art Gallery" (Figure 2). As months passed the word got around that "the Hagans can fend for themselves." Living on a cul-de-sac, spring, summer, and fall 2020 more than a dozen children rode their bikes and skateboards down our steep driveway. This diversion aside, 2020, as for many people, was one of the most difficult years of our lives.

Missouri Medicine Will Publish the Definitive History of the COVID Pandemic

In the centennial year of 2018, *Missouri Medicine* published[2, 3] an award-winning series of articles on the Great Influenza Pandemic of 1918. The authors were David S. McKinsey, MD, Joel P. McKinsey, MD, infectious disease specialists, and Maithe Enriquez, PhD, APRN. Our Journal is delighted to announce that this trio of authors will write a similar series of articles for early 2022 documenting the pandemic of our time, COVID-19.

Hope This goes Viral: All Physicians Need to Belong to MSMA

By the way, there are many reasons to belong to MSMA. It is among the top three most effective state medical societies and among the lowest five in annual dues. MSMA is the "Big Tent" for all Missouri physicians. MSMA leads the way, in advocacy and education! Joining MSMA is a smart business decision. The return on investment that members receive is far more than the cost of dues. To every physician or physician-in-training not belonging to MSMA, especially those of you that publish in its Journal, I cordially and sincerely invite you to join MSMA in 2021. Please visit www.msma.org/joinrenew to become a member. You may contact MSMA's Cassie Williams at cwilliams@msma.org if you have any questions.

References

1. Hagan III JC. Why me? Why now? Why prepare for sudden misfortune? *Missouri Medicine* 2012;109:182
2. McKinsey DS, McKinsey JP, Enriquez M. The 1918 Influenza in Missouri: Centennial Remembrance of the Crisis. (Part 1) *Missouri Medicine* 2018;115:183-188
3. McKinsey DS, McKinsey JP, Enriquez M. The 1918 Influence in Missouri: Centennial Remembrance of the Crisis (Part 2). *Missouri Medicine* 2018;115:319-324

MM

Missouri State Medical Association's COVID-19 Pandemic Presidency

by George J. Hruza, MD

My presidency started very low key with a few minutes on a Zoom call reciting the oath of office on April 4, 2020. Warren Lovinger, Jr., MD, visited all 114 Missouri counties during his term as MSMA President. I visited my home office, kitchen, TV room, and bedroom, and back again numerous times during my year. Mine was a truly virtual experience. Despite a lack of travel, MSMA has been engaged and successful at the state legislature for the benefit of our patients and Missouri physicians and virtually connected with our members statewide. We have kept you informed about the pandemic and worked with the state to get vaccines to all healthcare workers and vulnerable populations as quickly as possible.

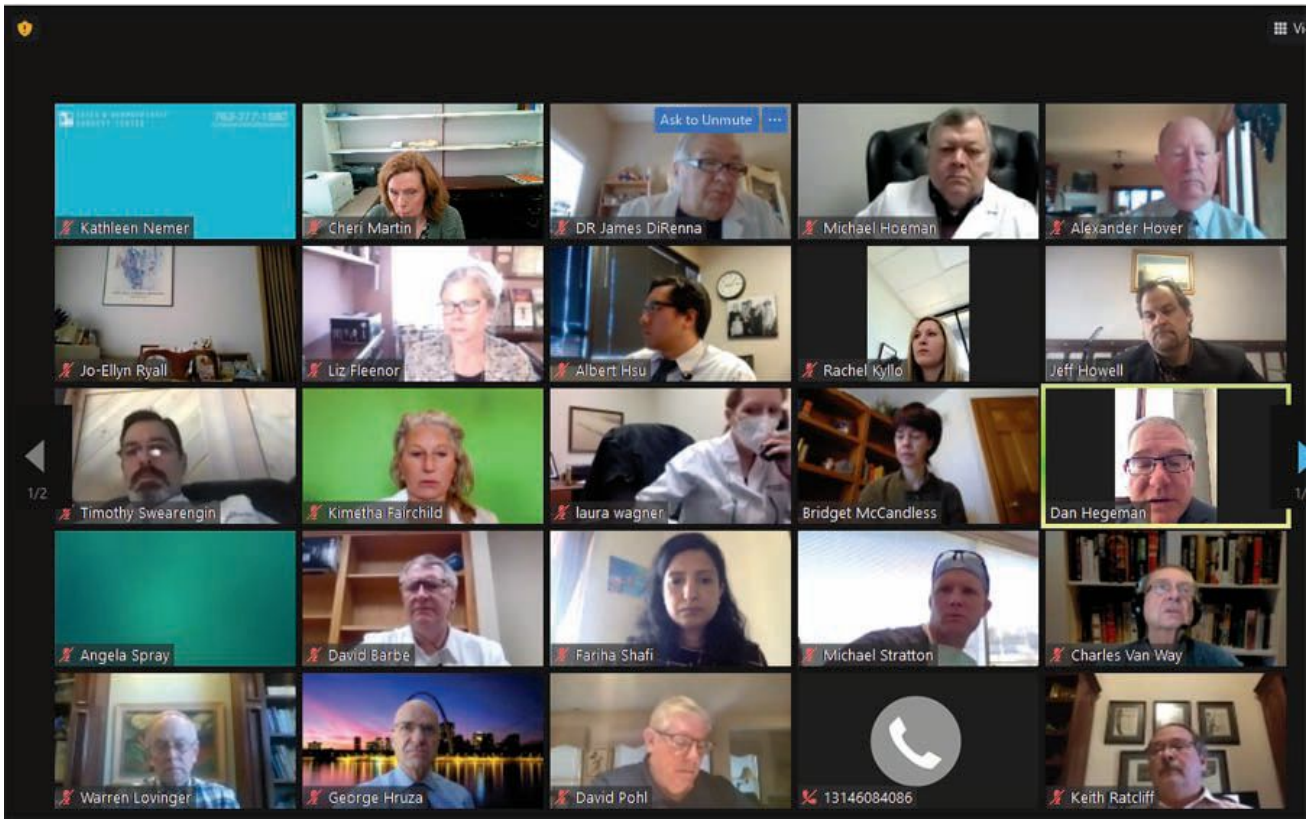
MSMA and Missouri physicians are very fortunate to have two professionals, Heidi Geisbuhler and Shantel Dooling, advocating for us in Jefferson City all year long. The 2020 legislative session was compressed and, at times, virtual, due to the pandemic. Despite the legislators being preoccupied with COVID-19, MSMA had significant successes. We were able to get legislation passed (SB 591), that tightened requirements on awarding punitive damages in medical malpractice cases. There has been a rapid increase of such claims since the non-economic cap was put in place to get around the cap. Now punitive damages can only be claimed in cases of "clear and convincing" intentional or malicious misconduct by the physician.

Hiring or having an associate join your practice usually means many months of working through the arcane credentialing process to get the new associate onto managed care plans without being able to see patients and bill the insurance companies for taking care of their subscribers. We were able to get legislation passed (HB 1682) that allows insurance companies to reimburse physicians for services provided to their subscribers while the credentialing process is completed with a credentialing decision required within two months down from three. The physician submits the bills once they have been credentialed. This is akin to the credentialing process that Medicare uses and should help new physicians hit the ground running to take care of their patients.

Physicians have far more extensive and longer clinical training with the training focused on independent medical decision making before becoming licensed to practice medicine. That makes physicians the appropriate leader of the healthcare team. Non-physician clinicians try to expand their scope of practice and ask for less or no physician supervision or collaboration every year. For the benefit of our patients to receive optimal care, MSMA continues to advocate to keep physicians as leaders of the healthcare team. In 2020, we were able to convince our legislators to keep the status quo by not advancing physical therapist direct access (HB 1869), APRN collaborative practice (SB 965, HB 1617, HB 1816, HB 2226), APRN licensure (SB 714, HB 1441), and CRNA scope (SB 863, HB 2057). There were two special sessions in 2020: one to deal with violent crime and another to deal with COVID-19 liability reform. Neither achieved its



George J. Hruza, MD, MBA, FAAD, FACMS, is the 2020-2021 MSMA President. He practices Dermatology in St. Louis, Missouri.



Even White Coat Day was a successful, virtual event with over 100 attendees/physicians from around the state!

goal, but overall, the 2020 legislative session was very good for Missouri physicians.

We are now in the middle of the 2021 legislative session, again disrupted multiple times due to COVID-19 outbreaks at the capitol. Most important for Missouri physicians is COVID-19 liability relief so that we can take care of patients without worrying about frivolous pandemic-related lawsuits. The legislation is on its way to, hopefully, make it into law. MSMA has been advocating for the elimination of requiring maintenance of certification participation for hospital and health insurer credentialing (Missouri passed such a ban a few years ago as it relates to state licensure); for truth in advertising (dealing with advertising one's board certification); for a statewide PDMP (patterned after the St. Louis County PDMP); and for insurance coverage for skin cancer screening.

MSMA has been testifying against bills to allow dentists to administer any vaccine; to allow non-physician clinicians to sign off on home health plans; to allow the establishment of a doctor patients relationship with an online questionnaire without in-person contact after the public health emergency has concluded; and to allow state government to overrule local and county health department decisions that they deem best for their population. I am sure there will be many other good and bad bills affecting our patients and Missouri physicians throughout the 2021 legislative session. MSMA will be at the Capitol every day to make sure that our voices are heard. Please make sure to respond to our calls to action by contacting your legislators to support our efforts on your behalf.

MSMA has kept and is keeping our members informed about all the legislative and advocacy happenings with weekly Zoom meetings. These meetings with legislators and our advocacy staff give regular legislative updates as well as our weekly *Legislative Report* throughout the session. We have also kept you informed on all aspects of COVID-19 through our website and weekly email communication of "5 Things you Need to Know." MSMA members can get the latest unfiltered

Get Involved!



by Jeff Howell, JD
MSMA Executive Vice President

Much of the value of MSMA membership is in the advocacy work we undertake for Missouri physicians here in Jefferson City. For over 100 years, MSMA has served as the physician's voice in the capitol. We're proud to be the standard bearer for the practice of medicine. No one is bigger; and no one does it better.

We strive to provide our members with opportunities to engage with legislators and decision-makers that affect your practice. For over a year, we've provided a weekly COVID conference call with the Director of the Department of Health and Senior Services. This year, we have begun holding Legislative Lunches on Fridays at noon, giving physicians facetime with various lawmakers. We had 14 elected officials participate in our 2021 Virtual White Coat Day.

Our advocacy on your behalf is not effective unless you are involved. Participate in these events. Volunteer for the Physicians of the Day program next year. Donate to MMPAC. A lack of participation leads legislators to believe that the MSMA legislative agenda is not important to physicians, so why should it be important to them?

If you are a member and are not receiving our advocacy publications, that means we don't have your email address. Please contact the MSMA office with that information so that we can show you where the value is in your membership.

Involvement. Advocacy. Membership.

Thanks for being an MSMA member.

information and get their questions answered on COVID-19 at the weekly Saturday morning calls arranged by MSMA with the Director of Missouri's Department of Health and Senior Services, Dr. Randall Williams.

Operation Warp Speed got two COVID-19 vaccines approved in less than a year. Healthcare workers (HCWs) and congregated facility residents and staff were the first category eligible to receive the vaccine. Employees of hospitals started receiving vaccine doses in December 2020. However, office-based physicians and staff seemed to not be included in the initial vaccine roll-out. MSMA went into action and worked with the Department of Health to make sure that office based HCWs be included in the vaccination effort. Hospitals were asked to vaccinate all HCWs (not just their employees or affiliated physicians) and county health departments also got into the action. Even the national guard helped out. By February 2021, all HCWs that wanted to get the vaccine should have been able to get it.

Leading MSMA during this COVID-19 year, while different than expected, was very satisfying due to the success we had at the legislature and helping our members cope with COVID-19, especially with vaccine access. I was honored to help inaugurate the St. Louis Metropolitan Medical Society, Boone County Medical Society, and Greene County Medical Society Presidents and Councils. I advocated for our members and patients at MSMA's March 2, 2021, White Coat Day with our state legislators and at the AMA's National Advocacy Conference February 22-25, 2021, with our members of Congress.

Finally, I want to thank our executive directors, Patrick Mills (2020) and Jeff Howell (2021) and MSMA staff, Benita Stennis, Carol Meyer, Cassie Williams, Cheri Martin, Heidi Geisbuhler, Liz Fleenor, and Shantel Dooling, for working tirelessly to keep MSMA strong, stable, and influential in Missouri. They made my job easy, but also very effective. This hard work benefits both our patients and members. **MM**

Physicians and Patients Score a Major Victory in Courts; Hospitals Lose

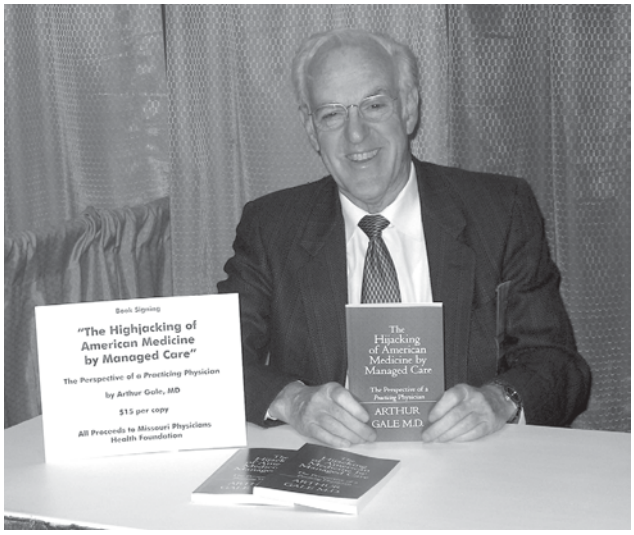
Hospitals' Opposition to Site Neutral Payments Prove They Are More Interested in Profiting from Owning Doctors than in Lowering Health Care Costs

by Arthur H. Gale, MD

When hospitals own physician practices Medicare pays them almost double what it pays physicians who practice independently. This needs to change!

Introduction: All Doctors Are Equal But Hospital-Employed Doctors Are More Equal

Employed physicians now exceed those who own their practices.[1] Most are primary care physicians who are owned by hospitals. A major reason for this is that when hospitals own physician practices Medicare pays them almost double what it pays physicians who practice independently. This needs to change! The explanation for this anomaly is that in the 1990s hospitals and managed care advocates convinced Medicare and the public that costs would decrease when doctors were employees of hospitals. The cost savings would take place through vertical integration, coordination, and economies of scale. Vertical integration is a code word for hospitals ownership of doctors.



Arthur H. Gale, MD, is a *Missouri Medicine* Contributing Editor and the author of numerous books on practice management. He is a retired Internal Medicine physician in St. Louis.

How Physician Payment Inequalities Were Developed

I also recall the promoters of managed care at that time saying that hospitals should structure themselves like General Electric which was one of the most successful and profitable corporations in America. I wondered why a corporation whose main goal is to generate profits for investors should serve as a model for hospitals which are primarily service institutions. Businesses often fail. Hospitals in general can't fail. They are a vital necessity for society. A recent book published in 2019 describes what one critic called the "devastating disintegration" of General Electric since it peaked in the 1990s. It is a much smaller company and worth far less today than it was then.[2] "Devastating disintegration" aptly describes our current profit driven health care system especially as it applies to Medicare.

Virtually no one today believes that vertical integration or the hospital employment of physicians lowers health care costs. Not even the hospitals. Over



the past 30 years health care costs have gone up not down especially in the hospital sector which at over 30% constitutes the largest single cost center in the entire health care economy.[3] Analysts know that the real reason that hospitals own physician practices is that it increases hospital profits. They write:

"Hospitals become more profitable when they employ doctors not only because they get paid more but because buying doctors expands the hospital market share which allows hospitals to negotiate higher reimbursements from all payers including Medicare which contributes to the upward cost spiral…As hospitals successfully negotiate with payors for higher reimbursement, payors cut payments to independent doctors making it harder for the doctors to resist offers of employment."[4] This analysis explains why it is so difficult for independent doctors to survive in practice.

Hospitals convinced Medicare to pay hospital-owned physicians in outpatient settings at nearly twice the rate that they pay independent physicians. I know of two internists who practiced internal medicine in the same office. Both were trained at the same institution. Both were board certified. One was owned by a hospital and one practiced independently. Medicare paid the hospital-owned physician nearly double the rate of the independent physician for both an office visit and complete physical exam. There is no valid reason for this. It's a classic example of corporate welfare.

Medicare is in crisis. The Medicare Trust Fund is expected to go bankrupt in 2024.[5] For years the Medicare Patient Advisory Commission (MedPAC) that advises Medicare on payment issues has not swallowed the hospital line and has advised Medicare to pay physicians in off-hospital campus locations at the same rate that it pays independent non-hospital owned physicians. About two years ago the department of Health and Human Services (HHS) implemented this rule.

Hospitals Go Ballistic to be Paid at Same Level as Independent Physicians

The hospitals panicked. Medicare payments constitute about 40% of their revenue.[6] Not only would they lose the extra government reimbursement for their offsite physicians but the lower Medicare reimbursement could cause many doctors to leave hospital employment. Even worse hospitals could lose market share and the lucrative referrals that primary care doctors make to hospital specialists and to hospital laboratory and radiology facilities.

Before Medicare could implement the new rules the American Hospital Association, the Association of American Medical Colleges and three health care organizations sued the Department of Health and Human Services (HHS). A Federal District Court ruled in favor of the hospitals. More recently a Federal Appeals Court unanimously reversed the lower court's

decision. The new Medicare rules stand. Medicare will no longer pay hospital employed physicians in outpatient settings more than it pays independent physicians.[7] Some authorities think that it is unlikely that the U.S. Supreme Court will allow this issue to come before it, but the hospitals are gearing up to present their case to the Supreme Court.[8]

This is a major victory for physicians, patients, and American taxpayers who finance Medicare. Physician groups including the two largest specialty societies—the American College of Physicians (ACP) and the American Academy of Family Practice (AAFP)—have long supported site neutral payments.[9] Health insurance companies, some business groups and others also support the new Medicare rule. It is also a victory for patients. As a result of the court decision they will have lower copayments and greater freedom of choice of physician.

Equal Payment Will Reduce Healthcare Costs and Insure Payment Equality

Under the new rule Medicare would pay all hospital-owned physician offices located off campus at the same rate as independent physicians. Under the new payment schedule the physician office rate for all physicians will be $39.76; beneficiary cost sharing will be $9.94 for a total of $49.70. Under previous HHS rules Hospital Outpatient Departments (HOPD) including facility fees were paid $98.70 for an office visit; beneficiary cost sharing was $24.68 for a total of $123.38.[10]

Initial savings for Medicare will be about $800 million per year. However, this is just the beginning. Medicare has much bigger plans for cutting costs in the future. Procedures that are now performed in hospitals will eventually be performed in outpatient settings. "Patients and Medicare pay more when the same services are delivered in hospital outpatient departments instead of independent physician practices for a wide variety of services—chemotherapy: $281 vs. $136; cardiac imaging: $2,078 vs. $655; and colonoscopy $1,383 vs. $625."[11]

The administration estimates that savings would be approximately $47.2 billion over ten years. The budget also proposes to eliminate payment disparities in outpatient care by applying site neutral payments for certain services performed at on-campus hospital outpatient departments which would increase savings to approximately $117.2 billion.[12]

Conclusion

Medicare has finally challenged the managed care-hospital canard that vertical integration reduces costs. It has finally said enough is enough. Only Medicare has the purchasing power to confront the hospitals and tell them we're not going to subsidize your out-of-control costs anymore. We're not going to pay equally well-trained doctors who perform equal work differently based on whether they are hospital-owned or not hospital-owned.

A question arises whether Medicare site neutral payments will eventually apply to on campus primary care physicians. Their work is essentially no different from primary care physicians who work in outpatient settings unless they take care of hospitalized patients (who more and more are being cared for by hospitalists.) If this should happen then there may be a significant exit of physicians from hospital employment.

That might not be such a bad thing. Physicians' take-home pay would decrease but they would not have hospitals treat them like factory workers demanding that they see patients on an assembly line basis; they could spend more time with patients; they would not have to take their electronic health records home at night for more hours of charting; they would have more freedom; they would have less burnout. Best of all they might even enjoy practicing medicine again.

References

1. Henry, Tanya Albert, Employed Physicians Now Exceed Those Who Own Their Own Practices.httPS://ama-assn.org/about/research/employed-physicians-now exceed –those- who-own- their-practices. Based on 2018 AMA Physician Practice Benchmark Survey
2. Gryta, Thomas, Mann, Ted, Lights Out, Pride Delusion, And The Fall Of General Electric, 2020.
3. American Medical Association; Policy Research Perspectives: National Health Expenditures, 2018.
4. Association of Independent Doctors (AID) Comment on CMS Site Neutrality; 1/13/2021.
5. Levitt, Larry, The Language of Health Care Reform, JAMA, January 19, 2021.
6. Gee, Emily, The High Price of Hospital Care, Center for American Progress, 6/26/2019.
7. Morse, Susan, Appeals Court Sides With HHS on Site Neutral Payments. Health Care Finance, July 17 2020.
8. Cohrs, Rachel, Hospitals Will Need Supreme Court's Help to stop site-neutral, 340B Cuts, Modern Health Care, October 19, 2020.
9. Alliance for Site Neutral Payments, accessed 1/29 /21.
10. Ibid.
11. Ibid.
12. Alliance for Site Neutral Payment Reform Commends Inclusion of Site Neutral Payment Reform FY 2021 Budget, February 11, 2020. **MM**

Higher Consciousness Through Self-Inquiry Can Improve Cardio Metabolic Outcomes, Mental Health, and Resilience

by Anand Chockalingam, MD, Smrita Dorairajan, MD & Kavin Anand

Heartful Living is our unique cardiac wellness program based on self-inquiry. This meditative system based on Siddha Yoga, positive psychology, and mindfulness, has helped reduce cardiac symptoms, procedures, and medicines all while enhancing confidence and optimism. We share a few illustrative cardiac cases to outline our program. Higher consciousness, through numerous tools and mind-body methods, is at the core of this program. We start with a couple of illustrative cases and explore the basis and scope of self-inquiry in improving health.

Illustrative Cases

Case 1

A 60-year-old white woman presented in spring 2020 with poorly controlled hypertension of 25 years duration. Despite six medications, her BP was over 200/110mmHg on several occasions at home. She was anxious about BP control and leg edema at initial clinic visit when BP was 174/84mmHg, BMI 37.6 and weight 115.3Kg. She engaged with our self-inquiry program and started fasting with mindfulness practice. At six months, although she has not lost any weight yet, her BP is well controlled on only three medications. Her confidence has increased, and she feels more energetic than ever before.



Anand Chockalingam, MD, (left), and Smrita Dorairajan, MD, are both at the Harry S Truman VA Medical Center, Columbia, Missouri, and in the Division of Cardiovascular Medicine, Department of Medicine, University of Missouri-Columbia, Columbia, Missouri. Kavin Anand is at Stanford University, Stanford, California.

Case 2

A 59-year-old woman developed heart failure with preserved ejection fraction due to morbid obesity, weight 133kg, BMI 47 as well as cirrhosis and functional limitations. She has lost 67 pounds, over 22% of initial weight, over the last two years (Figure 1). She is more confident and enthusiastic now. Echocardiographic diastolic parameters have improved. She is enthusiastic about her future, on fewer medications, and anticipates losing another 67 pounds over the next two years.

What is the Real Scope of Health?

We believe health is the freedom to pursue one's passions. This requires at every stage of life identifying with activities, pursuits, and causes that are genuinely interesting. Once an individual recognizes this core concept, it becomes easier to accept responsibility for lifestyle choices and health. Connecting with or discovering new interests, especially when older, requires willingness to explore and experiment. Despite supervised weight loss with rigorous research protocols, 50-80% of the weight is regained within two to five years.[1] Self-inquiry appears to succeed through changes at the subconscious level. We have numerous patients naturally sustaining health gains beyond five to ten years. Chronic kidney disease, typically considered irreversibly progressive, tends to improve with this program.[2] As is often the case, anxiety and hypertension appear to have propagated each other in Case 1. When we address mood and outlook, sustaining lifestyle improvements long term becomes easier. While we routinely see BP reduction with weight loss, this patient appears to have benefited primarily from the mindfulness component of our program. Case 2 highlights the potential to enhance self-confidence and meaningful engagement with life, and thereby improve

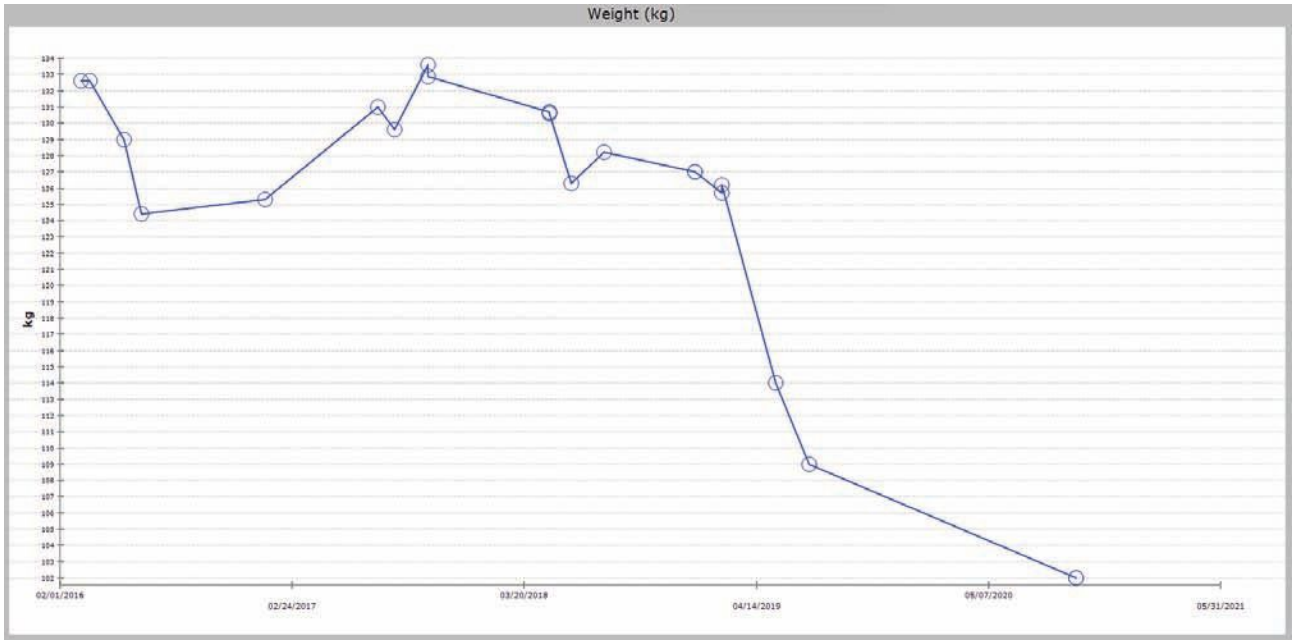


Figure 1. Illustrative case 2 weight graph in kg over last few years from the electronic medical records, where HUGE fasting and intentional weight loss significantly improves heart failure.

survival and quality of life in complex heart failure patients.

Self-Inquiry Based Cardiac Wellness Program

Self-inquiry is simply introspecting on the question "who am I?" Siddha, meaning 'aiming for perfection,' is the Tamil medical system with a rich 5,000-year tradition. Siddha way of life encourages primary prevention, mental wellbeing, and holistic health through yoga while offering natural and herbal cures for several ailments and chronic diseases.[3] Bodhidharma popularized ancient Siddha martial arts and self-inquiry methods in the Orient, now widely practiced as Kung-fu and Zen philosophy.[4] Since 2015, we have formally offered "Heartful Living," a self-inquiry based cardiac wellness program, in mid-Missouri for patients, families, healthcare providers, and physicians. This is organized through the whole health initiative at Harry S Truman Veterans Hospital for veterans with cardiac disease as well as the local community at no cost.

This program is unique, incorporating positive psychology, mindfulness methods, and Siddha yoga with evidence-based cardiology. Participants attend eight weekly hour-long sessions with 30 minutes of didactics, 15 minutes of different self-inquiry mindfulness practices, and 15 minutes of open discussion. We tailor the program to individual requirements and set daily goals to practice during the week at home. The key topics of diet, exercise, sleep, stress, time management, optimism, mindfulness, altruism, service, and other ideas for adding meaning to life are covered. Medical management is deferred to patient's providers. Participants gain a new perspective on consciousness that is simple, intuitive, and self-explorable. Improvements in cardiac symptoms and risk factors naturally ensue from this self-inquiry. As patients gain a deeper mind-body connection, exercise capacity, compliance and self-reported sense of well-being improve significantly (Figure 2). With nearly 90% diabetes and 80% heart disease attributed to lifestyle and our own research demonstrating importance of adolescent outlook and mood, we have now opened this initiative to students and family members of cardiac patients.[5, 6] Primordial prevention is several-fold cost effective when we enhance physical health and mental wellbeing from childhood.

Consciousness

We interpret life events as 'good' or 'bad,' based on our beliefs and hopes. There is, however, considerable individual variation in deriving meaning and happiness. Consciousness is our perception of ourselves and the world and the basis for experiencing life. Consciousness is awareness by the mind of self and the world, which in

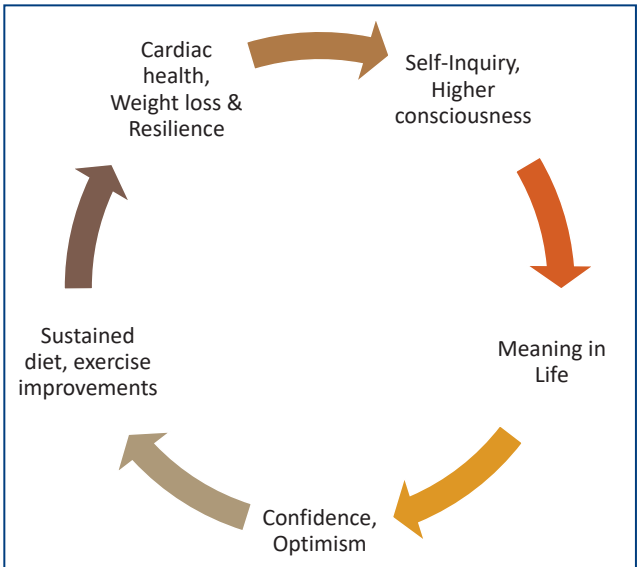


Figure 2. Self Inquiry initiated with HUGE, hunger gratitude experience, results in higher consciousness leading to progressive gains in confidence and cardiac risk predictors, which in turn reinforces more self-inquiry, sustaining the long-term improvements in health.

turn determines the response to one's surroundings.[7-9] Based on our perception of the self, we can discern three states of consciousness (Figure 3).

1. The predominant state for most people is 'mind consciousness.' People identify with their thoughts as their true self, react to life events in an endless loop and this becomes the entire experience of life. Just like thoughts or dreams, life becomes a roller-coaster ride when the mind is the self.

2. A minority of people operate naturally through kindness towards others (family, friends, colleagues) or dedicate themselves to a higher value (ideals, cause, calling). Their thoughts and personal interest take back seat in pursuing 'the bigger picture.' This 'heart-consciousness' is selfless kindness which offers a natural freedom, higher energy, and ease of movement through the challenges of life. This enables passionate living with deeper empathy.

3. The awakened or enlightened state is very rarely attained. Very few people operate at this expanded state of consciousness. This is truly living free, where the self is boundless, and life simply flows.

The three states are fluid without distinct boundaries. The same person can identify at one instance with his thoughts and trivial stresses while at another time as meaningful integral part serving a bigger purpose. How one operates in each situation is determined by his level of awakening or intensity.

Consciousness is not theory or philosophy for the mind to assimilate. Thus, consciousness eludes comprehension even to the most intelligent amongst us. On the other hand, various levels of consciousness can be verified as our personal experience of reality.

Origin of Human Consciousness

Pre-humans did not have 'self-consciousness' and related with the natural world more like modern apes.[10] With their limited physical strength, pre-human populations were small, and thrived on eating fruits and nuts as well as scavenging the leftovers of big cats' prey. With evolution, approximately 200,000 years ago, our thinking and mental capacity attained a critical mass, [11] There was no turning back after gaining this cortical brainpower, which helped us rapidly ascend to the top of the food chain. For the first time in evolution this was brought about by the analytical mind. Our thinking opened new doors -- we discovered strength in groups, invented clever devices and weaponized fire. Bigger, faster and stronger animals could not match our mind's innovative tools and collective strength. Thus, mankind's ascent as the master of the natural world coincided with thought-identification or mind consciousness.

Our population expanded, and the hunter-gatherer ancestors found it hard to sustain our growing population. About 10,000 years ago we began farming and settling along riverbeds. Through agriculture, humans were able to produce far more food and our population began to grow exponentially. This surplus of resources enabled specialization of labor and gave birth to the early waves of civilization. Not only did our numbers grow, our collective human knowledge began to compound, rapidly separating us from animals:

1. Animals can only learn intuitively through experience. Instinct helps them relate to their environments and manage natural threats.

2. Animals don't perceive time the way we do. They lack the imagination to project a future reality different from their own past or prior generations.

3. For animals, little logical knowledge or specific memory is accumulated or passed on to subsequent generations.

Human knowledge, however, is far more potent due to the prefrontal cortex.[11] Critical thinking, memory, language, and learning keep advancing with each generation, making us unique. The thinking, analytical conscious mind has been talking to us loud and clear for 200,000 years now. We therefore perceive

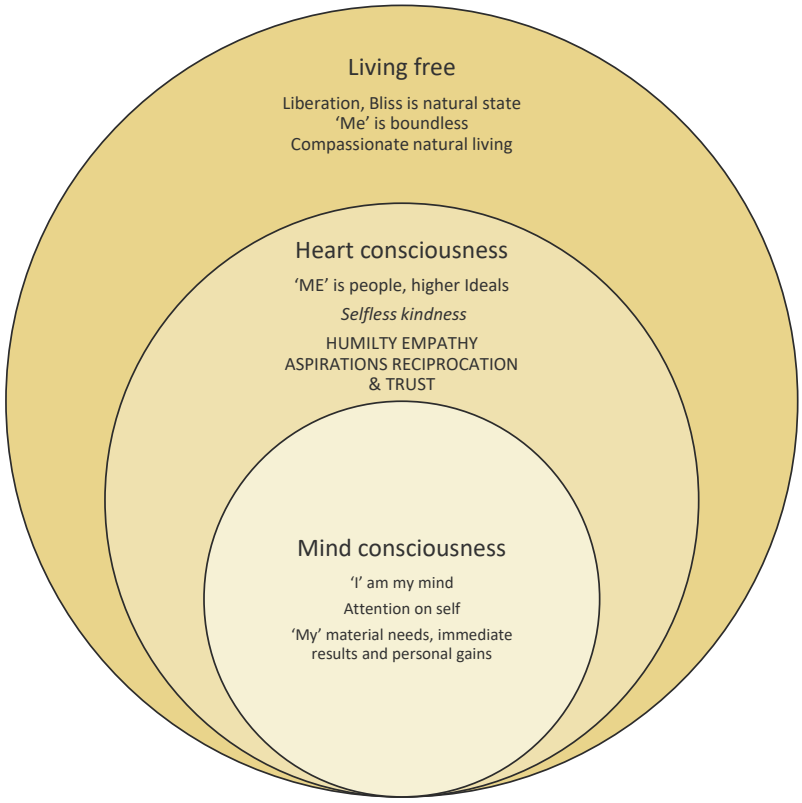


Figure 3. Mind Consciousness: Our core identification is with our thoughts as our real self and attention is towards our immediate challenges. Heart Consciousness: The individual self is less pronounced due to naturally identifying with close people or higher ideals. This is the path to self-realization through kindness.

ourselves distinctly from childhood and project our peculiar preferences and dislikes as our personality. With the new information that we have assimilated over many generations, humans have understandably forgotten several aspects of our pre-human selves. Instinct, intuition, and 'reflexes' are broadly grouped together as animal behavior to be controlled and outgrown. Religion, culture, and education systematically curb our innate natural self from early childhood and 'cultivate' humans to conform to modern society.

Mind Consciousness

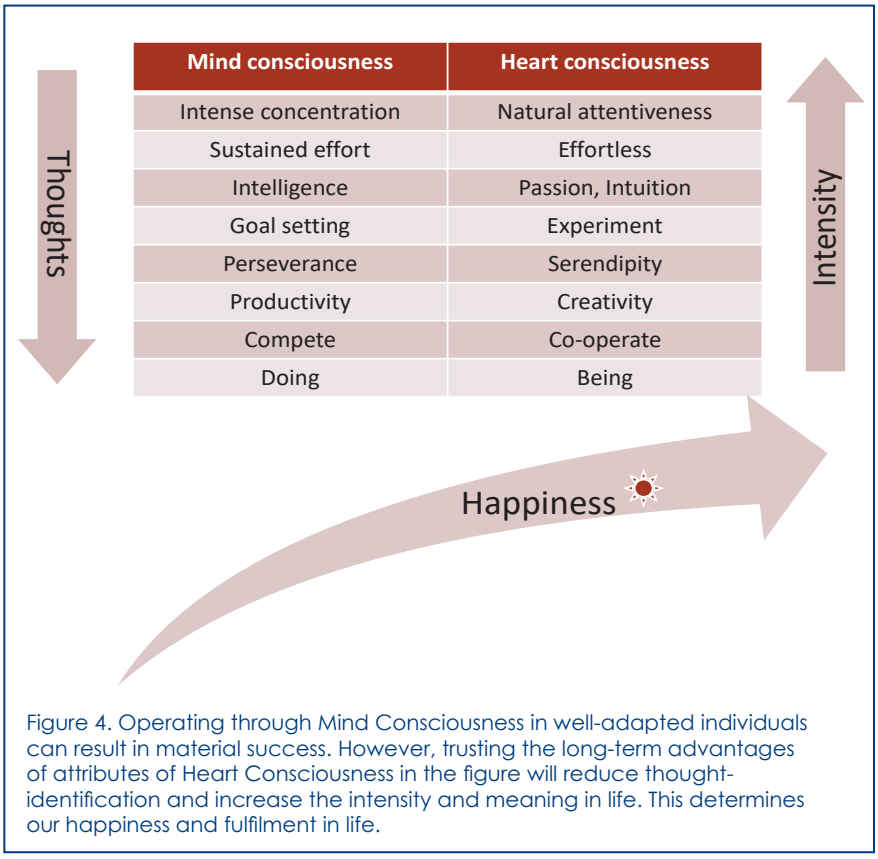
We became self-aware and ascended to the apex of the food chain. We owed this to our mind and superior intelligence. We naturally identified with our thoughts and the mind as our real 'self.' The mind remained superior to every other force in the natural world and allowed the intelligentsia to rule over the others. Power and praise reinforced the crucial role of the thinking mind in surviving and succeeding as civilization became increasingly complex. Self-esteem and self-awareness are integral to the self-image, which is specific to an individual and his/her lifespan. Our use of the word 'mind' typically implies thought-identification that really began in prehistoric times.

The mind has enabled us to learn languages, memorize vast amount of knowledge, and thrive in societies.[12] Education and learning utilize specific aspects of the mind to achieve excellence in specialized arts, skills and crafts. In nature, all deer graze and all tigers hunt, while we humans have been specializing and acquiring particular skills for the last 10,000 years. We have long forgotten our ability to survive in the wild. We now rely on the collective specialized skills, to make the products constituting modern life.

The collective gains for humanity owed to the mind are plenty and indisputable, but the mind is also the source of our individual pain and suffering. Humans feel pressured to perform throughout life. Anxiety and depression are increasing. The world appears insecure and seems constantly on the verge of collapse. The mind is now the source of our insecurities and despair. Artificial goals, increasing expectations and false beliefs contribute to illness and disease. Our stress, fears and biases arise in the mind and impact our quality of life.

Heart Consciousness

'Selfless kindness' or heart consciousness is the next level of human evolution. Instead of the conscious mind, we dive deeper down and naturally identify with our 'heart' or subconscious self. Its origin dates back to our primitive animal past where we remember to trust our instincts and intuition. It allows us to lead a better life today, less bound to daily stress and deadlines. It gives us a future where we are more awake and living spontaneously in the moment. We are all moving in this direction, naturally but slowly.[13] Just like water



Mind consciousness	Heart consciousness
Intense concentration	Natural attentiveness
Sustained effort	Effortless
Intelligence	Passion, Intuition
Goal setting	Experiment
Perseverance	Serendipity
Productivity	Creativity
Compete	Co-operate
Doing	Being

Figure 4. Operating through Mind Consciousness in well-adapted individuals can result in material success. However, trusting the long-term advantages of attributes of Heart Consciousness in the figure will reduce thought-identification and increase the intensity and meaning in life. This determines our happiness and fulfilment in life.

flows downwards, consciousness flows upwards. Life is inherently efficient and moves ahead using the least possible effort. This is the ability to relate with the world through child-like eyes. The mind is needed as the foundation for this new and elevated perception of reality. The mind can be stilled by meditation or self-inquiry. This trust in our natural instincts and belief in our intuition can be nurtured despite the challenges of modern society.

Our mind is a double-edged sword. It helps us clearly see our individual interests and safely navigate our environment. At the same time, it hinders our instinctive surrender to nature and incessantly raises warning alarms. This is the mind refusing to accept reality as it is. It wishes to ascribe higher meaning and special purpose for its existence beyond what nature confers. It refuses to accept its own miniscule place in the larger scheme of things, our frailty and imminent mortality.

Heart consciousness is intensity, energy—excitement arising from kindness. This allows the logical mind to continue thinking and raise its alarms as usual. The mind is still turned on but is now muffled by a much louder identity. There is a deeper level of intensity that the individual has awoken to. Here the subconscious is experienced as the self. We can experience the confidence and clarity of several million years of evolution, and this is part of our natural state. This is inherent to us and does not require effort or memorization. This primitive 'knowledge' long pre-dates cortical logic and learning.

Figure 4 illustrates how the mind values effort, pursues growth, and recognizes achievement. While this holds true in the short term, it also leads to anxiety and stress. The heart accepts the being intuitively and allows life to unfold. There is no feeding the ego and little claim to individual uniqueness or special prowess. With this comes more sustained meaning in life, happiness, and fulfilment without the anxiety for rapid rewards and daily reaffirmations. Bhagavad Gita says, "do your duty, do not worry about the results." To completely devote years of effort with no expectations of fruition would seem ludicrous to linear thinking—but this is the essence of the teaching. The ease to accept all outcomes comes from a deeper trust, humility, and seeing our limited scope in the bigger scheme of things.

Living Free

Life is change and growth. Our body is perceived in movement. Our mind is perceived in thought. The heart is perceived in kindness. Intensity is the key. A year's worth of life experiences accumulated with the mind is attained in a moment of higher consciousness at the heart level. In our modern society, we have become accustomed to carrying our baggage around: the mind. We see life as an endless cycle of hard work, stress, and exhaustion. However, life is not destined to be this way. The burdens of the mind can be eased; the first step in doing so is to realize that there is a better path. Consciousness can be elevated effortlessly by letting go of our thought-identity with its false beliefs. Thoughts cannot be stopped, but they can become

less pronounced and not define our being. The mind has a limited role in this elevated reality. With higher consciousness, life gains energy. Every effort contributes to the common good, and we find through helping others, we are adding meaning to our lives.

The inner 'heart' can be felt through the acronym: **H**umility and gratitude, **E**mpathy, our true **A**spirations and goals, **R**eciprocation and gaining **T**rust all around. When connected with HEART our intensity naturally rises. This 'thought-free' intensity has scientifically been described as flow state or zone.[14] Siddha philosophy of tolerance, equality, and empathy have been at the core of individual wellness and societal vitality as described in Tholkappiyam, the oldest Tamil grammar text 5,000 years ago.[3] Thiruvalluvar, a Siddha poet and philosopher, directly addresses flow as the highest level of enthusiasm for life itself. Accepting anything less was a disgrace for Tamils 2,000 years ago.[15] Every year during the Tamil harvest festival, Pongal, the rice boils and overflow symbolizing this celebration of life. With gratitude, consciousness spontaneously expands to encompass more of existence. Thus, HEART consciousness is the road to higher consciousness and liberation.

Health in the Future

Self-inquiry has the potential to improve health and mindset. While we use over a dozen tools, Hunger Gratitude Experience (HUGE) is intuitive and universally applicable. Identifying with people or circumstances that we are grateful for is the first step. Next is deeper mind-body connection gained through exploring, accepting, and relating directly with hunger through fasting. Experiencing a deeper gratitude for life automatically ensues when this process is explored and deepens self-awareness. Based on their practice, authors find this tool effective in inspiring a wide spectrum of people. Advanced heart disease, chronic kidney disease, and long-standing type II diabetes improve significantly. Patients find it natural and safe sustaining over 30% weight loss for 10-15 years with HUGE fasting. Similarly, physicians find it is easier to focus, cope with burnout, and experience more empathy towards their patients. Students report lesser anxiety as well as better academic and athletic performance.

Exploring space, taking the first step on the moon, Armstrong said "one small step for man is one giant leap for mankind." Exploring the inner world, gaining invaluable insight into ourselves, and taking the first step inwards towards self-inquiry may transform our health individually and allow our species to thrive in harmony with nature.

Conclusion

The logical mind seeks growth and dominance over the external world. Thought-identification was natural and essential for our survival. Tapping into the vast potential of our subconscious is possible through tools that promotes selfless kindness or HEART consciousness. Cardiac patients with numerous comorbidities benefit sustainably and profoundly with self-inquiry. This path is both ancient and modern; it will lead to our awakening. Our ability to overcome thought-attachment, expand consciousness and celebrate life may determine our health and destiny.

References

1. Hall KD, Kahan S. Maintenance of Lost Weight and Long-Term Management of Obesity. Med Clin North Am. Jan 2018;102(1):183-197. doi:10.1016/j.mcna.2017.08.012
2. Ricardo AC, Anderson CA, Yang W, et al. Healthy lifestyle and risk of kidney disease progression, atherosclerotic events, and death in CKD: findings from the Chronic Renal Insufficiency Cohort (CRIC) Study. Am J Kidney Dis. Mar 2015;65(3):412-24. doi:10.1053/j.ajkd.2014.09.016
3. Weiss R. Recipes for Immortality : Healing, Religion, and Community in South India: Healing, Religion, and Community in South India. . Oxford University Press; 2009; 80.
4. Powell W. Martial Arts. MacMillan Encyclopedia of Buddhism. MacMillan Reference USA; 2004:214-218.
5. Willett WC. Balancing life-style and genomics research for disease prevention. Science. Apr 26 2002;296(5568):695-8. doi:10.1126/science.1071055
6. Srinivas S, Rajendran S, Anand K, Chockalingam A. Self-reported depressive symptoms in adolescence increase the risk for obesity and high BP in adulthood. Int J Cardiol. Oct 15 2018;269:339-342. doi:10.1016/j.ijcard.2018.07.089
7. Consciousness. Dictionarycom: Random House Inc.
8. Niculescu AB, 3rd, Schork NJ, Salomon DR. Mindscape: a convergent perspective on life, mind, consciousness and happiness. J Affect Disord. Jun 2010;123(1-3):1-8. doi:10.1016/j.jad.2009.06.022
9. Vithoulkas G, Muresanu DF. Conscience and consciousness: a definition. J Med Life. Mar 15 2014;7(1):104-8.
10. Heyes C. New thinking: the evolution of human cognition. Philos Trans R Soc Lond B Biol Sci. Aug 5 2012;367(1599):2091-6. doi:10.1098/rstb.2012.0111
11. Sherwood CC, Subiaul F, Zawidzki TW. A natural history of the human mind: tracing evolutionary changes in brain and cognition. J Anat. Apr 2008;212(4):426-54. doi:10.1111/j.1469-7580.2008.00868.x
12. Cosmides L, Tooby J. Evolutionary psychology: new perspectives on cognition and motivation. Annu Rev Psychol. 2013;64:201-29. doi:10.1146/annurev.psych.121208.131628
13. Nowak MA, Page KM, Sigmund K. Fairness versus reason in the ultimatum game. Science. Sep 8 2000;289(5485):1773-5. doi:10.1126/science.289.5485.1773
14. Csikszentmihalyi M, Larson R. Validity and reliability of the Experience-Sampling Method. J Nerv Ment Dis. Sep 1987;175(9):526-36. doi:10.1097/00005053-198709000-00004
15. https://www.ytamizh.com/thirukural/kural-971/, accessed 1.15.2021.

Disclosure

The website www.HiLifeJourney.org is a self-inquiry based nonprofit aiming to sustainably improve health and resilience. *Seeking Hunger* is book authored by AC to encourage self-inquiry and health through mindful eating. **MM**

Leading a Horse to Water AND Making Him Drink…Recommendations for Dealing with Non-Adherent Patients

by Christina Moore, JD

Patient misunderstanding is only one of many reasons for patient non-adherence.

My father was a very smart man and loved telling stories. One of his favorites was about a time when he was in the Army and went to a doctor for an infection on his foot. He described in detail the large pills the doctor prescribed and how much trouble he had swallowing them. After a couple weeks, he could not figure out why the pills were not working. At a follow up appointment, he learned that he was supposed to dissolve the large pills in water and soak his feet, and not swallow the pills! Fortunately, my dad was fine despite this misunderstanding, and we were able to enjoy a few laughs. Misunderstandings happen all of the time in life, and of course, healthcare is no different. Patient misunderstanding is only one of many reasons for patient non-adherence.

The old English proverb "you can lead a horse to water, but you can't make him drink," comes to mind regarding this issue. Physicians can make the best recommendations for their patients, but they cannot make them adhere to them. Patient non-adherence can be demonstrated in many ways including a patient's failure to schedule or keep appointments, failure to obtain recommended diagnostic testing (e.g., lab or x-rays), failure to fill or take medications as prescribed, failure to report worsening symptoms, or engaging in conduct that is contrary to what a health care provider has recommended. This issue is not a new problem for patients or their health care providers. This article will discuss the staggering statistics relating to patient non-adherence, provide an overview of the risk issues for health care providers, and provide some recommendations, touching on some patient-centered, value-based healthcare innovation options available to physicians and patients that could be embraced to help with this problem.



Christina B. Moore, JD, from the St. Louis office of Husch Blackwell wrote this article. Husch Blackwell represent a full spectrum of healthcare providers and other businesses in regulatory compliance and litigation matters. The information contained in this article should not be construed as legal advice or a legal opinion on any specific facts or circumstances. The contents are intended for general information purposes only, and readers are encouraged to consult their own attorney concerning their specific situation and specific legal questions.

The Problem: How Many Aren't Drinking the Water

Here are some staggering statistics:

- Patient no-show rates for scheduled appointments "were reported from 12% to 80% in various healthcare settings."[1]
- The cost to the United States for patient no-shows is estimated to be as much as $150 billion a year.[2]
- Patients "who failed to keep just one appointment with a primary care physician were 70% more likely to not return to that primary care within 18 months."[3]
- "3.6 million people in the U.S. do not obtain medical services due to transportation barriers."[4]
- Medication non-adherence causes an estimated 125,000 avoidable deaths per year.[5]
- Medication non-adherence costs between $100 billion and $289 billion annually in preventable health care costs.[6]

- Among United States adults (40-79), almost 70% used one or more prescription drugs in the past 30 days.[7]
- 20-30% of medication prescriptions are never filled.[8]
- Approximately "50% of medications for chronic disease are not taken as prescribed."[9]
- One-third of kidney transplant patients do not take their anti-rejection medications.[10]
- 41% of heart attack patients do not take their prescribed blood pressure medications.[11]
- One-half of children suffering from asthma do not use their inhalers at all or do not use them consistently.[12]
- The World Health Organization (WHO) noted that "increasing the effectiveness of adherence interventions may have a far greater effect on the health of the population than any improvement in specific medical treatments."[13]

Risk Concerns: When the Horse Doesn't Drink the Water

A study performed by the Controlled Risk Insurance Company (CRICO) insurance program which includes all of the Harvard medical institutions and their affiliates, provides some perspective on the amount of medical malpractice cases involving patient non-adherence. CRICO established a national benchmarking system and developed a way to track medical malpractice claims impacted by patient non-adherence. Using clinical coders to assign certain codes, CRICO captured relevant instances of non-adherence regarding: (1) recommended treatment; (2) follow-up calls or appointments; or (3) medication recommendations. For all cases reviewed from 2007–2016, "11 percent had one or more of these contributing factors (12 percent of the high-severity cases)."[14]

Patients should share in the responsibility for their own care, but a significant amount of responsibility is placed on a health care provider to ensure follow-up and adherence with patients. Indeed, in many cases, "[b]elieving that a physician has a better understanding of the ramifications of a patient's failure to pursue or continue treatment than does the patient, a jury may impose a greater burden upon the physician."[15] This may be especially true if a patient suffers from any mental illness.

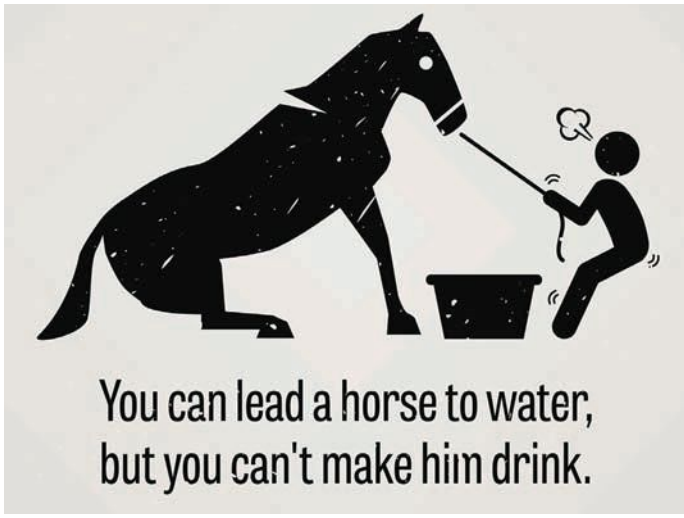
Not all states treat patient's non-adherence the same with respect to legal liability. Historically, the law only allowed victims of a tort to sue for compensation if they had no role in, nor responsibility for, the cause of the alleged injury, a legal doctrine called contributory negligence. That doctrine could provide some harsh results and most states, including Missouri, use another system. Missouri is a pure comparative fault state.[16] Under the pure comparative fault principles, "the injured party's own negligence is compared to that of the negligence of defendant to determine whether any damages awarded should be diminished in proportion to the amount of negligence attributable to that plaintiff."[17] In other words, "a plaintiff's negligence that concurs with that of the defendant does not relieve the defendant from liability. It merely diminishes the amount of damages that the plaintiff can recover."[18] "Comparative fault is an affirmative defense in which the defendant must prove that the actions or omissions of the plaintiff contributed to the plaintiff's loss to negate or reduce the defendant's legal responsibility."[19]

In a medical malpractice action in Missouri, the court may apply comparative fault and consider the patient's negligence so long as that negligence is a proximate cause of the alleged injury.[20] To be a proximate cause of an injury, a patient's negligent act must "have been simultaneous and cooperative with the defendant's negligent act."[21] But, "[c]ourts have been reluctant to impose joint liability upon a patient in a malpractice lawsuit for the condition which caused him to seek the physician's assistance, even if the patient negligently imposed the condition upon himself."[22] In other words, if a patient injures himself through his or her own negligence, he or she is still entitled to medical treatment that is not negligent. For example, in the *Van Vacter* case, the defendant doctor instructed his patient to quit smoking, exercise, and lower his weight and cholesterol level after suffering a heart attack. The patient did not comply with his physician's instructions including failure to take his prescribed medication.[23] A few years later, he presented to the hospital, was evaluated and sent home and died of a heart attack the next morning. The jury originally apportioned 93% fault to the patient. The court overturned this verdict and remanded the case for a new trial finding that patient's negligence in failing to follow the doctor's recommendations was not a proximate cause of his fatal heart attack because it only gave rise

to his condition and the occasion for the defendant physicians' negligence.[24]

Courts have allowed a patient's conduct to form the basis for comparative fault in a number of circumstances such as when "a patient who delays in seeking or returning for medical treatment, who fails to follow a physician's advice or instructions, who furnishes false, incomplete, or misleading information to his or her physician, or who attempts to treat his or her own injury before seeking medical attention."[25]

This doesn't have to apply to patients!



For instance, a court reduced a plaintiff's verdict involving a situation where a nurse was found to be negligent with respect to an injection after the patient failed to seek follow up care for seven weeks after experiencing symptoms of an infection from the injection site.[26] In another case, a patient was found 50% at fault where he lost his finger due to an infection. The court noted that the plaintiff had received both oral and written instructions including a discharge instruction sheet which plaintiff had signed off on noting that he received and understood the wound care instructions for his finger. The instructions advised the patient to be on the lookout for an infection, but despite the severe pain he suffered, he waited days before seeking help. The court reduced the award for failure to follow the physician's instructions after treatment.[27] As it is a physician's duty to fully advise and inform a patient of the treatment recommended, courts consider the patient's "fault" in light of what he or she knew or should have known. Therefore, if a court finds that a physician did not properly inform the patient of the recommended treatment, the patient's negligence may not be considered in allocating fault.

In a more significant case of non-adherence, a plaintiff's intervening conduct may actually be considered an independent cause absolving a defendant from liability entirely.[28] In *Williams*, a defendant physician avoided liability by showing that the plaintiff's conduct was a "new and independent force" that was the "responsible, direct, and proximate cause of his injury."[29] In that case, it was undisputed that the defendant physician provided medical instructions that the patient should seek a follow-up examination if he experienced any symptoms. It was also undisputed that the patient understood the instructions, admitted that he was aware of his family history of heart disease and realized that he might be having a heart attack but chose to ignore his symptoms and delay treatment. The defendant physician was held not negligent as a matter of law.[30] These cases reveal not only the importance of clearly advising patients of recommendations and making sure the patient understands the recommendations, but the need also to document in the patient's medical records both the recommendations and the patient's understanding and importance of them.

Not only is there a medical malpractice risk associated with ensuring patient compliance, there is potentially another risk with value-based alternative payment models. As one article noted, "with Medicare's growing emphasis on value-based care, many physicians now also have a financial stake in ensuring that patients take the medicine they need"[31] and adhere to the medical guidance provided. In fact, some have argued that the traditional fee-for-service model does not provide the necessary incentives for individual physicians to address this issue as it rewards physicians for providing more services, not based on quality or improved outcomes. As such, it is argued that "[e]ffective change will not happen until key players decide to take on this challenge and reimbursement systems are changed to reward health systems that improve medication adherence and chronic disease control."[32] Recent rule changes reflect the Department of Health and Human Services' (HHS) continued push to reward value based medicine as part of its Regulatory Sprint to Coordinated Care ("Regulatory Sprint").

On November 20, 2020, HHS published two final rules that "aim to reduce regulatory barriers to care coordination and accelerate the transformation of the healthcare system into one that pays for value and promotes the delivery of coordinated care."[33] The goals of the Regulatory Sprint include encouraging and improving "a patient's ability to understand treatment plans and make empowered decisions" and incentives for providers to "coordinate, collaborate, and provide patients with tools to be more involved."[34] With these new rules, HHS created a new anti-kickback safe harbor for patient engagement and support programs to allow the provision of tools to encourage patient adherence with treatment or medication use, follow-up, or management of an ongoing disease or condition with certain conditions. By mentioning these new rules, this article is not focused on, nor intended to provide, fraud and abuse analysis or advice, but intended to provide a reminder of the trend towards reimbursement based on value-based medicine and the additional incentive to address the issue of patient non-adherence with innovative solutions contemplated by these new rules.

Recommendations: How To Make Them Drink the Water

A common theme throughout the preamble for the new HHS rules is the government's encouragement for creative, innovative, and flexible solutions to promote patient engagement tools. Examples include:

- "As a threshold matter, the definition of 'value-based purpose' was crafted to provide parties with flexibility to develop innovative care arrangements and strategies specific to the needs of their target patient populations;"[35]
- "This rule aims to increase options for parties to create a range of innovative arrangements eligible for safe harbor protection;"[36]
- "To avoid inadvertently limiting which tools and supports advance specified goals and provide [value-based enterprise] participants flexibility and the opportunity to innovate, we are not providing an exhaustive list of tools and supports;"[37] and
- HHS believes that the safe harbor "will expand opportunities for innovation in how industry stakeholders engage and support patients, including arrangements involving remote patient monitoring."[38]

As such, providers should think outside the box and consider innovative solutions to assist their patients in adhering to medical advice. But, if such solution could be viewed as providing remuneration thus potentially implicating Stark or the Federal Anti-Kickback Law, please seek legal guidance to ensure compliance with all federal and state laws and regulations.

Sometimes the First Step is Getting Them to the Water: Addressing Patient No-Shows

In order to address patient non-adherent issues such as patient no-shows, providers need to determine which patients are non-adherent and why.[39] Certainly talking with each patient and individually reviewing their records can identify which patients may be non-adherent, but that can be a monumental task. With the use of electronic medical records (EMR) and other data collection sources, physicians could develop a way to track relevant patient data to quickly determine if patients are scheduling and keeping the appointments as recommended. In addition, there are new products available that interface with the EMR to assist with online scheduling and data collection, allowing easy analysis and tracking of patient populations and scheduling issues. Such tools may include predictive analytics to determine what type of patients are most likely to be non-compliant or at risk and assist in identifying a solution.[40]

At a minimum, it may be helpful to track the no-show rate. By tracking you can see what works with your patient population as you try different ways to reduce the no-shows. Providers can explore different ways of handling patient reminders – live calls, robocalls, text messages or messages via a patient portal or other secure electronic messaging system. One organization found it effective to schedule calls four days prior to an appointment. When no one answered the call, they implemented calls every day until the scheduled appointment.[41] In addition, changing the timing of the reminder calls may make a difference.

It is also important to understand that some patients miss appointments because they simply cannot get there. Transportation was found to be the third most commonly cited issue for older adults in obtaining health care services.[42] The issue could relate to not wanting to travel a long distance for a short appointment, not being able to drive – physically or not having a car, or simply not planning ahead of time

to arrange for transportation. If someone has difficulty physically getting to an appointment, providing reminders several days in advance may assist the patient in having sufficient time to arrange for transportation. On the reminder call, a friendly inquiry as to whether the patient has any issues traveling to the appointment may be helpful so those issues can be addressed. If the patient notifies the staff a couple days before the visit of the need for transportation, it may help for the staff to make arrangements with local churches, Uber, Lyft, paratransit services provided through the Americans with Disabilities Act, insurance company provided transportation or other public services. In certain circumstances, as set forth in the OIG's safe harbor, providers may offer free transportation to their patients.[43]

In addition, where appropriate, virtual visits through telemedicine can be very helpful. In fact, in April, the Dean of the School of Medicine for Saint Louis University noted that patient no-show rate for SLUCare dropped to nearly zero from a usual rate of 20 percent with the increased use of telemedicine visits.[44] While not all types of situations allow for a virtual visit, providers should consider if there are ways that a virtual visit can work, and whether it is feasible to add tools such as remote patient monitoring devices or applications through a patient's mobile device that could securely track and transmit objective data to a patient's health care provider. Forgetting an appointment or transportation issues are only two issues that may impact a patient to adhere to an appointment, and obviously knowing the reason is essential in addressing non-adherent issues with your patient.

Why the Horse Doesn't Drink the Water

The American Medical Association recently set out eight reasons why patients fail to take their medications as prescribed: fear, cost, misunderstanding, too many medications, lack of symptoms, mistrust, worry and depression.[45] The Centers for Disease Control (CDC) sets out these reasons a little differently as five types of factors including socioeconomic, health care system, medical, therapy-related and patient-related.[46] Regardless, investigating issues of non-adherence with your patients and their families is necessary in order to address the issues.

Lack of understanding may be as simple as my dad's story about how to use the tablets he was prescribed for his feet. Recognizing that time is limited with patients, explaining treatment in multiple formats can improve understanding and promote correct use. You can do this by confirming the patient's understanding by asking them to repeat the recommendations to you, allowing time for questions, and providing clearly written paper instructions with photos. If a patient portal is available, sharing detailed instructions and links to reliable websites through the portal is also recommended. Many patients try to research issues and self-diagnose themselves so it may be helpful to alleviate some fears about medications by directing patients to reliable information and also include some recommendations about sources to avoid. The latter is typically a source of misinformation and fear.

Lack of understanding may be caused by limited English proficiency, visual impairment, or hearing impairment. It is estimated that patients with limited English proficiency equate to more than 7% of the United States population, 4%-6% of the United States population have a hearing impairment, and 6% of patients over 65 have visual disabilities.[47] A patient will likely not be able to adhere to medical recommendations if there is a basic lack of understanding due to any of these communication barriers. Section 1557 of the Patient Protection and Affordable Care Act (ACA) prohibits discrimination on the because of race, color, national origin, age, disability or sex in certain health care programs. Accordingly, covered entities must take reasonable steps to provide meaningful access to individuals with communication barriers which may include the provision of language assistance services.[48] In this regard, be aware of your obligations to ensure that a patient understands your instructions.

The cost of medications, testing, prescribed therapies or treatments may not be known to the patient (or the provider) so it is important to be mindful of the affordability and discuss options with the patient such as lower cost generics or alternatives. Also, invite the patient to call if the prescription or treatment turns out to be cost prohibitive so you can evaluate other options. Encourage your staff to be creative and resourceful and inform patients of various patient assistance programs including RxAssist, a medication assistance resource center. As mentioned above, transportation issues are very common in older patients and not just for travel to and from appointments, but may also make it difficult for your

patient to obtain medications as recommended. In the preamble to the final rule, HHS noted certain examples of anticipated arrangements based on the new value-based safe harbors including the provision of a free prescription pickup service to expedite the patient's adherence to the physician's ordered treatment.[49] In addition, providers are encouraged to fully utilize all aspects of the EMR such as setting up reminders to follow-up with a patient after prescribing a new medication or treatment to ensure that the patient obtained the prescription, inquire whether it is helping, and determine if there are any concerning side effects.

There are also mobile tracking and gamification apps that may assist your patient with medication compliance including reminder notifications, providing dosing information and medication schedule support, and include features that have the ability to contact a patient's friend or family member when the patient forgets to take the medicine or has not indicated such on the app.[50]

If a patient is taking a number of medications, encourage the patient to use one pharmacy and take advantage of devices to help take the medications at the right time such as a pill case, using a mobile device for alerts or engaging a pharmacy such as PillPack which delivers medications to a patient's home that is separated on the prescribed dose and schedule – including separate packaging for each day with all pills to be taking at that specific time. This article touches on just a few of the noted AMA reasons for non-adherence and just a few ways to address those issues, but health care providers will likely discover many more after investigating these issues with their patients.

Tracking the Horse to the Water Source

"Many physicians do an excellent job of communicating with their patients and work very hard to facilitate adherence but fail to give themselves credit for these efforts because they don't adequately document them. Documentation is key in managing risk associated with nonadherent patients."[51] Incidents of non-adherence should be carefully notated in the patient's record making sure to document in a non-judgmental matter – essentially document what you discussed with the patient. Document all efforts to contact a patient for follow-up and any acknowledgement of the patient's understanding.

The following is an example of such a notation:

> "Patient called after missing a second scheduled appointment and encouraged to reschedule another appointment and maintain regular appointments. The patient states that he changed jobs and that his insurance will not be effective for ninety days and requests to wait at least 90 days for a new appointment until this insurance kicks in. The risk of delay was discussed with the patient to include the possibility of permanent vision loss or blindness if not regularly checked given his family history of glaucoma. The patient stated that he understood the information provided and risks. I have asked my staff to investigate and advise him of any financial assistance that may be available and schedule an appointment as soon as possible as directed by the patient."

Of course, timely completion of records is always recommended as it assists with capturing the necessary detail about an encounter with a patient, but it is also critical for subsequent care, including care from other providers. In addition, for risk management purposes, as plaintiff attorneys can obtain much more detail about a patient's medical records including when a chart has been completed. More importantly, your notes may be available for patients through a patient portal, and as such, clearly documenting the patient encounter provides another reminder to your patient about the treatment plan and may also assist the patient in adhering to the treatment plan. Templates and macros in electronic medical records can be helpful including developing certain custom prompts for your particular patient population. When using prompts or templates, make sure the record reflects the specific visit with your patient and you avoid using the cut and paste option in the record. In addition, while it may be cost prohibitive in some practices, a medical scribe may be helpful to provide efficiency, documentation, and productivity.

Leading a Horse to Water AND Making Him Drink

As with horses and water, patient non-adherence may always be a problem. Recognizing the various reasons and identifying your non-adherent patients and why they are the way they are may be the critical first step in addressing the problem. Providers are encouraged to be thoughtful, creative, and innovative in solving these problems. Sometimes these solutions can be very simple – for my dad, a simple printout

of instructions including a photograph might have eliminated his good story. Fortunately, he had many other good stories to tell.

References

1. Marbough, D., Khaleel, I., Shanqiti, K., Tamil, M., Simsekler, M. Ellaham, S., Alibazoglu, D., Alibazoglu, H. (2020). Evaluating the Impact of Patient No-Shows on Service Quality. Risk Manag Healthc Policy, 13, 509-517. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7280239.
2. Sachin H. Jain, Missed Appointments, Missed Opportunities: Tackling the Patient No-Show Problem, Forbes, Oct. 6, 2019, available at https://www.forbes.com/sites/sachinjain/2019/10/06/missed-appointments-missed-opportunities-tackling-the-patient-no-show-problem/?sh=d1195a5573bd [hereinafter Forbes].
3. Forbes, *supra* note 2.
4. Transportation and the Role of Hospitals. (November 2017), American Hospital Association, http://www.hpoe.org/Reports-HPOE/2017/sdoh-transportation-role-of-hospitals.pdf.
5. Kleinsinger, F. (2018). The Unmet Challenge of Medication Nonadherence. Perm J, 22, 18-033. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6045499/ [hereinafter Kleinsinger].
6. See id.; Brody, J. (2017). The Cost of Not Taking Your Medicine. New York Times. Retrieved from https://www.nytimes.com/2017/04/17/well/the-cost-of-not-taking-your-medicine.html. [hereinafter Brody]
7. Prescription Drug Use Among Adults 40-79 in the United States and Canada. (2019). Centers for Disease Control and Prevention, National Center for Health Statistics. Retrieved from https://www.cdc.gov/nchs/data/databriefs/db347-h.pdf.
8. Brody, *supra* note 6.
9. Brody, *supra* note 6.
10. Brody, *supra* note 6.
11. Brody, *supra* note 6.
12. Brody, *supra* note 6.
13. Adherence to Long-Term Therapies: Evidence for Action. (2003). World Health Organization. Retrieved from https://www.who.int/chp/knowledge/publications/adherence_introduction.pdf?ua=1.
14. Hoffman, J. (2018). Malpractice cases involving non-adherent patients. CRICO. Retrieved from https://www.rmf.harvard.edu/Clinician-Resources/Newsletter-and-Publication/2018/SPS-March-Non-Adherent-Patients.
15. McNary, A. (2015). Avoiding Risk with Nonadherent Patients. Innovations in Clinical Neuroscience, 12(3-4), 37-40. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4420169/ [hereinafter McNary].
16. *Gustafson v. Benda*, 661 S.W.2d 11, 15 (Mo. banc.1983); *Lipp v. Ginger C., L.L.C.*, 229 F. Supp.3d 1018, 1020 (W.D. Mo. 2017).
17. *Lipp v. Ginger C., L.L.C.*, 229 F. Supp.3d 1018, 1020 (W.D. Mo. 2017) (*citing Cornell v. Texaco, Inc.*, 712 S.W.2d 680, 682 (Mo. banc. 1986)).
18. *Allison v. Sverdrup & Parcel & Assocs., Inc.*, 738 S.W.2d 440, 451 (Mo. Ct. App. 1987).
19. *Magill v. United States*, No. 4:05CV547MLM, 2006 WL 1153810, at *4 (E.D. Mo. May 1, 2006).
20. *Van Vacter v. Hierholzer*, 865 S.W.2d 355, 358 (Mo. Ct. App. 1993); see generally *Floyd v. Thompson*, 201 S.W.2d 390, 393 (Mo. 1947).
21. *Van Vacter*, 865 S.W.2d at 358.
22. *Campbell v. Lake Regional Medical Management, Inc.*, 2020 WL 4741914 (W.D. Mo Aug. 14, 2020); *citing Van Vacter v. Hierholzer*, 865 S.W.2d at 358-59.
23. *Van Vacter*, at 356.
24. *Id.* at 359.
25. *Campbell v. Lake Regional Medical Management, Inc.*, 2020 WL 4741914 (W.D. Mo Aug. 14, 2020) *citing Mercer v. Vanderbilt Univ., Inc.*, 134 S.W.3d 121, 129 (Tenn. 2004).
26. *Love v. Park Lane Med. Ctr.*, 737 S.W.2d 720 (Mo. 1987).
27. *Shelton v. United States*, 804 F. Supp. 1147, 1159 (E.D. Mo. 1992)
28. *Williams v. Birkeness*, 34 F.3d 695, 697 (8th Cir. 1994) *citing Eidson v. Reproductive Health Servs.*, 863 S.W.2d 621, 626-627 (Mo. Ct. App. 1993).
29. *Id.*
30. *Id.*
31. Value-based Rx, How physicians can manage affordability, adherence. (2017). Medical Economics. Retrieved from https://www.medicaleconomics.com/view/value-based-rx-how-physicians-can-manage-affordability-adherence.
32. Kleinsinger, *supra* note 5.
33. See HHS Press Release, available at https://www.hhs.gov/about/news/2020/11/20/hhs-makes-stark-law-and-anti-kickback-statute-reforms-support-coordinated-value-based-care.html; *see also* Centers for Medicare & Medicaid Services, Medicare Program; Modernizing and Clarifying the Physician Self-Referral Regulations, 85 Fed. Reg. 77493 (Dec. 2, 2020); *see also* Department of Health and Human Services, Office of Inspector General, 42 CFR Parts 1001 and 1003 RIN 0936–AA10 Medicare and State Health Care Programs: Fraud and Abuse; Revisions to Safe Harbors Under the Anti-Kickback Statute, and Civil Monetary Penalty Rules Regarding Beneficiary Inducements [hereinafter New Anti-Kickback Rules], 85 Fed. Reg. 77684 (Dec. 2, 2020).
34. Centers for Medicare & Medicaid Services, Medicare Program; Modernizing and Clarifying the Physician Self-Referral Regulations, 85 Fed. Reg. 77493 (Dec. 2, 2020).
35. New Anti-Kickback Rules, 85 Fed. Reg. 77720.
36. New Anti-Kickback Rules, 85 Fed. Reg. 77774.
37. New Anti-Kickback Rules, 85 Fed. Reg. 77803.
38. New Anti-Kickback Rules, 85 Fed. Reg. 77796.
39. McNary, *supra* note 15.
40. Forbes, *supra* note 2; *see also* Campbell, J. (2019, August). Healthbox, Improving Medication Compliance: Five Innovative Approaches. Healthbox. Retrieved from https://www.healthbox.com/blog/improving-medication-compliance-five-innovative-approaches/ [hereinafter Healthbox].
41. Forbes, *supra* note 2.
42. Forbes, *supra* note 2.
43. 42 C.F.R. §1001.952(bb).
44. Brennan, V. (2020). What comes next: How embrace of telemedicine in St. Louis provides clues to post-COVID health care market. St. Louis Business Journal. Retrieved from https://www.bizjournals.com/stlouis/news/2020/04/23/what-comes-next-how-embrace-of-telemedicine-in-st.html.
45. AMA, Patient Support & Advocacy, 8 Reasons Patients Don't Take Their Medication, Dec. 2, 2020, available at https://www.ama-assn.org/delivering-care/patient-support-advocacy/8-reasons-patients-dont-take-their-medications.
46. Strategies and Emerging Interventions for Improving Medication Adherence, August 2017, Science-in-Brief, available at https://www.cdc.gov/dhdsp/pubs/docs/SIB_feature_Aug2017.pdf.
47. Pope, T., New Regulations Require Better Communication with Patients Who Have Disabilities and Limited English Proficiency, ASCP Post (Jan. 25, 219), available at https://ascopost.com/issues/january-25-2019/new-regulations-require-better-communication-with-patients-who-have-disabilities-and-limited-english-proficiency/.
48. Department of Health and Human Services: Nondiscrimination in Health Programs and Activities; Final Rule, 81 Fed. Reg. 31376, May 18, 2016; *see also* 42 C.F.R. Part 92.
49. New Anti-Kickback Rules, 85 Fed. Reg. 77881.
50. Healthbox, *supra* note 40.
51. McNary, *supra* note 15.

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Serving on the Navy's Hospital Ships During the Response to COVID-19: Perspective from Two Deployed Missouri Physicians

by Gavin P. Dunn, MD, PhD & Brad Bernstein, MD

The sailors of the USNS Comfort and USNS Mercy, as well as those who served in other efforts across the country, should be proud of their service to the country in spring 2020. Indeed, COVID-19 has touched every corner of the globe,

In the spring of 2020 as the COVID-19 global pandemic swept across the United States and around the world, the Department of Defense mobilized the armed forces in an historic response to assist the civilian medical infrastructure to protect American lives. In a matter of days to weeks, active duty and reserve personnel from the United States Army, Navy, Air Force, and Marine Corps were rapidly deployed to cities facing near existential crises as hospital systems operated at or beyond their breaking points due to the numbers of infected patients.

As part of this response, the United States Navy stood up the USNS Mercy (T-AH-19) and USNS Comfort (T-AH-20) hospital platforms under Task Force 130.1. As United States Navy Reserve Medical Corps Officers—one a neurosurgeon (G.P.D.) and the other an anesthesiologist (B.A.B.)—based in St. Louis, Missouri, we will review and reflect on our experiences on both ships and provide some "lessons learned" in a dynamic global environment.

As COVID-19 was gripping Seattle and increasing in New York City in mid-March, there was tremendous concern that our country's hospital system would not be able to support a suddenly large number of critically ill COVID-19 patients as well as the rest of the civilian population with serious medical conditions. Facing a world-class medical system suddenly in extremis, the Department of Defense directed the Navy's hospital ship assets to the epicenters of escalating infection. To this end, the USNS Mercy was activated to support Los Angeles and the surrounding counties followed shortly thereafter by the USNS Comfort to New York City. Both ships, under the aegis of Military Sealift Command, are staffed by civilian mariners, but have the same command triad as shore-based military treatment facilities (MTFs). Both hospitals were also supported by a Commodore and his line staff. Because both ships had 1,000 patient beds, 12 operating rooms, and state of the art imaging technology, their mission was to acutely expand the local civilian capacity to provide patient care by becoming another large hospital

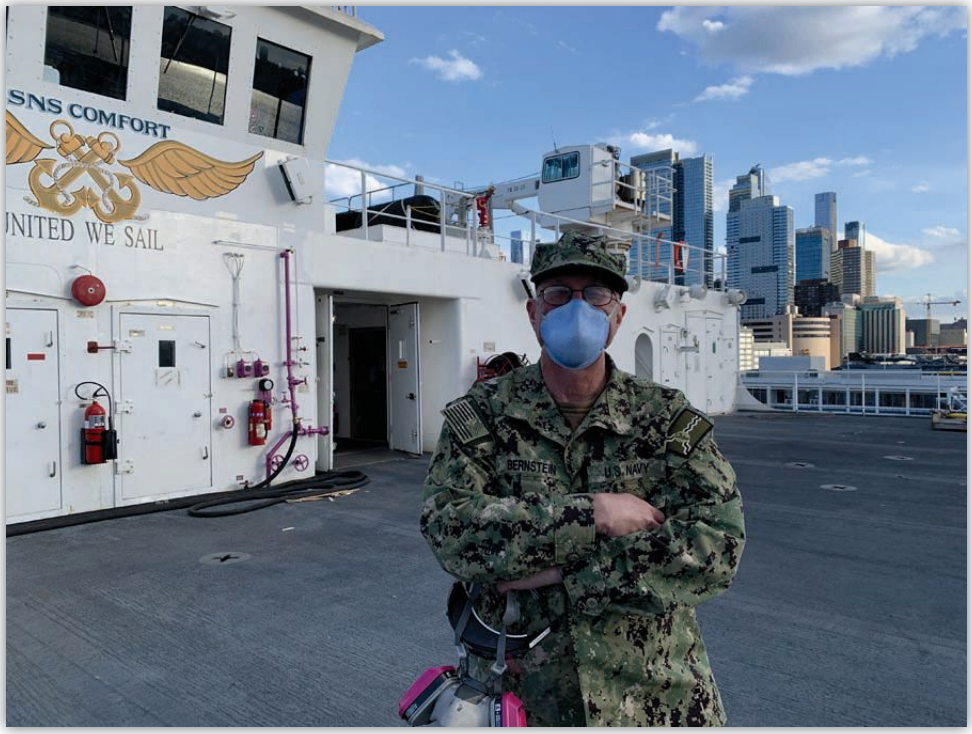




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in the region to offload local centers that were beyond capacity.

The speed with which the mission developed was stunning. Both ships, in "maintenance availability" status at the time of activation, were ready to get underway within five days and required nearly herculean efforts by the crew. Active duty and reserve providers were notified to report to their respective ships within several days. One of the authors was mobilized over a weekend and slept in a bunk in a stateroom of the USNS Mercy in San Diego by Sunday evening. This rapid deployment was only possible because of a highly effective logistics on the active-duty side, the superb readiness of the Navy Medicine Reserve community—both force-wide and at the level of our St. Louis Navy Operational Support Command—and the deep level of support shown by our civilian employers and colleagues. Moreover, there was outstanding support from the active duty subspecialty communities. To a member, the reserve community was highly enthusiastic and humbled to serve the country in this way; although many had deployed in other theaters previously, this mission was the first deployment for a large proportion including the authors. Once each ship was fully staffed, the reserve and active duty groups integrated seamlessly to execute the mission. Everyone's journey to Navy medicine is unique and, together, forms the incredibly rich tapestry of this community. The working relationships between active and reserve sailors was a success story of this deployment.



Brad Bernstein, MD, on the deck of the USNS Comfort docked at Pier 90 in NYC.

Once underway, both ships became high-functioning hospitals by the time they reached their destinations and began to treat patients shortly thereafter. The mantras from the USNS Mercy and USNS Comfort were "Ready on Arrival" and "United We Sail/Comfort of the Sick on the Sea"—both were true. We were incredibly impressed by the high-quality care delivered by providers from all backgrounds including MTFs, the VA, civilian academic institutions, and civilian private practice settings. These diverse backgrounds stimulated a strong desire to learn from each other, and as a result, both ships formed "Grand Rounds" talks during which speakers delivered presentations on areas of expertise. We also noted the advanced COVID-19 testing capacity that was quickly established on board. On the USNS Mercy, several cutting edge COVID-19 testing platforms were developed and validated in a period of days, which undoubtedly played a crucial role in mission success. Naturally, "Semper Gumby" (Always Flexible) was a constant refrain due to the quickly changing parameters of each mission. In the case of the USNS Comfort, the ship transitioned from a non-COVID to COVID facility, necessitating berthing of most personnel off the ship to maximize safety while taking care of COVID patients onboard. Similarly, personnel of the USNS Comfort also ultimately transitioned to berthing onshore to maximize individual safety.

As the missions for both platforms concluded, it was clear that we and others had learned a great deal from the efforts of Navy Medicine to provide support to the civilian community. As distressed as New York City was during the zenith of its COVID-19 infections, the USNS Comfort treated only a modest number of patients. Although several articles in the press pointed to a complex set of regulations that made it challenging to transfer patients, other factors were likely in play. Specifically, it will be important to understand the role that health care economics played in the willingness of local hospitals to transfer patients not only to the USNS Comfort, but also to field hospitals in locations nationwide. Effectively, a brand-new hospital opened in each city virtually overnight, and at a time when every hospital was hemorrhaging financially, it may have been difficult to untangle "assistance" from "competition" in some settings. It remains a tragic paradox during this entire pandemic—the very hospitals tasked with caring for the sick are simultaneously under staggering financial constraints. In the case of the USNS Mercy, limited patient volume had more to do with the success that California experienced in early and aggressive social mitigation tactics which decreased the slope of COVID-19 infections. Overall, it is important to understand all of the critical vectors when trying to support civil authorities in instances where there is overlap between civilian and military functions. We also recognize that patients admitted to each hospital ship often experienced difficulty communicating with their families ashore, which will be important to resolve in the future.



Gavin Dunn, MD, PhD, (left) in the operating room on the USNS Mercy.

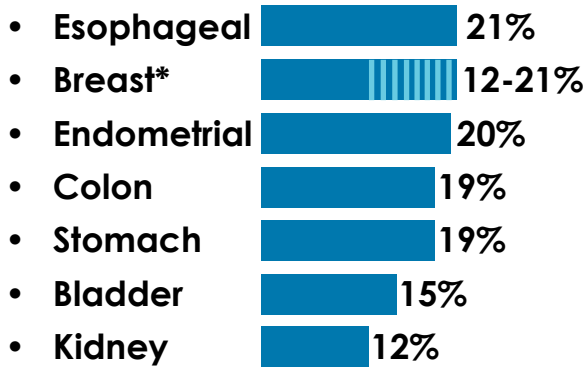
The sailors of the USNS Comfort and USNS Mercy, as well as those who served in other efforts across the country, should be proud of their service to the country in spring 2020. Indeed, COVID-19 has touched every corner of the globe, and the members of Task Force 130.1 did their part to answer an early call from a nation in distress, reeling from a new and uncertain specter, and trying to find its way through the darkness. These platforms are highly valuable assets that will surely be deployed to other turbulent areas in the years ahead. However, the value of our Navy's hospital ships, albeit substantial, was perhaps not the central lesson from these mobilizations. The most impressive asset that we saw as mobilized members of the United States Navy was its people—ready to serve in missions at home and abroad.

Disclosure

This manuscript reflects the sole perspectives of the authors and does not represent, in any way, the views of the United States Navy and/or the Department of Defense. **MM**

1 PICTURE = 1,000 WORDS

Estimated decreases in risk of cancer with high levels of physical activity



*Estimate ranges from 12-21% Source: National Cancer Institute

Conditions Favoring Increased COVID-19 Morbidity and Mortality: Their Common Denominator and its Early Treatment

by Eliot Shevel, BDS

Abstract

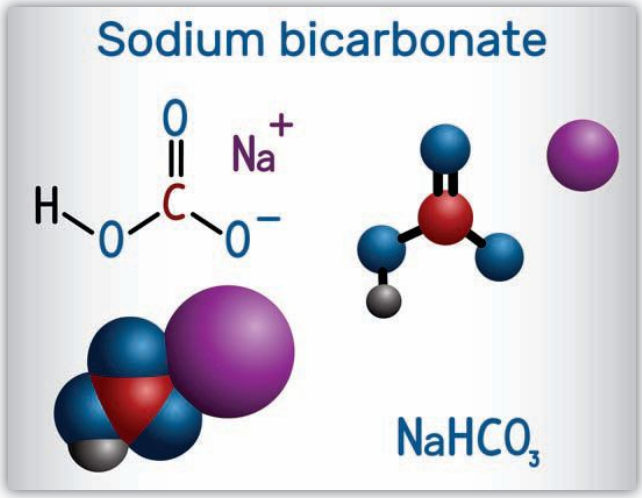
The factors contributing to increased morbidity and mortality in SARS-CoV-2 infection are diverse, and include diabetes, obesity, Chronic Obstructive Pulmonary Disease (COPD), advanced age, and male sex. Although there is no obvious connection between these, they do have one common denominator—they all have a tendency towards lower urine pH, which may indicate a lower-than-normal tissue pH. Furthermore, it has been shown that lower pH has two important negative influences: 1) it enhances viral fusion via the endosomal route, thereby facilitating viral multiplication; and 2) it facilitates increased production of inflammatory cytokines, thereby exacerbating the cytokine storm. This paper discusses published literature on lower tissue/interstitial pH in those diseases/co-morbidities that are known risk factors of severe COVID-19, and hypothesize that small doses of baking soda could be a simple, cost-effective, and rapid method of reducing both morbidity and mortality in COVID-19 patients.

Introduction

Morbidity and mortality with COVID-19 are increased with diabetes, obesity, chronic obstructive airways disease, advancing age, and in males. The common denominator is a tendency toward a lower urine or tissue pH, as listed here:



Eliot Shevel, BDS, DipMFOS, MB, BCh, is head of the South African Headache Society, the South African affiliate of the International Headache Society. He is founder and practices at The Headache Clinic in Johannesburg, South Africa.



1. Diabetes. Patients with type 2 diabetes exhibited a significantly lower 24-hour urine pH (5.45 ± 0.27 versus 5.90 ± 0.42; P < 0.01),[1, 2] and low urine pH is in itself an independent predictor of diabetes.[3]

2. Obesity in males. Obesity is significantly correlated with lower urinary pH (≤5.5) in men,[4, 5] and urine pH shows a stepwise decrease with increasing Body Mass Index.[6]

3. Chronic Obstructive Pulmonary Disease (COPD). A consequence of hypercapnia due to alteration of gas exchange in COPD patients is an increase of H^+ concentration.[7]

4. Advanced age. With increasing age, there is a significant increase in the steady-state blood H+ ($p < .001$), and reduction in steady-state plasma HCO3 ($p < .001$), indicative of a progressively worsening low-level metabolic acidosis.[8] The decline of urine pH with age was highly significant. The fall in urine pH with age was monotonic, and, except for the final hexile in women, every hexile was significantly lower than the previous,[9] and males.[10, 11]

5. Urine pH reflects acid–base balance and is readily measurable.[12] Average urine pH is usually 6.0 - slightly acidic, but the normal range is 4.5 to 8.0. The pH of the blood is tightly regulated between 7.35 and 7.45. Plasma and interstitial fluid contain similar amounts of bicarbonate buffer, blood additionally

has powerful pH buffering protein molecules such as haemoglobin and albumin. Because of this difference, interstitial fluid pH is more variable than that of plasma.[1] Consequently, in conditions with mild but not severe acidosis the normal pH range of interstitial fluids can vary much more than that of the blood.

This article highlights the possible role of low interstitial fluid pH in SARS-CoV-2 infections and explains the mechanisms by which the increased acidity that occurs in the five groups of people listed above may increase both morbidity and mortality in COVID-19.

There are two ways that increased interstitial fluid acidity may adversely affect COVID-19 prognosis: low pH enhances viral fusion and entry into cells via the endosomal route,[13, 14] thereby facilitating viral multiplication, and low pH increases the production of inflammatory cytokines,[15] exacerbating the cytokine storm and the dire consequences thereof.

Viral Fusion

For all enveloped viruses such as SARS-CoV-2, a critical event during the entry of the virus into cells is the fusion of the viral envelope with the membrane of the host cells,[16] enabling viral multiplication.[17] The process ends with transfer of viral genomes inside host cells, where viral replication takes place.[14] Disruption of the SARS-CoV-2 fusion mechanism offers a potential therapeutic target.[18]

It has been shown that fusion of Corona viruses does not occur at neutral pH and that fusion activation is a direct low-pH-dependent process occurring within acidic endosomes. Little or no fusion occurred above a pH of 6.0. The pH optimum for fusion was 5.0 at 37°C, where fusion occurred rapidly.[17] Viral fusion proteins undergo dramatic transitions during membrane fusion. For viruses such as SARS-CoV-2 that enter through the endosome, these conformational rearrangements are typically pH sensitive. A low pH enhances virus entry into the cell, facilitating viral replication and proliferation.[19] Conversely, virus entry into cells is inhibited by inhibitors of pH-dependent endocytosis.[17] It has previously been suggested that future antiviral approaches targeting coronavirus fusion may need to take into account a rapid virus-cell fusion reaction with a low-pH-dependent trigger.[17]

Inflammatory Cytokines and Low pH

There is strong evidence favouring the existence of links between acid-base balance and cytokine concentrations with acidosis as potential factor for the trigger threshold of the inflammatory response.[15] The pH of the extracellular milieu affects a wide range of immunological functions,[20, 21] with a lower pH enhancing cytokine production.[22, 23]

There is also a body of evidence showing that low interstitial fluid pH is a common feature associated with the course of inflammatory reactions against pathogenic microorganisms in peripheral tissues.[24-26] These studies strongly suggest links between acid-base balance and cytokine concentrations, with low pH as a potential trigger of the inflammatory response.[15]

Low pH is among the most common abnormalities seen in patients suffering from severe pulmonary and systemic illness. In these patients, the mainstay of therapy is treatment of the underlying condition, and not correction of the pH. Although studies suggest that low pH itself has profound effects on the host, particularly in the area of immune function,[27] some consider the acidosis to be protective, especially in the presence of lung inflammation.[28]

Increased mortality in COVID-19 patients is a consequence of the increased inflammatory response and the excessive cytokine production—the so-called "cytokine storm." The loss of local control of the release of these cytokines leads to systemic inflammation and potentially deleterious consequences.[29] Studies analyzing cytokine profiles from COVID-19 patients have suggested that the cytokine storm correlates directly with lung injury, multi-organ failure, and the poor prognosis of severe COVID-19.[30] Reducing cytokine production during the management of COVID-19 patients would doubtless improve survival rates and reduce mortality.[30]

Discussion

Abnormalities in systemic acid-base balance represent attractive targets for COVID-19 therapy. Interstitial fluid pH is easily altered and rendering its pH more alkaline may indeed alter both viral load[19] and the immune response.[27] Interstitial fluid pH is easily rendered more alkaline by the oral administration of small doses of bicarbonate of soda. Normalizing the pH of the interstitial fluid in susceptible individuals may reduce both virus multiplication and cytokine production. One of the major factors affecting acidity is diet. Foods that make the urine more acidic include grains, fish, high protein foods, and sugary foods. Alkaline foods that reduce the acidity are nuts, vegetables, and most fruits. Changing to a more alkaline diet can reduce the acidity of the urine. Unfortunately,

this takes time, and is of little help with COVID-19, as in COVID-19 the tissues must be made less acidic as quickly as possible after a positive COVID-19 test. It is easier and quicker to reduce the body's acidity levels by taking bicarbonate of soda It is interesting to note that the use of bicarbonate of soda to treat viruses has a precedent—as long ago as the 1920s, bicarbonate of soda was widely used to treat flu. Now the flu virus is not a Corona virus, but what is important is that the flu virus also enters the cell by endocytosis in order to multiply—that is, it enters the cells by the same mechanism as the COVID-19 virus. Bicarbonate of soda is widely used as an antacid and millions of people use it regularly for dyspepsia without problems or adverse side effects. It is cheap, readily available at any grocery store without a prescription, and is safe in the recommended dose of a level teaspoon in warm water four times a day.

Viral replication occurs in most cases during the first week or so of being infected. Consequently, the use of bicarbonate of soda to reduce viral multiplication would only be beneficial during this period. The indications for its use in susceptible groups would be either a positive COVID-19 test or in patients with mild disease, preferably as soon as possible after on first onset of symptoms. It must be emphasized that there is no evidence that reducing the tissue acidity in susceptible individuals will prevent COVID-19 infection, and neither does the evidence suggest that it would be of any value once severe manifestations have developed. On the contrary, the presence of acidosis once lung inflammation is present may reduce mortality.[28]

Conclusion

This manuscript presents evidence suggesting in patients with early COVID-19 infection, treating the mild acid/base imbalance as early as possible in the progression of the disease may impede virus fusion and replication, as well as slow down or reduce the inflammatory changes in general. This might be done safely and inexpensively with bicarbonate of soda. In COVID-19 patients with mild disease and risk factors, would alkalinization be a useful therapeutic strategy to prevent severe illness? Only time and more extensive research will tell. I'm saying it's time for more extensive research to tell.

References

1. Marunaka Y. Roles of interstitial fluid pH in diabetes mellitus: Glycolysis and mitochondrial function. World J Diabetes. 2015;6(1):125-135.
2. Maalouf NM, Cameron MA, Moe OW, et al. Metabolic basis for low urine pH in type 2 diabetes. Clin J Am Soc Nephrol. 2010;5(7):1277-1281.
3. Hashimoto Y, Hamaguchi M, Nakanishi N, et al. Urinary pH is a predictor of diabetes in men; a population based large scale cohort study. Diabetes Res Clin Pract. 2017;130:9-14.
4. Song JH, Doo SW, Yang WJ, et al. Influence of obesity on urinary pH with respect to sex in healthy Koreans. Urology. 2011;78(6):1244-1247.
5. Negri AL, Spivacow FR, Del Valle EE, et al. Role of overweight and obesity on the urinary excretion of promoters and inhibitors of stone formation in stone formers. Urol Res. 2008;36(6):303-307.
6. Najeeb Q, Masood I, Bhaskar N, et al. Effect of BMI and urinary pH on urolithiasis and its composition. Saudi J Kidney Dis Transpl. 2013;24(1):60-66.
7. Bruno CM, Valenti M. Acid-base disorders in patients with chronic obstructive pulmonary disease: a pathophysiological review. J Biomed Biotechnol. 2012;2012:915150.
8. Frassetto L, Sebastian A. Age and systemic acid-base equilibrium: analysis of published data. J Gerontol A Biol Sci Med Sci. 1996;51(1):B91-99.
9. Menezes CJ, Worcester EM, Coe FL, et al. Mechanisms for falling urine pH with age in stone formers. Am J Physiol Renal Physiol. 2019;317(7):F65-F72.
10. Worcester EM, Bergsland KJ, Gillen DL, et al. Mechanism for higher urine pH in normal women compared with men. Am J Physiol Renal Physiol. 2018;314(4):F623-F629.
11. Waters WE, Sussman M, Asscher AW. Community study of urinary pH and osmolality. Br J Prev Soc Med. 1967;21(3):129-132.
12. Welch AA, Mulligan A, Bingham SA, et al. Urine pH is an indicator of dietary acid-base load, fruit and vegetables and meat intakes: results from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk population study. Br J Nutr. 2008;99(6):1335-1343.
13. Kamadurai HB, Qiu Y, Deng A, et al. Mechanism of ubiquitin ligation and lysine prioritization by a HECT E3. Elife. 2013;2:e00828.
14. Dimitrov DS. Virus entry: molecular mechanisms and biomedical applications. Nat Rev Microbiol. 2004;2(2):109-122.
15. Casimir GJ, Lefevre N, Corazza F, et al. The Acid-Base Balance and Gender in Inflammation: A Mini-Review. Front Immunol. 2018;9:475.
16. Earp LJ, Delos SE, Park HE, et al. The many mechanisms of viral membrane fusion proteins. Curr Top Microbiol Immunol. 2005;285:25-66.
17. Chu VC, McElroy LJ, Chu V, et al. The avian coronavirus infectious bronchitis virus undergoes direct low-pH-dependent fusion activation during entry into host cells. J Virol. 2006;80(7):3180-3188.
18. Malik AH, Zaid S, Yandrapalli S, et al. Corrigendum to 'Trends and Outcomes with Transcatheter versus Surgical Mitral Valve Repair in Patients >80 Years of Age' [The American Journal of Cardiology 125 (2020) 1083-1087]. Am J Cardiol. 2020;128:220.
19. Harrison JS, Higgins CD, O'Meara MJ, et al. Role of electrostatic repulsion in controlling pH-dependent conformational changes of viral fusion proteins. Structure. 2013;21(7):1085-1096.
20. Lardner A. The effects of extracellular pH on immune function. J Leukoc Biol. 2001;69(4):522-530.
21. Martinez D, Vermeulen M, Trevani A, et al. Extracellular acidosis induces neutrophil activation by a mechanism dependent on activation of phosphatidylinositol 3-kinase/Akt and ERK pathways. J Immunol. 2006;176(2):1163-1171.
22. Zampieri FG, Kellum JA, Park M, et al. Relationship between acid-base status and inflammation in the critically ill. Crit Care. 2014;18(4):R154.
23. Steele PM, Augustine NH, Hill HR. The effect of lactic acid on mononuclear cell secretion of proinflammatory cytokines in response to group B streptococci. J Infect Dis. 1998;177(5):1418-1421.
24. Edlow DW, Sheldon WH. The pH of inflammatory exudates. Proc Soc Exp Biol Med. 1971;137(4):1328-1332.
25. Simmen HP, Battaglia H, Giovanoli P, et al. Analysis of pH, pO2 and pCO2 in drainage fluid allows for rapid detection of infectious complications during the follow-up period after abdominal surgery. Infection. 1994;22(6):386-389.
26. Simmen HP, Blaser J. Analysis of pH and pO2 in abscesses, peritoneal fluid, and drainage fluid in the presence or absence of bacterial infection during and after abdominal surgery. Am J Surg. 1993;166(1):24-27.
27. Kellum JA, Song M, Li J. Science review: extracellular acidosis and the immune response: clinical and physiologic implications. Crit Care. 2004;8(5):331-336.
28. Kregenow DA, Rubenfeld GD, Hudson LD, et al. Hypercapnic acidosis and mortality in acute lung injury. Crit Care Med. 2006;34(1):1-7.
29. Jaffer U, Wade RG, Gourlay T. Cytokines in the systemic inflammatory response syndrome: a review. HSR Proc Intensive Care Cardiovasc Anesth. 2010;2(3):161-175.
30. Ragab D, Salah Eldin H, Taeimah M, et al. The COVID-19 Cytokine Storm; What We Know So Far. Front Immunol. 2020;11:1446.

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MSMA Members in the News

Did you make the news? Submit your success story and photo to lfleenor@msma.org.



Amy K. Patel, MD, is *Missouri Medicine's* new Radiology Editorial Board member for the Journal. She is a Breast Radiologist, Medical Director, Liberty Hospital Women's Imaging, and Assistant Professor of Radiology at the University of Missouri-Kansas City School of Medicine, Kansas City, Missouri. She is also the Associate Editor of Digital Media for the *Journal of the American College of Radiology*.

She replaces **John H. Niemeyer, MD**, who has served the Missouri Medicine Editorial Board since 2007. With our thanks, Dr. Niemeyer is receiving the *Missouri Medicine* Distinguished Service Award for his 14 years of dedicated service. He practices radiology at Missouri Baptist Medical Center in St. Louis, Missouri.



Robert Corder, MD, an OB/GYN in St. Joseph, received the President's Silver Medal Volunteer Service Award at the Kirby Puckett Center there. Staff at the center said Dr. Corder's dedication to rehabilitating lives during the pandemic made him worthy of the honor.



Inderjit Singh, MD, an Internal Medicine physician in St. Louis, recently jointed the National Kidney Foundation Serving Eastern Missouri, Metro East, and Arkansas Advisory Board. Dr. Singh currently serves as President of Gateway Nephrology.



Jennifer Page, MD, was recently installed as the St. Louis Metropolitan Medical Society President. She is a Physical Medicine and Rehabilitation Specialist and Medical Director of Acute Rehabilitation at Mercy Hospital South.

The following physicians were installed as officers to serve with Dr. Page in 2021: **Erin Gardner, MD**, president-elect; **Mark Gunby, DO**, vice president; **Robert A. Brennan, Jr., MD**, secretary-treasurer; and **Jason K. Skyles, MD**, immediate past president.

Four physicians were installed as Councilors serving three year terms from 2021 through 2023: **Sara Hawatmeh, MD; Otha Myles, MD; David Niebruegge, MD;** and **Farheen Raja, MD**. **MM**

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Premier Peer-Reviewed Journal: Thanks Dr. Hagan

It has been my privilege to serve on the editorial board of *Missouri Medicine* in Internal Medicine, reluctantly stepping down after thirty-plus years. I have watched it grow from an average journal with an occasional interesting medical article to one of the premier peer-reviewed journals in the country.

This transition from average to outstanding is entirely the result of the dedication, intellect, and hard work of our Editor, Dr. John Hagan, and it has been my pleasure and honor to work with him over these past two decades. And while he is always busy thanking and giving credit to everyone on the editorial board, it occurred to me that no one is thanking him for all that he has done to make the Journal the outstanding, nationally recognized publication that it has become.

So, on behalf of the editorial board of the Journal, past and present, and all the Journal's readers, I want to thank Dr. Hagan for his incredible dedication and hard work. Missouri physicians should know what a gem Dr. Hagan has been for the medical community.

John S. Daniels, MD
Retiring Internal Medicine
Missouri Medicine Editorial Board Member, St. Louis

Use of Convalescent Plasma in the Management of COVID-19

The article, "COVID-19 Convalescent Plasma: From Donation to Treatment - A Systemic Review & Single Center Experience," published in January/February 2021 issue of *Missouri Medicine*, discusses convalescent plasma (CP) as a treatment for COVID-19 infection, the limitations that could arise in recruiting donors, coordinating care, and delivering the therapy, particularly in the early phase of the pandemic. The use of CP in the U.S. was granted under the Expanded Access Program based on the assumption that plasma from recovered individuals could potentially contain antibodies to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, the antibody levels in the plasma units were unknown at the time of transfusion. Based on early analysis on efficacy and safety and lack of effective treatment, the Food and Drug Administration (FDA) supported the emergency use of COVID-19 CP.

Since then, studies have yielded mixed results. Clinical trials focusing on patients with COVID-19 who had moderate to severe illness failed to show significant clinical benefit. Observational studies showed that transfusion of CP to hospitalized COVID-19 patients with higher antibody levels and transfusion within three days yielded greater reductions in mortality. In subgroup analyses, the lower risk of death within 30 days of plasma transfusion in the high-antibody titer group was only seen among non-intubated patients before transfusion. However, these studies had significant limitations and potential biases and some were underpowered, making it difficult to conclude whether CP transfusion has any role in the treatment of patients with COVID-19.

On the other hand, serious adverse events after CP transfusion were not frequent and were similar to standard plasma transfusion. In the U.S., most common risks of plasma transfusion are non-infectious including transfusion reactions and allergic reactions.

Based on this available date and published literature, the National Institutes of Health COVID-19 treatment guidelines determined that "the data are insufficient to recommend for or against" the use of CP. The Infectious Diseases Society of America and American Association of Blood Banks recommended the use of CP to be limited to clinical trials stating that the benefit of CP will likely to occur in patients who are not critically ill and who received high antibody plasma unit titers within 72 hours of diagnosis or hospital admission.

Until more well conducted randomized controlled studies are completed, routine provision of CP for patients with COVID-19 should be discouraged. The administration of high-antibody titers CP should be limited to clinical trials, and those who have mild disease at high risk of progression early in the course of their illness.

References

1. Libster R, Pérez Marc G, Wappner D, Coviello S, Bianchi A, Braem V, et al. Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults. The New England journal of medicine. 2021.
2. Budhai A, Wu AA, Hall L, Strauss D, Paradiso S, Alberigo J, et al. How did we rapidly implement a convalescent plasma program? Transfusion. 2020;60(7):1348-55.
3. Tobian AAR, Shaz BH. Earlier the better: convalescent plasma. Blood. 2020;136(6):652-4.
4. Joyner MJ, Bruno KA, Klassen SA, Kunze KL, Johnson PW, Lesser ER, et al. Safety Update: COVID-19 Convalescent Plasma in 20,000 Hospitalized Patients. Mayo Clinic proceedings. 2020;95(9):1888-97.
5. Piechotta V, Chai KL, Valk SJ, Doree C, Monsef I, Wood EM, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. The Cochrane database of systematic reviews. 2020;7(7):Cd013600.
6. adminstration USfD. FDA In Brief: FDA Updates Emergency Use Authorization for COVID-19 Convalescent Plasma to Reflect New Data. 2021,February 4th.

Dima Dandachi, MD, MPH
Medical Director of the HIV/AIDS Program; Medical Director of Outpatient Antimicrobial Therapy and Vascular Access Team; Division of Infectious Diseases, Department of Medicine, University of Missouri Healthcare
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Insulin Resistance: The Inconvenient Truth

by Anand Chockalingam, MD, Pandiyan Natarajan, MD, Puvithra Thanikachalam, MD & Radha Pandiyan, MD

What is the origin of the term 'insulin resistance'? Is insulin resistance the cause or the consequence? Does insulin resistance routinely require long-term medications?

The term Insulin Resistance (IR) was first introduced by Professor Wilhelmina Faltu in 1931 and this was reiterated by Sir Harold Percival Himsworth in 1936.[1] Interestingly, insulin therapy was introduced before this in 1922.[2] Most of the early patients required increasingly large doses of insulin to control hyperglycemia. As early forms of insulin were impure and derived from nonhuman species, people often developed antibodies to therapeutic insulin leading to resistance.[3] In the present era of recombinant human insulin, anti-insulin antibodies do not raise to levels sufficient to impair insulin action.



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The modern-day understanding and clinical spectrum of IR has changed markedly. IR may be defined as a subnormal glucose response to endogenous and/or exogenous insulin. Physiological stress like pregnancy (placental lactogen) may lead to IR. Pathological stress with excess counter-regulatory hormones like cortisol, growth hormone, catecholamines, and glucagon may also cause IR. Also, medications (glucocorticoids, antiretrovirals, oral contraceptives), or medical conditions such as lipodystrophy, genetic defects in insulin-signaling pathways (Type A insulin resistance) and blocking autoantibodies against the insulin receptor (Type B insulin resistance) may lead to IR. Rare inherited conditions like Leprechaunism, Rabson-Mendenhall syndrome and lipodystrophy disorders may warrant genetic testing and appropriate management to limit IR-related mortality.[4]

IR has been implicated in the causation of many conditions like polycystic ovarian syndrome (PCOS), Type 2 Diabetes mellitus, the metabolic syndrome, fatty liver and coronary artery disease. The precise basis for the link between IR and these clinical conditions is not yet identified. In all these conditions it is widely believed that the cells are resistant to the action of insulin. Insulin levels are variable in patients with Type 2 diabetes mellitus, PCOS, and in the metabolic syndrome. Failure of beta cells to produce insulin may be the issue in some. There is no consistent relationship between insulin levels and occurrence or

severity of the condition in patients with PCOS. Estimation of insulin levels are no longer recommended for the diagnosis of PCOS.[5] Relative calorie excess and sedentary lifestyle in all these conditions may contribute to the elevation in serum insulin levels.

IR can be diagnosed by IV glucose/insulin tolerance testing or from individual blood tests like HOMA- IR ASSAY or Quicki assay.[6] While these tests can also be performed in a medical practice, we often encounter them in research settings. Insulin level is not routinely measured in Type 2 diabetes mellitus and metabolic syndrome. Insulin levels when estimated do not show a consistent pattern in patients with Type 2 diabetes mellitus. In some portion of IR patients, beta cell failure with low serum insulin levels coexists. More often, insulin level is positively correlated to glucose levels. As the blood glucose level goes up, insulin level goes up too. When patients can still produce enough insulin, elevated serum insulin is the consequence of raised glucose level and not the cause of it.

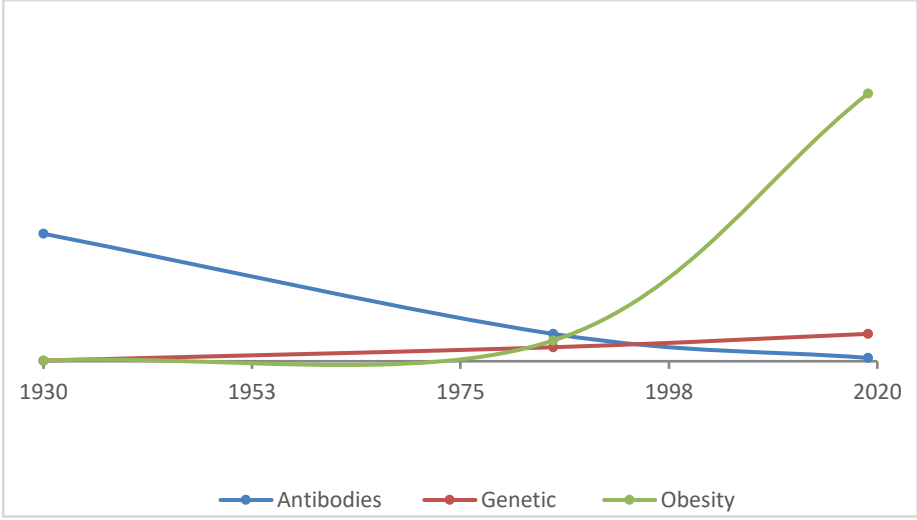


Figure 1. Label of Insulin resistance – changing etiology over last 100 years

The term 'Insulin Resistance' (IR) originally described antibodies to animal forms of insulin in 1930s, while genetic etiology for IR remains a small fraction. The dramatic increase in IR over the last 2-3 decades corresponds to the obesity epidemic. IR is not formally quantified but presumed to be the basis for several metabolic derangements. This distracts from the real issue of over nutrition, sedentary habits and obesity.

With the worldwide obesity epidemic, some physicians find it increasingly impolite to confront their patients with the real problems of sedentary habits, over-eating, sugar-added food/beverage consumption and resultant obesity. Intellectualizing and reframing 'insulin resistance' as an independent medical entity allows for lifelong palliation with numerous diabetic medications, downstream expensive cardiovascular and peripheral revascularization procedures as well as excess morbidity and mortality.

IR as originally described has taken a back seat with the bulk of the current patient population being comprised of obesity-related derangements and complications (Figure 1). Deregulation of fatty acid metabolism and mitochondrial dysfunction may genetically predispose some to IR. Thin patients with PCOS may have IR as an independent medical condition and require medications. Improved lifestyle, emphasizing diet, exercise, stress control, and optimal sleep can specifically improve IR, reduce medication requirement and enhance long term outcomes in all these conditions.

Much of the modern IR epidemic is due to inflammation, sugar-added diet, stress-related neurohumoral activation, and visceral adiposity. Type 2 diabetics typically respond to increasing serum insulin- either exogenous formulations or sulphonylurea mediated endogenous stimulation- indicating that IR is not the primary issue. Over time, the term 'IR' has assumed new meaning and is thought of as the very basis for PCOS, Type 2 Diabetes Mellitus and Metabolic Syndrome. All these conditions have significant over-nutrition and weight gain as the underlying pathophysiological basis. A recent UK diet study resulted in 86% remission and withdrawal of antidiabetic medications with 15kg weight loss.[7] Calorie restriction increased longevity across the animal kingdom mediated by dramatic cardiometabolic risk reduction seen in primates.[8,9] Even amongst healthy normal weight humans, 25% calorie restriction

reduces IR significantly and future risk of diabetes with tremendous public health potential.[10]

In conclusion, insulin resistance is widely misunderstood among clinicians and patients alike. The originally described condition in diabetics developing antibodies to impure early insulin formulations, and thus requiring dose escalations, has become exceedingly rare now. Genetic forms account for a small minority of real IR in non-obese healthy individuals. In most Type 2 diabetics, elevated insulin level is the consequence of raised glucose load and not the cause of it. IR is often not an independent medical condition requiring long term medications. Obesity needs to be addressed as such, directly and specifically. Targeting diet, exercise, and weight reduction offers a window of opportunity to resolve 'insulin resistance' and oftentimes cure metabolic syndrome minimizing chronic disease management with medications.

References

1. Gale EA. Commentary: the hedgehog and the fox: Sir Harold Himsworth (1905-93). Int J Epidemiol. 2013;42(6):1602-1607. doi:10.1093/ije/dyt202
2. Quianzon CC, Cheikh I. History of insulin. J Community Hosp Intern Med Perspect. 2012;2(2):10.3402/jchimp.v2i2.18701. Published 2012 Jul 16. doi:10.3402/jchimp.v2i2.18701
3. Kahn CR, Rosenthal AS. Immunologic reactions to insulin: insulin allergy, insulin resistance, and the autoimmune insulin syndrome. Diabetes Care. 1979;2(3):283-295. doi:10.2337/diacare.2.3.283
4. Semple RK, Savage DB, Cochran EK, Gorden P, O'Rahilly S. Genetic syndromes of severe insulin resistance. Endocr Rev. 2011;32(4):498-514. doi:10.1210/er.2010-0020
5. Lewandowski KC, Płusajska J, Horzelski W, Bieniek E, Lewiński A. Limitations of insulin resistance assessment in polycystic ovary syndrome. Endocr Connect. 2018;7(3):403-412. doi:10.1530/EC-18-0021
6. Buchanan TA, Watanabe RM, Xiang AH. Limitations in surrogate measures of insulin resistance. J Clin Endocrinol Metab. 2010;95(11):4874-4876. doi:10.1210/jc.2010-2167
7. Lean MEJ, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. Lancet 2018; 391: 541–51
8. Masoro, E. J. Caloric restriction. Aging 10, 173–174 (1998)
9. Mattison JA, Roth GS, Beasley TM, et al. Impact of caloric restriction on health and survival in rhesus monkeys from the NIA study. Nature. 2012;489 (7415):318-321
10. Kraus WE, Bhapkar M, Huffman KM, Pieper CF, Krupa Das S, Redman LM, Villareal DT, Rochon J, Roberts SB, Ravussin E, Holloszy JO, Fontana L; CALERIE Investigators. 2 years of calorie restriction and cardiometabolic risk (CALERIE): exploratory outcomes of a multicentre, phase 2, randomised controlled trial. Lancet Diabetes Endocrinol. 2019 Sep;7(9):673-683. doi: 10.1016/S2213-8587(19)30151-2. Epub 2019 Jul 11. PMID: 31303390; PMCID: PMC6707879.

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Washington University in St. Louis
School of Medicine

Washington University Division of Plastic and Reconstructive Surgery Plays Critical Role in Developing Specialty

by Justin Sacks, MD, MBA

The Washington University (WashU) School of Medicine Division of Plastic and Reconstructive Surgery has played critical roles in developing the specialty in the United States and the world abroad. It is a Division rich in history, discovery, and research. It is part of a historic Department of Surgery lead by Timothy Eberlein, MD, the Director of the Alvin J. Siteman Cancer Center, the Spencer T. and Ann W. Olin Distinguished Professor and Bixby Professor. The Division of Plastic and Reconstructive Surgery program in 2020 was 100 years old. Plastic Surgery has come of age during the 20th century and will further help transform medicine in the 21st-century and beyond.

The WashU Division of Plastic and Reconstructive Surgery sat atop leadership in the early origins of the specialty in the United States. Vilray P. Blair, MD, served as the first chief of the Division at the Medical School from 1925-1955. Blair treated soldiers in World Was I with complex maxillofacial injuries, and his paper on "Reconstructive Surgery of the Face" set the benchmark for facial reconstruction. Blair's visionary leadership helped transform the American Association of Plastic Surgery and led to the American Board of Plastic Surgery formation as an independent specialty board. James Barrett Brown, MD, became the chief of Plastic Surgery in 1955 and served until 1968. He pioneered work using large skin grafts to treat severe burns in wounded warriors; his work also led to hand surgery innovations. ohn E. "Jack" Hoopes, MD, served as chief of the Division of Plastic and Reconstructive Surgery from 1968 until 1970. He then became Chief of Plastic Surgery at Johns Hopkins University School of Medicine in Baltimore, Maryland. There he trained generations of trainees carrying on the WashU legacy. Following Hoopes, Paul M. Weeks, MD, was the Chief of Plastic and Reconstructive Surgery from 1970-1996. In addition to being a leader in hand trauma and tendon repair, Weeks helped promote plastic surgery residency training at Washington University and nationwide. His groundwork fostered the development of a truly integrated plastic surgery residency. Susan Mackinnon, MD, took over in 1996 and ran the Division for 23 years until 2019. Dr. Mackinnon lead a Division that focused on all aspects of Plastic and Reconstructive Surgery, specifically Nerve Surgery. Clinical, basic, and translational research involved advances in peripheral nerve surgery culminating in the first human nerve cadaveric transplant.

In the last several decades, the WashU Division of Plastic Surgery program has continued to advance the field with the highest quality graduates. These graduates have populated academic and private practices across North America and the globe. We train three categorial integrated Plastic Surgery residents per year over six years. We also teach hand



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and microsurgical fellows and offer additional peripheral nerve fellowship training. Shortly we will be offering a microsurgical fellowship. Our program has adopted the mantra of clinical, educational, research, and innovation excellence.

In February 2020, I started as the Shoenberg Professor and Chief, Division of Plastic and Reconstructive Surgery in the Department of Surgery at Washington University in St. Louis. Before this, I spent the last decade at Johns Hopkins School of Medicine, where I was the Vice-Chair of Clinical Operations and Director of Oncological Reconstruction. Before Johns Hopkins, I was on faculty at the MD Anderson Cancer Center in Houston, Texas, and completed fellowships and training at the University of Pittsburgh Medical Center and Mount Sinai School of Medicine in New York City. My practice encompasses head to toe cancer, trauma, and aesthetic reconstruction. My training and previous experience inform the path of the future state of the WashU Plastic and Reconstructive Division moving forward.

The Washington University School of Medicine was founded in 1895. The main medical campus encompasses Barnes Jewish Hospital and St. Louis Children's Hospital, which has over 1,300 beds. There are 15 hospitals within the BJC healthcare system with over 3,000 beds. NIH funding is over $500 million per year, and the school of medicine is continually ranked in the top 10.

We currently have 16 full-time faculty. Our Division is committed to clinical education research and innovation. We have 10 core clinical programs within the Division of Plastic Surgery that we are currently growing: aesthetic surgery, breast surgery, adult craniofacial, pediatric and craniofacial plastic surgery, general reconstructive surgery, hand surgery, limb salvage, lymphedema surgery, nerve surgery, and transgender surgery. Each clinical program has a leader who is responsible for clinical, educational, and research initiatives. We have a separate freestanding aesthetic surgery facility called West County Plastic Surgery, which caters to aesthetic surgery in an academic environment. We have expanded outside Barnes Jewish Hospital into the community at Alton Northeast Hospital, Christian Northeast Hospital, Progress West and are looking to expand throughout the BJC Health Care system.

New novel programs have begun such as Lymphedema Surgery, managing patients with upper and lower extremity lymphedema. This center of excellence will offer the full host of conservative management, including imaging, medical therapy, and surgical optimization. Specifically, patients requiring lymphatic rewiring with lymph node transfer and/or lymphovenous bypass will be studied over time. The basic science of lymphedema will be investigated in the lab, and clinical outcomes research will be initiated with a prospectively managed database. This novel collaboration for lymphedema care involves a multi-disciplinary team of infectious disease, bariatric surgery, primary care, hematology/oncology, physical medicine and rehabilitation, physical and occupational therapy, and orthopedic surgery.

A novel collaboration between Acute and Critical Care Surgery, Vascular Surgery, and Plastic Surgery for Limb Preservation has started. This specific service focuses on treating patients with peripheral vascular disease to preserve limb form and function using sophisticated limb salvage and free tissue transfer. Transgender surgery will also be expanding for both facial reconstruction, top, and bottom surgery. Future programs will involve Vascularized Composite Allotransplantation involving the abdominal wall, face, and hand. We will have a concerted effort between immunology, transplant surgery, and our Division.

Our plastic surgery residency program will continue to expand. It routinely recruits medical students from around the country and world. We will continue to advance the education platform and explore competency-based learning and novel ways to train residents in the future. Our Plastic Surgery Research Laboratories is led by Matthew Wood, MD, an NIH-funded basic science researcher who focuses on nerve regeneration. The research laboratory contains over 2,000 feet of wet lab space and 4,000 feet of office space. We have five operating microscopes and a full host of research infrastructure to perform basic science at the highest level in tissue engineering, immunology, and nerve physiology. It is an exciting time to be part of the Division of Plastic and Reconstructive Surgery in the Department of Surgery at Washington University School of Medicine. These articles highlighted by our faculty reveal our exciting clinical, basic science, and translational research projects.

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Family-Centered Pediatric Plastic Surgery Care

by Kamlesh B. Patel, MD, Kristin D. Pfeifauf, JD & Alison Snyder-Warwick, MD

Washington University in St. Louis
School of Medicine

A family-centered pediatric plastic surgery care model can be used to increase satisfaction, improve health outcomes and follow-up, decrease burden of care, and improve efficiency of resource utilization.



Kamlesh B. Patel, MD, MSc, (above), Kristin D. Pfeifauf, JD, and Alison Snyder-Warwick, MD, are in the Division of Plastic and Reconstructive Surgery, Washington University, St. Louis, Missouri.

Abstract

Our multidisciplinary cleft palate and craniofacial center was established in 1978 and manages more than 5,000 active patients from birth to skeletal maturity. Over the past four years we have implemented a complex family-centered reorganization, with the goal of improving care and patient retention. Through our implementation of a family-centered approach, we have also decreased treatment burden, need for secondary procedures and cost of care. [1-12]

Introduction

A multidisciplinary, team-based approach has long been standard of care for patients with craniofacial anomalies and has provided the basis for a multidisciplinary care model in many other fields of medicine[4] (Figure 1). This care model allows patients to see multiple practitioners in a single visit, rather than attending separately scheduled appointments with each necessary provider, and it facilitates collaborative care planning amongst providers. Our families attend a multidisciplinary team clinic annually to consult with various providers as appropriate to patient age and diagnosis, including their plastic surgeon, orthodontist, speech-language pathologist, otolaryngologist, amongst others (Figure 2). American Cleft Palate-Craniofacial Association Standards (the Standards) provide a nationally accepted, disease-centered framework for delivery of multidisciplinary cleft care. However, the Standards afford flexibility for teams to design their clinics to best suit their patients' and providers' needs and resources. As a result, teams across the country demonstrate distinct approaches to organization, clinical protocols and other integral care components.[4,6]

In structuring their clinics, teams often have little or no understanding of families' treatment concerns, needs, and preferences, and teams typically base their process of care decisions on provider experience, without regard to the family's perspective.[13] In contrast, a family-centered model incorporates patient and parent concerns, needs, and preferences into care decisions, in order to attain outcomes meaningful to families and providers alike.

Family-centered care is a critical healthcare improvement aim of the Institute of Medicine and a high priority focus area

for the National Institutes of Health and Agency for Healthcare Research and Quality.[7] Evidence-based medicine has shown family-centered care to be positively associated with clinical effectiveness, patient safety and care satisfaction.[14] Higher care satisfaction correlates with better follow-up and retention, which in turn leads to improved clinical outcomes.[15] At present, poor follow-up and retention are a substantial hindrance to long-term, complete care for medically complex craniofacial patients, which family-centered model could mitigate.[3] Moreover, a shift to a family-centered model will enable cleft teams to adjust the care process to minimize care burden and improve patient quality of life (QOL).[16]



Figure 1. Multidisciplinary Cleft-Craniofacial team members at St. Louis Children's Hospital.

Over the past four years, our team has managed our transition to a family-centered model with a focus on obtaining optimal outcomes with minimum burden. Here we summarize our multidisciplinary and systematic approach to improve care of patients within our cleft and craniofacial clinic.

Medically-Complex Craniofacial Patients

Patients with craniofacial anomalies, including craniosynostosis, cleft palate, and craniofacial microsomia, are considered medically complex, and they are followed from birth to skeletal maturity (15-18 years of age). Craniosynostosis is the abnormal early fusion of a cranial suture resulting in irregular head shape. Patients can present with single-suture involvement or more complex multi-suture synostosis, and the overall incidence of craniosynostosis is as high as 1 in 1,700 births.[17]

Surgical management of patients with craniosynostosis is complex, requiring the expertise of both a plastic surgeon and a neurosurgeon, and necessitating adequate long-term multidisciplinary follow-up. Orofacial clefts (including cleft palate) are the most common congenital facial anomalies in the world, with nearly 250,000 new cases diagnosed annually worldwide, and an estimated prevalence in the United States of 1 in 690 live births.[18] In these children, a variety of health domains related to patient QOL, including speech, hearing, breathing, oral health, feeding, appearance, and psychosocial functioning, are affected. In light of their complex needs, children with orofacial clefts (including cleft lip and palate) undergo a multitude of surgical and nonsurgical treatments during their childhood. Throughout this process, they interact with a number of healthcare providers across multiple disciplines regarding different aspects of their care, including plastic surgery for correction of the lip and palate, speech therapy for treatment of speech deficits, otolaryngology for airway and hearing compromise, audiology for treatment of hearing loss, dentistry for oral healthcare, nutrition for feeding difficulty, and psychology for psychosocial issues related to their diagnosis. Children with craniofacial microsomia are born with a constellation of symptoms that includes orbit involvement, mandibular hypoplasia, microtia (pinna underdevelopment), nerve involvement, and soft tissue hypoplasia.[19] Surgical repair for craniofacial microsomia varies on the severity of the anomaly but can include the need for bone-anchored hearing aids, facial reconstruction (such as surgical distraction osteogenesis), and intensive ophthalmological care. At our center, the timing of surgical procedures for craniosynostosis, cleft

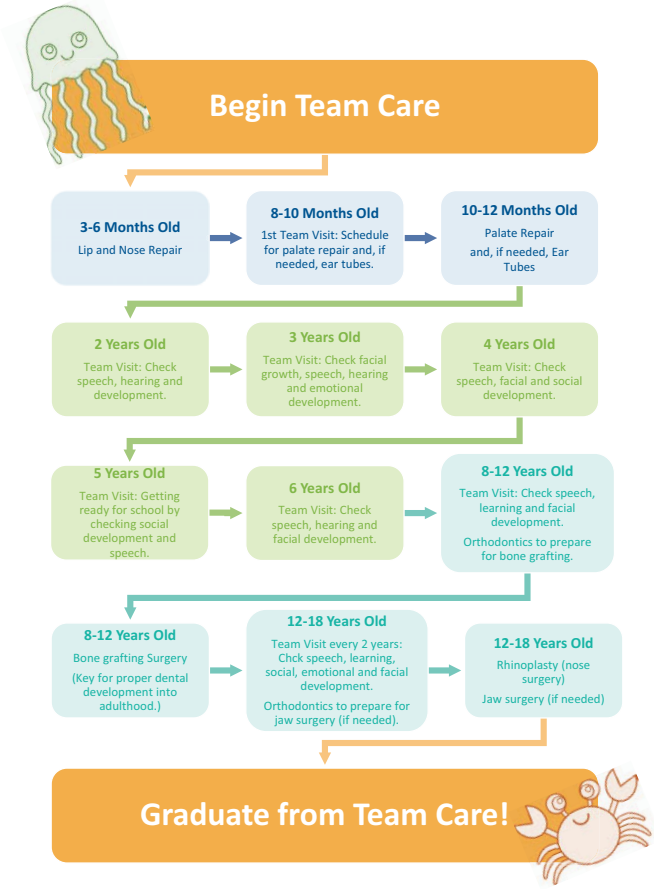


Figure 2. Cleft Lip & Palate timeline for care.

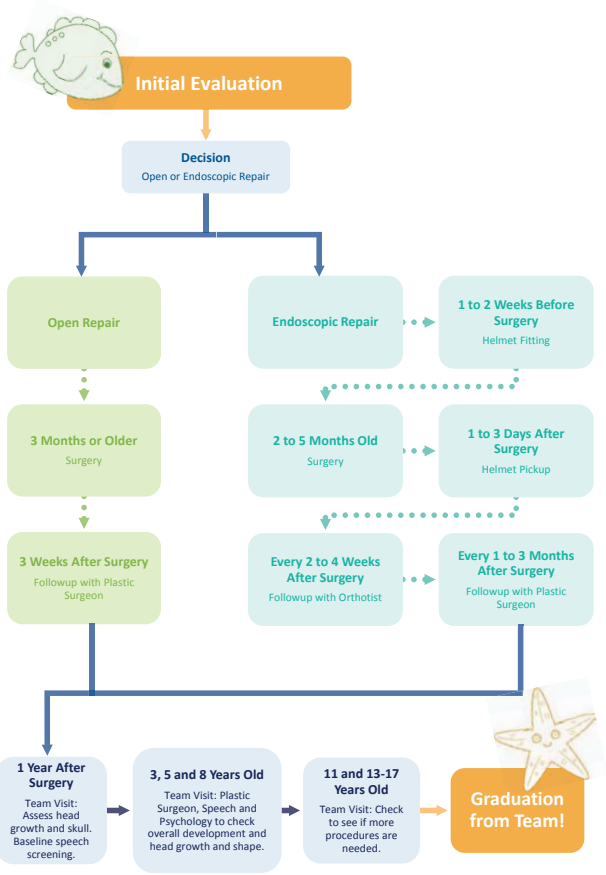


Figure 3. Nonsyndromic craniosynostosis timeline for care from birth to skeletal maturity. New protocol minimizes clinic visits and need for additional imaging.

palate and craniofacial microsomia is guided by the ultimate goal of decreasing the number of secondary procedures and decreasing overall treatment burden.

Multidisciplinary Team Care

A multidisciplinary, team-based approach has been standard of care for patients with craniofacial anomalies since 1938, and our center was established in 1978 as the first cleft and craniofacial team to serve the Midwest region. Our team members include surgeons from Plastic Surgery and Otolaryngology, as well as a Speech-Language Pathologist (SLP), Dentist, Orthodontist, Psychologist, Audiologist, and Geneticist, enabling practitioners to better meet patients' complex needs. As an American Cleft Palate-Craniofacial Association (ACPA)-approved team, we closely adhere to ACPA Standards. Specifically, the ACPA established minimum standards of care for cleft palate and craniofacial teams in the 1990s and adopted its Standards for Cleft and Craniofacial Teams in 2008.[20] Only teams who adhere to these Standards are eligible to be listed by the ACPA as approved teams.

The Standards establish the minimum requirements for multidisciplinary cleft and craniofacial team care. These criteria also afford teams flexibility to organize to best meet the needs of their individual patient populations, geographic locations, resources and treatment environments. We found a wide variation of clinical protocols and approaches to clinic administration in teams across the United States.[4] Combined with the complex, multidisciplinary nature of cleft palate and craniofacial care, the diversity of clinical protocols causes substantial variation in care costs and resource utilization.[4] The estimated total cost for each new case of cleft lip and palate is

roughly $175,000, and clinical protocol options influence cost of care, patient and provider resource utilization, medical outcomes, family-reported QOL, and family-reported satisfaction with outcomes and care. Our team has continually strived for the transition of cleft and craniofacial care to a value-driven, family-centered model of care, in an effort to lower care burden and overall costs of care (Figure 3).

Family-Centered Care

Over the past few decades, medicine has transitioned to a family-centered model (in the context of adult medicine, patient-centered).[14,21,22] For example, the American Academy of Pediatrics (AAP) has established that family-centered care is a critical component of clinical decision-making and stresses that patients and families should have the opportunity to collaborate with providers in all aspects of care.[14] The implementation of family-centered improvements increases patient and family satisfaction and QOL, and decreases burden of care.[23] Moreover, family-centered care improves clinical effectiveness and patient safety across diseases, study designs, population groups, and outcome measures.[14,24] Family-centered care is also associated with decreased healthcare costs and healthcare utilization and improved patient follow-up. [14,21,25,26]

Despite its well-recognized benefits, a family-centered care model has been slow to reach cleft and craniofacial centers. Cleft and craniofacial care has traditionally been driven by underlying diagnosis rather than family needs, values and preferences, and the traditional approach often burdens families unnecessarily.[13,27,28] In contrast, a family-centered model would be carefully designed to meet families' specific needs, concerns, and preferences.[13,28] Over the past four years, in our effort to achieve this improved model of care, we developed and implemented our own plan for team reorganization that aligned with our setting and patient population.[7] We followed a systematic, collaborative approach to accomplish this in an efficient, organized way. As a result of our efforts, we find we are better able to serve our patient population and meet families' unique needs while substantially lowering burden of care. For example, we found our improvements increased our multidisciplinary team clinic capacity by 38% (improving patient access to clinic), decreased the time families spent in clinic and reduced the overall frequency of clinic visits.

Shared Decision Making

Shared Decision Making (SDM) is an important component of family-centered care and is a process by which families and practitioners communicate to reach medical decisions based on the best available evidence and factors specific to the patient.[29-31] The SDM model is most beneficial when there is clinical equipoise between surgical treatment options, ensuring that families are well informed and involved in the treatment process.[29] Our center developed a decision aid for families that present with a child with craniosynostosis.[6] Two surgical treatment methods for single-suture craniosynostosis are open cranial vault remodeling (open repair) and endoscope-assisted craniectomy with use of postoperative molding helmet (endoscopic repair).[32] Both open and endoscopic repair are used in patients under six months of age, but each has specific benefits and challenges. To help families understand the treatment options, we actively use our decision aid, to ensure families understand the diagnosis and select the treatment option that is best for them.

Surgical Innovations to Decrease Treatment Burden

Pediatric plastic surgery care requires providers to consider timing of procedures that will provide the desired outcome. Managing patients with congenital anomalies adds an additional level of complexity, as surgeons must consider the impact of surgical treatment on facial growth. The ultimate goal is to obtain the best outcome for the child, while minimizing the total number of procedures and need for secondary procedures.

For patients with craniosynostosis, we have successfully obtained this goal in partnership with the Department of Neurosurgery at Washington University and St. Louis Children's Hospital. In 2006, we started the minimally invasive endoscopic program for the management of patients with craniosynostosis. Over the past 14 years, we have



Figure 4. Left, child with right unilateral coronal craniosynostosis. Left, 1-year after completion of helmet molding therapy and endoscopic-assisted treatment.



Figure 5. Left, child with a bilateral cleft lip and palate. Right, 5-years after bilateral cleft lip and nose repair.

become a national leader in publishing outcomes that have guided centers around the country. In both the minimally invasive treatment and traditional open treatment of patients with craniosynostosis, we have decreased the need for secondary procedures, need for additional computed tomography imaging (thereby limiting ionizing radiation exposures), while maintaining safety for all patients treated during this time with no episodes of significant morbidity and mortality. [8,9,11,12,33] (Figure 4.)

Patients with cleft lip and palate require four to five surgical procedures during their lifetime (lip repair, palate repair, alveolar bone graft, septorhinoplasty, and possible orthognathic surgery). The most common need for secondary procedures in patients with cleft lip and palate are need for lip or nasal revision due to continued irregularities or hyperresonance resulting from inadequate palatal closure during speech. To help reduce the need for secondary lip or nasal procedures, our team includes pediatric Dentists to perform alveolar molding of the asymmetric maxilla to create symmetry in the bony segments of the maxilla. This allows the surgical team to obtain better symmetry in the soft tissue components of the upper lip and nose.[34] (Figure 5.) This strategy has significantly decreased the need for secondary palatal procedures following primary palate repair. Our group has also shown that our more aggressive dissection and retropositioning of the muscles within the soft palate results in improved speech outcomes relative to the traditional surgically conservative approach utilized by many teams.[10]

Conclusion

Our team has moved toward a family-centered model by modifying care protocols and treatment techniques to decrease cost and treatment burden while customizing care to meet our families' unique and varying needs. Family-centered care is a high-priority focus area in healthcare and

its implementation leads to better outcomes, satisfaction and quality of life for families. Family-centered care also decreases care burden and improves healthcare efficiency, including with regards to resource utilization. Our center's move toward a family centered model has enabled us to best serve families in light of their needs, preferences and values, while simultaneously strengthening our clinical efficiencies and lowering families' burden of care.

References

1. Skladman R, Grames LM, Skolnick G, et al. Adult Quality of Life Post Cleft Palate Repair: A Comparison of Two Techniques. J Craniofac Surg 2017; 28(4): 909-14.
2. Pfeifauf KD, Snyder-Warwick A, Skolnick GB, Naidoo SD, Nissen RJ, Patel KB. Primer on State Statutory Mandates of Third-Party Orthodontic Coverage for Cleft Palate and Craniofacial Care in the United States. Cleft Palate Craniofac J 2018; 55(3): 466-9.
3. Cooper DC, Peterson EC, Grellner CG, et al. Cleft and Craniofacial Multidisciplinary Team Clinic: A Look at Attrition Rates for Patients With Complete Cleft Lip and Palate and Nonsyndromic Single-Suture Craniosynostosis. Cleft Palate Craniofac J 2019; 56(10): 1287-94.
4. Pfeifauf KD, Patel KB, Snyder-Warwick A, Skolnick GB, Scheve S, Naidoo SD. Survey of North American Multidisciplinary Cleft Palate and Craniofacial Team Clinic Administration. Cleft Palate Craniofac J 2019; 56(4): 508-13.
5. Padovano WM, Snyder-Warwick AK, Skolnick GB, et al. Evaluation of Multidisciplinary Team Clinic for Patients With Isolated Cleft Lip. Cleft Palate Craniofac J 2020; 57(7): 900-8.
6. Pfeifauf KD, Said AM, Naidoo SD, et al. Evaluation of the Patient-Practitioner Consultation on Surgical Treatment Options for Patients With Craniosynostosis. J Craniofac Surg 2020; 31(5): 1186-90.
7. Pfeifauf KD, Snyder-Warwick AK, Scheve S, et al. One Multidisciplinary Cleft and Craniofacial Team's Experience in Shifting to Family-Centered Care. Cleft Palate Craniofac J 2020; 57(7): 909-18.
8. Zubovic E, Lapidus JB, Skolnick GB, Naidoo SD, Smyth MD, Patel KB. Cost comparison of surgical management of nonsagittal synostosis: traditional open versus endoscope-assisted techniques. J Neurosurg Pediatr 2020: 1-10.
9. Ha AY, Skolnick GB, Chi D, et al. School-Aged Anthropometric Outcomes After Endoscopic or Open Repair of Metopic Synostosis. Pediatrics 2020; 146(3).
10. Nguyen DC, Patel KB, Skolnick GB, et al. Progressive Tightening of the Levator Veli Palatini Muscle Improves Velopharyngeal Dysfunction in Early Outcomes of Primary Palatoplasty. Plast Reconstr Surg 2015; 136(1): 131-41.
11. Han RH, Nguyen DC, Bruck BS, et al. Characterization of complications associated with open and endoscopic craniosynostosis surgery at a single institution. J Neurosurg Pediatr 2016; 17(3): 361-70.
12. Nguyen DC, Farber SJ, Skolnick GB, et al. One hundred consecutive endoscopic repairs of sagittal craniosynostosis: an evolution in care. J Neurosurg Pediatr 2017; 20(5): 410-8.
13. Abbott MM, Meara JG. Value-based cleft lip-cleft palate care: a progress report. Plast Reconstr Surg 2010; 126(3): 1020-5.
14. Committee On Hospital C, Institute For P, Family-Centered C. Patient- and family-centered care and the pediatrician's role. Pediatrics 2012; 129(2): 394-404.
15. Prakash B. Patient satisfaction. J Cutan Aesthet Surg 2010; 3(3): 151-5.
16. Wong KW, Forrest CR, Goodacre TE, Klassen AF. Measuring outcomes in craniofacial and pediatric plastic surgery. Clin Plast Surg 2013; 40(2): 305-12.
17. French LR, Jackson IT, Melton LJ, 3rd. A population-based study of craniosynostosis. J Clin Epidemiol 1990; 43(1): 69-73.
18. Group IW. Prevalence at birth of cleft lip with or without cleft palate: data from the International Perinatal Database of Typical Oral Clefts (IPDTOC). Cleft Palate Craniofac J 2011; 48(1): 66-81.
19. Horgan JE, Padwa BL, LaBrie RA, Mulliken JB. OMENS-Plus: analysis of craniofacial and extracraniofacial anomalies in hemifacial microsomia. Cleft Palate Craniofac J 1995; 32(5): 405-12.
20. Teams CoAo. CAT Approval Procedures Manual. http://www.acpa-cpf.org/team_care/commission_on_approval_of_teams/cat_approval_procedures_manual/ (accessed July 29, 2016 2016).
21. Bertakis KD, Azari R. Patient-centered care is associated with decreased health care utilization. J Am Board Fam Med 2011; 24(3): 229-39.
22. Medicine Io. Crossing the Quality Chasm: A New Health System for the 21st Century, 2000.
23. Wong Riff KWY, Tsangaris E, Goodacre TEE, et al. What Matters to Patients With Cleft Lip and/or Palate: An International Qualitative Study Informing the Development of the CLEFT-Q. Cleft Palate Craniofac J 2018; 55(3): 442-50.
24. Doyle C, Lennox L, Bell D. A systematic review of evidence on the links between patient experience and clinical safety and effectiveness. BMJ Open 2013; 3(1).
25. Clay AM, Parsh B. Patient- and Family-Centered Care: It's Not Just for Pediatrics Anymore. AMA J Ethics 2016; 18(1): 40-4.
26. Herrin J, Harris KG, Kenward K, Hines S, Joshi MS, Frosch DL. Patient and family engagement: a survey of US hospital practices. BMJ Qual Saf 2016; 25(3): 182-9.
27. Association ACP-C. Standards of Team Care for Cleft Palate and Craniofacial Teams. http://www.acpa-cpf.org/team_care/standards/ (accessed May 23, 2017.
28. Long R. Understanding the Burden of Care.
29. Doumit GD, Papay FA, Moores N, Zins JE. Management of sagittal synostosis: a solution to equipoise. J Craniofac Surg 2014; 25(4): 1260-5.
30. Geiger F, Liethmann K, Hoffmann F, Paschedag J, Kasper J. Investigating a training supporting Shared Decision Making (IT'S SDM 2011): study protocol for a randomized controlled trial. Trials 2011; 12: 232.
31. Gartner FR, Bomhof-Roordink H, Smith IP, Scholl I, Stiggelbout AM, Pieterse AH. The quality of instruments to assess the process of shared decision making: A systematic review. PLoS One 2018; 13(2): e0191747.
32. Renier D, Marchac D. Craniofacial surgery for craniosynostosis: functional and morphological results. Ann Acad Med Singapore 1988; 17(3): 415-26.
33. Parikh RP, Snyder-Warwick A, Naidoo S, Skolnick GB, Patel KB. Impact of an Event Reporting System on Resident Complication Reporting in Plastic Surgery Training: Addressing an ACGME and Plastic Surgery Milestone Project Core Competency. Plast Reconstr Surg 2017; 140(5): 736e-45e.
34. Patel KB, Mulliken JB. Correction of the vestibular web during primary repair of unilateral cleft lip. Plast Reconstr Surg 2014; 134(4): 600e-7e.

Disclosure

None reported. **MM**

Cutting Edge Craniomaxillofacial Trauma Reconstruction

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Future directions for technology and craniofacial surgery entail achieving greater precision and accuracy in the actual surgical procedure.



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Abstract

Facial injuries remain a significant source of morbidity in trauma. Due to the variety and unpredictable patterns of injuries associated with either blunt or ballistic mechanisms, advanced diagnostic imaging and complex management options are necessary. Multidisciplinary collaboration is essential to optimize the care of craniomaxillofacial trauma.

Introduction

Facial trauma can encompass skin, muscles, nerves, blood vessels, and bones. There can be a combination of those structures and range from simple to complex. About one-third of facial fractures have concomitant soft tissue trauma. The precise incidence and epidemiology of facial trauma is dependent on demographic factors such as socioeconomic status, age, gender, and mechanism of injury. Furthermore, it can be confounded by underreporting and treatment of these injuries. Facial fractures alone presenting to the emergency room is around half-a-million per year in the United States.[1] We know that these types of injuries occur more in young males than females, and are most frequently the result of accidents, assaults, falls, and motor vehicle collisions (MVC).[2] Despite mandatory implementation of airbags and seatbelts, MVCs remain the most significant cause of facial trauma all over the world. Facial trauma needs to be performed in a holistic and multidisciplinary setting as there can be multiple associated injuries. Fractures of the skull, intracranial injuries (10%), cervical spine injury, and upper extremity injuries are not uncommon.[1,3] A collaboration between plastic surgery and the multiple surgical, medical and radiologic subspecialties is critical to patient care and recovery.

Mechanisms of Facial Injury

Two broad categories of facial injury mechanisms include blunt versus ballistic. Two case examples are presented to compare and contrast what may be required to manage these types of trauma.

Case 1

A young male was assaulted with a fist resulting in cheek depression. Additionally, he felt that his teeth did not fit together appropriately. After a thorough evaluation by emergency medicine, trauma surgery, plastic surgery, and ophthalmology, the patient underwent a craniomaxillofacial CT scan. The facial bones are organized into units that can break in relatively predictable patterns when subjected to blunt forces (e.g., falls, assault, MVC). The images were 3D reconstructed revealing displaced fractures to his

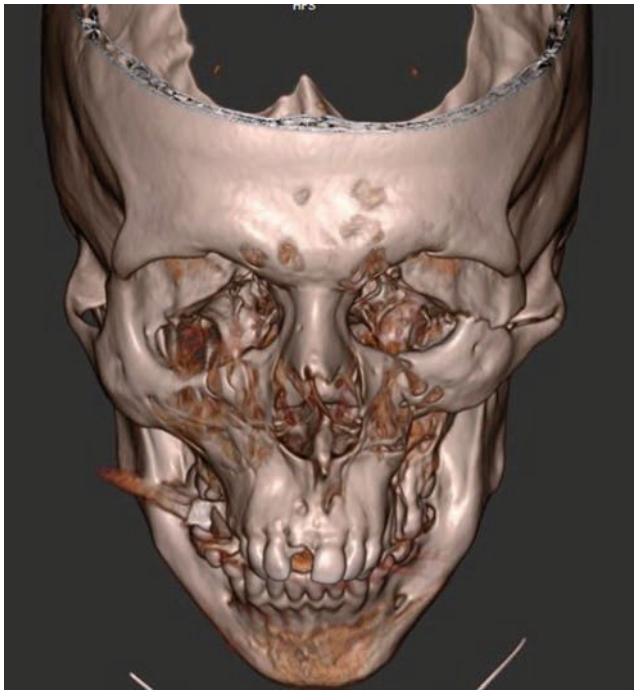


Figure 1. A three-dimensional reconstructed image of the craniomaxillofacial CT scan showing left orbital floor fracture zygomatico-maxillary-complex fracture.



Figure 2. Intraoperative use of the O-arm CT scanner (Medtronic. Minneapolis, MN). A craniomaxillofacial CT scan takes about two minutes and allows for immediate feedback of fracture reduction and hardware placement.



Figure 3. A three-dimensional reconstructed image of the intra-operative CT scan showing adequate fracture reduction and placement of left orbital floor implant and hardware fixation.

left orbital floor and a depressed zygomatico-maxillary-complex (ZMC) fracture (Figure 1). His injuries required surgery, but he had no other injuries and was discharged home safely on a soft diet and did not require any antibiotics.[4] Several days later, the patient underwent operative reduction and internal fixation with plates and screws of his orbit and ZMC fractures. Optimal reduction of these fractures is essential to vision, facial function, and form. To aid with this three-dimensional process, we utilize an intra-operative O-arm (Medtronic. Minneapolis, MN). CT scan is used to obtain images after the surgery but before the patient is woken up from surgery (Figure 2). It allows us to confirm the places of the implants, plates, and screws and the opportunity to re-adjust as necessary during a single operation. Figure 3 shows the 3D reconstructed picture of the intra-operative CT scan after fracture reduction and fixation with orbital floor implant, plates and screws (Stryker. Kalamazoo, MI).

The use of imaging technology in evaluating, planning, and management of complex facial injuries is evolving into the standard. Pre-operative CT scan are the gold standard for diagnosing facial fractures and are widely used in the post-operative setting to confirm repair.[5-7] With advancements in equipment,

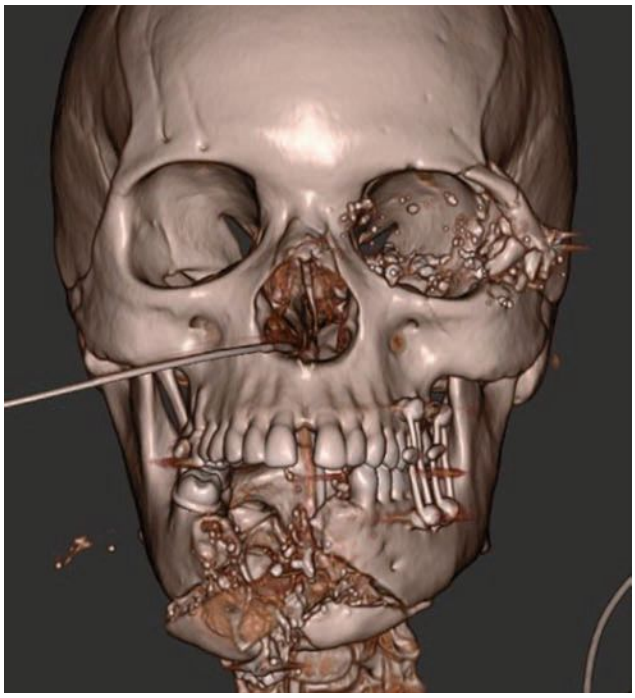


Figure 4. A three-dimensional reconstructed image of the pre-operative CT scan showing displace and comminuted fracture of the anterior mandible after a ballistic injury.

CT scanners are now more portable and less costly and produce high-quality images. Intraoperative CT is a powerful tool to evaluating bony anatomy and has been used by surgeons to assess the skull, skull base, and spine, and is becoming increasingly accessible.[8] The literature supports the routine use of intraoperative CT for orbital, pan-facial, and complex ZMC, LeFort, and naso-orbital-ethmoidal fractures.[9]

Case 2

A young woman suffered a gunshot wound to the mandible that resulted in a severely displaced and comminuted fracture. The pre-operative 3D CT reconstruction showed multiple fragments of her anterior mandible (Figure 4). After being deemed safe for surgery by multiple surgical specialists, the patient was taken to the operating room for initial debridement of devitalized tissue and repair of as many disrupted structures as possible. At the end of this surgery, it was apparent that standard bony fracture reduction and fixation with plates and screws would not be feasible or optimal for patient recovery.

A team consisting of industry (Stryker. Kalamazoo, MI), engineers (3D Systems. Rock Hill, SC) and plastic surgeons with training in craniofacial surgery and microsurgical reconstructive surgery was assembled

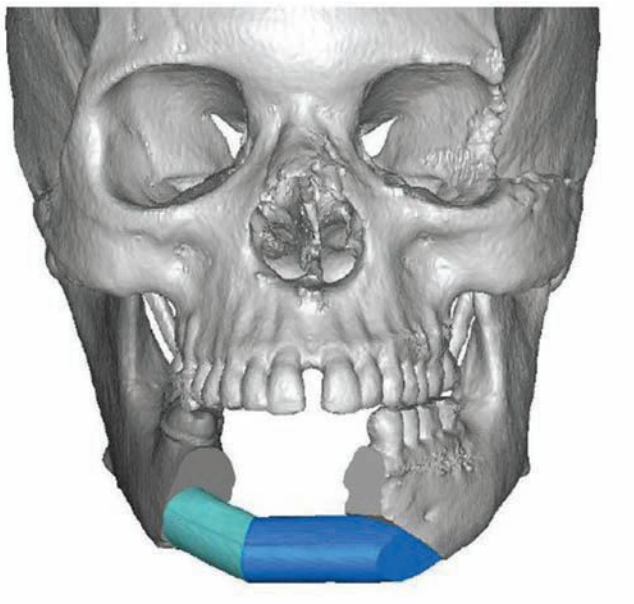


Figure 5. Virtual surgical planning rendering by 3D Systems (Rock Hill, SC) showing vascularized free fibular bone flap in reconstruction of missing mandible.

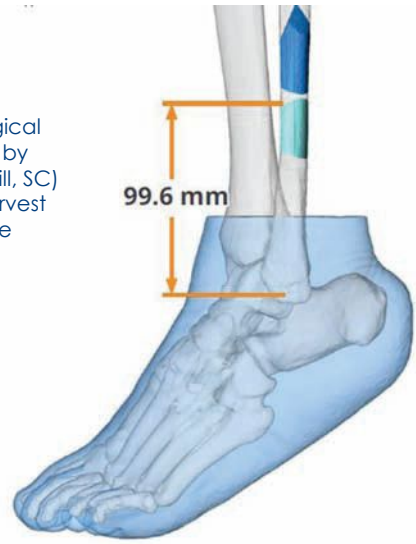


Figure 6. Virtual surgical planning rendering by 3D Systems (Rock Hill, SC) showing precise harvest and bony cuts in the fibula.

to tackle this problem. Through virtual surgical planning (VSP) using pre-operative CT scans of the face and lower extremities, a segment of the patient's fibula was shaped into a new mandible to reconstruct what she was missing (Figure 5). In a subsequent operation, this bone from her leg was brought with its blood supply and connected to her facial blood vessels as a vascularized free-fibular flap (Figure 6). Once this was accomplished, the patient had a complete mandible with which she could resume eating and speaking normally again without any significant impact to her ability to walk.

Ballistic injury to the face presents a unique and challenging dilemma for the surgeon. There can be significant and unpredictable disruption of normal anatomy planes of soft tissue and bone. Much of what we know about management of ballistic and blast injuries come from military combat. Identifying the problem and restoring form and function with good support structures and healthy soft tissue coverage as close to the time of injury are the core principles.

Sequencing and execution of the different operations by a multidisciplinary team in craniofacial microsurgical reconstruction following trauma is complex. These cases test the surgeon's technical and creativity abilities to optimize functional and aesthetic outcomes. A wide variety of free flap options exist for reconstructing facial defects, each with their own unique strengths and limitations. This patient with a large mandibular defect was reconstructed with a free fibular flap. Hidalgo first described this flap in mandibular reconstruction over three decades ago and it still remains one of the most commonly used for its reliability and versatility.[10] The free fibular flap provides quality bone stock and can be harvested with different tissues (e.g. muscle, fascia, skin). It is limited by the patient's own bone length, pedicle length, and potential for leg weakness and ankle instability.[11]

Computer-assisted surgery started in the 1980s and has since become increasingly integrated into complex craniomaxillofacial reconstruction.[12,13] Virtual surgical 3D simulation and planning has many advantages (i.e. analysis, planning, virtual surgery, printout of guides or implants, verification of actual to planned results).[14] Despite these, it should be stressed that technology cannot replace a surgeon's clinical judgement or technique.

Conclusion

Future directions for technology and craniofacial surgery entail achieving greater precision and accuracy in the actual surgical procedure. Collaboration between experts within plastic surgery provides greater breadth of experience and better care and outcomes for patients.

References

1. Allareddy V, Allareddy V, Nalliah RP. Epidemiology of facial fracture injuries. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2011;69(10):2613-2618.
2. VandeGriend ZP, Hashemi A, Shkoukani M. Changing trends in adult facial trauma epidemiology. The Journal of craniofacial surgery. 2015;26(1):108-112.
3. Mithani SK, St-Hilaire H, Brooke BS, Smith IM, Bluebond-Langner R, Rodriguez ED. Predictable patterns of intracranial and cervical spine injury in craniomaxillofacial trauma: analysis of 4786 patients. Plastic and reconstructive surgery. 2009;123(4):1293-1301.
4. Linkugel AD, Odom EB, Bavolek RA, Snyder-Warwick AK, Patel KB. Systemic Preoperative Antibiotics with Mandible Fractures: Are They Indicated at the Time of Injury? Craniomaxillofac Trauma Reconstr. 2018;11(1):35-40.
5. Boyette JR, Pemberton JD, Bonilla-Velez J. Management of orbital fractures: challenges and solutions. Clin Ophthalmol. 2015;9:2127-2137.
6. Marinho RO, Freire-Maia B. Management of fractures of the zygomaticomaxillary complex. Oral and maxillofacial surgery clinics of North America. 2013;25(4):617-636.
7. Manson PN, Markowitz B, Mirvis S, Dunham M, Yaremchuk M. Toward CT-based facial fracture treatment. Plastic and reconstructive surgery. 1990;85(2):202-212; discussion 213-204.
8. Schichor C, Terpolilli N, Thorsteinsdottir J, Tonn JC. Intraoperative Computed Tomography in Cranial Neurosurgery. Neurosurgery clinics of North America. 2017;28(4):595-602.
9. Cuddy K, Khatib B, Bell RB, et al. Use of Intraoperative Computed Tomography in Craniomaxillofacial Trauma Surgery. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2018;76(5):1016-1025.
10. Hidalgo DA. Fibula free flap: a new method of mandible reconstruction. Plastic and reconstructive surgery. 1989;84(1):71-79.
11. Momoh AO, Yu P, Skoracki RJ, Liu S, Feng L, Hanasono MM. A prospective cohort study of fibula free flap donor-site morbidity in 157 consecutive patients. Plastic and reconstructive surgery. 2011;128(3):714-720.
12. Vannier MW, Marsh JL, Warren JO. Three dimensional CT reconstruction images for craniofacial surgical planning and evaluation. Radiology. 1984;150(1):179-184.
13. Toth BA, Ellis DS, Stewart WB. Computer-designed prostheses for orbitocranial reconstruction. Plastic and reconstructive surgery. 1988;81(3):315-324.
14. Steinbacher DM. Three-Dimensional Analysis and Surgical Planning in Craniomaxillofacial Surgery. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2015;73(12 Suppl):S40-56.

Disclosure

None reported. **MM**

State-of-the-Art Lymphedema Surgery Treatment Program

by Rachel Skladman, MD, Rachel A. Anolik, MD & Justin M. Sacks, MD, MBA

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Improving the quality of life for patients with lymphedema is central to our goal. Clinical and basic science research focused on the pathophysiology of lymphedema propels our mission forward.



Rachel Skladman, MD, Rachel A. Anolik, MD, (above), and **Justin M. Sacks, MD, MBA, FACS**, are in the Division of Plastic and Reconstructive Surgery, Washington University, St. Louis, Missouri.

Abstract

The purpose of this article is to describe the multidisciplinary lymphedema surgery treatment program at Washington University in St. Louis. In this article, we discuss our collaboration with colleagues in medicine and therapy for conservative management and lymphedema staging. We describe our preferred imaging modalities for diagnosis, staging, and surgical treatment. Finally, we provide an overview of the surgical procedures we perform and our surgical treatment algorithm.

Introduction

Lymphedema is a progressive, debilitating condition that affects up to 250 million people worldwide.[1] Lymphedema is characterized by an accumulation of fat or fluid—most commonly in the upper or lower extremity—that results in progressive swelling, pain, numbness and tingling.[1,2] Eventually, patients develop hypertrophy, acanthosis, and hyperkeratosis that results in skin breakdown.[2] A feared consequence of lymphedema is the development of cellulitis, lymphangitis, and lymphatic malignancies.[2] To prevent such complications, clinicians aim to diagnose and treat lymphedema at its early stages. The International Society of Lymphology staging guidelines are provided in Figure 1.

Lymph fluid flows throughout the network of lymphatic channels, moving by contraction of skeletal muscles. An insult to the transport of lymphatic fluid results in the accumulation of protein-rich fluid, excess water, blood cells, and cellular products.[3] As flow of lymphatic fluid becomes impaired, the remaining lymphatic vessels dilate and valves fail to maintain unidirectional flow of fluid. Persistent lymphatic stasis results in the accumulation of proteinaceous fluid and induces inflammation—causing cellular proliferation, deposition of fat, and fibrosis of lymphatic vessels.[3,4] Lymphedema results when the lymphatic pumping potential becomes overwhelmed, resulting in the accumulation of fluid in the subcutaneous tissue.[3]

Etiology

Causes of lymphedema can be divided into two groups: primary and secondary lymphedema. Primary lymphedema is caused by a developmental abnormality and may present at birth, during adolescence, or during adulthood. A genetic mutation is implicated in 30% of patients, most commonly the vascular endothelial growth factor (VEGF) signaling pathway is implicated.[5]

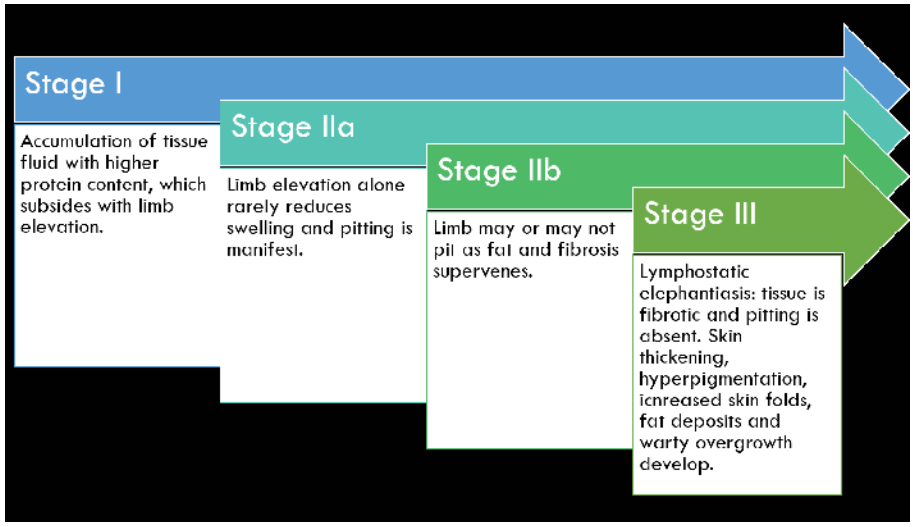


Figure 1: International Society of Lymphology Lymphedema Staging Guidelines



Figure 2: Presenting Symptoms of Lymphedema

However, most cases of lymphedema amenable to surgical management are caused by an insult to the lymphatic system which may be infectious, cancerous, or traumatic. In the developing world, secondary lymphedema is primarily caused by infection with microfilaria *Wuchereria bancrofti*, which affects up to 300 million people world-wide.[3,5] In the Western world, lymphedema is iatrogenic, most commonly secondary to the treatment of breast, gynecologic, and skin cancer.[5] Most commonly, lymphedema results secondary to breast cancer. The risk of breast cancer-related lymphedema (BCRL) increases with axillary lymph node dissection, adjuvant radiotherapy, and regional nodal irradiation.[5] The combination of lymphadenectomy and post-radiation scarring damages the lymphatic system and results in lymphadematous swelling of the upper or lower extremity.[6] The incidence of BCRL after mastectomy ranges from 24%-49% and from 4%-28% after lumpectomy.[4] Historically 20%-50% of patients undergoing axillary lymph node dissection developed secondary lymphedema, but this number has decreased to 5%-7% with the advent of sentinel lymph node biopsy.[3]

As a result of fluid accumulation patients experience heaviness, numbness, tingling, and pain of the extremity (Figure 2).[3,7] Lymphedema is associated with a decreased quality of life, embarrassment due to the cosmetic appearance of the affected limb, and financial burden. Patients report a decreased ability to perform activities of daily living and maintain employment.[3,8,9]

Multidisciplinary Lymphatic Disease Diagnosis

Surgical planning for the management of lymphatic disorders requires advanced imaging techniques for lymphatic mapping. Historically, the gold standard for the diagnosis of lymphedema was lymphoscintigraphy.[10] First introduced in 1953, it has been the primary imaging modality used to definitively diagnose patients with extremity lymphedema. Lymphoscintigraphy uses radioactive contrast, Technetium-99m sulfur-colloid, to provide images of the lymphatic system and assess lymphatic flow. The

colloid tracer is injected into the first webspace of the hands or feet; is taken up by lymph nodes; and then enters the lymph ducts. A gamma scanner is used to follow the movement of radioactive material. The amount of radiotracer absorbed throughout the lymphatic system indicates the function of lymphatic channels and drainage of lymph to nodal basins. Lymphoscintigraphy assesses the speed of lymph node drainage (transport index) to semi-quantitatively understand the severity of lymphedema and identify lymphatic channel blockage. The measurement is based on the speed of uptake and time to reach the lymph nodal basin. Delayed uptake indicates partial blockage; absent uptake indicates complete blockage of lymphatic flow.[11] Lymphoscintigraphy does not provide a dynamic visualization of lymphatic vessels and lymph nodes. Due to the slow movement and absorption of colloid, lymphoscintigraphy has limited temporal and spatial resolution.[12, 13]

In recent years, Magnetic Resonance Imaging (MRI) has emerged as a new method for the diagnosis of lymphatic diseases due to its high sensitivity for depiction of abnormal lymph vessels without the use of a radioactive isotope.[13,14] At our institution, Magnetic Resonance Lymphangiography (MRL), which uses Gd- BOPTA (gadolinium benzyloxypropionictetraacetate) has emerged as the preferred imaging modality for the visualization and diagnosis of lymphatic disorders. This modality allows for the dynamic assessment of lymphatic architecture and drainage. Three-dimensional visualization of lymphatic channels assesses for morphological abnormalities. Due to the specificity of gadolinium contrast for the lymphatic system, it is possible to visualize finely detailed morphological abnormalities in lymphatic vessels—even for vessels as small as 1mm. MRL is able to visualize distinct intranodal structural pathology and allow for real-time lymph flow monitoring. The high spatial resolution of MRL has profound implications for the surgical management of lymphedema: MRL can localize the damage to the lymphatic system so that the appropriate vessels for lymphovenous anastomosis can be determined preoperatively. The 3D assessment of lymph vessels helps guide intraoperative lymph node and vessel transplantation.[14] Volumetric assessment of the limb and the 3D depiction of the relationship between lymphatic vessels and the venous system is a useful guide both pre- and intraoperatively. Additional information on the severity of lymphedema, degree of fat accumulation, and volume of muscle is also beneficial for surgical planning.[14] MLR demonstrates extra-lymphatic abnormalities, including: the location of edema, deposition of fat, and tissue fibrosis to distinguish lymphedema from other types of edema. The higher spatial resolution; depiction of structurally abnormal lymphatic channels; 3D images; and absence of ionizing radiation have positively impacted our clinical practice and microsurgical outcomes.

We use fluorescent lymphangiography for intraoperative lymphatic mapping. Indocyanine Green (ICG) is injected into the web space of the digits. Fluorescence lymphangiography detects the near-infrared light emitted by the indocyanine green dye which demonstrates the path of lymphatic vessels.[15,16] Only functioning lymphatics take up ICG which allows clinicians to distinguish functioning lymphatics from non-functioning lymphatics. ICG can demonstrate disruption of lymphatic flow, tortuous abnormal lymphatics, and dermal backflow— which is diffuse leakage of dye into the interstitium as a result of lymphatic vessel abnormality. The subdermal pattern of ICG uptake correlates the degree of dilatation and fibrosis in the lymphatics.[6] Most commonly, ICG is used for evaluating lymphatic transport, the presence of functional lymphatics, and the distribution of dermal backflow.[5,15,16] Intraoperative ICG allows surgeons to make incisions precisely over the functional lymphatic vessels for the lymphovenous anastomosis. Identifying the appropriate functioning lymphatic vessel for bypass is the step most important for success of the operation.[15,16] The use of ICG has been shown to reduce operative times and improve outcomes while simultaneously allowing for the accurate assessment of disease severity and ISL staging.[15] ICG findings positively correlate with lymphoscintigraphy when used to determine disease severity, while being a less invasive and lower cost test.

We obtain MRI lymphangiography preoperatively for disease staging and treatment planning. We use the ICG intra-operatively to

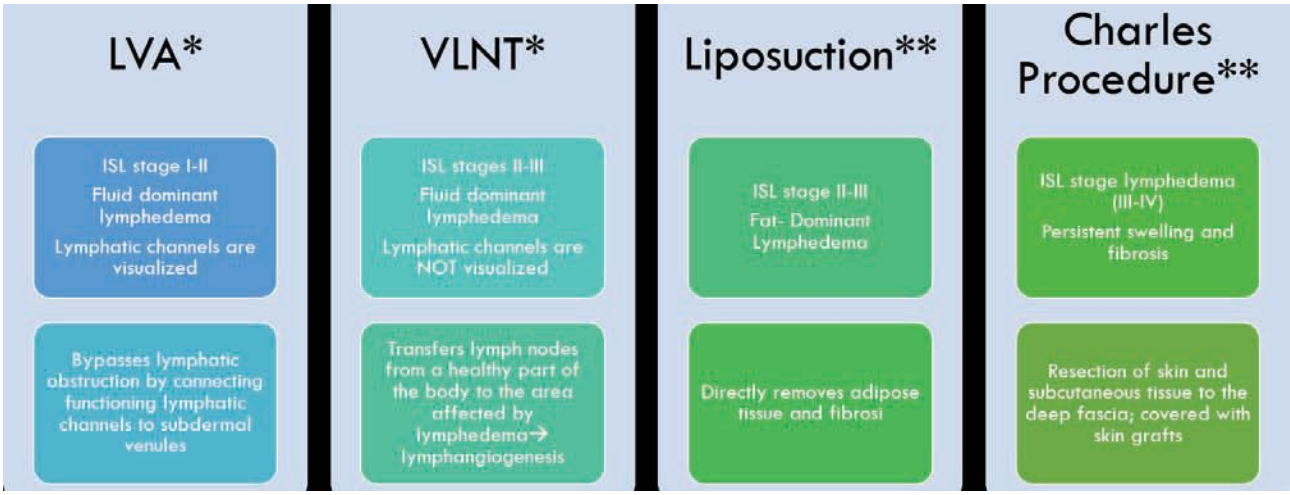


Figure 3: Brief Surgical Guide of Operative Procedures

identify dermal lymphatics for lymphovenous anastomosis. In the operating room, it is our practice to confer all ICG findings with the MRI lymphangiography such that all channels identified on MRI assessment are also marked out with ICG before incision.

We have partnered with lymphedema therapists in both the physical and occupational therapy department for preoperative optimization and disease staging. Our therapists perform circumferential measurements to compare volume differences between the affected and unaffected limbs and monitor the progression of symptoms over time.

We have begun to use bioimpedance spectroscopy using the SOZO® bioimpedance spectroscopy device (ImpediMed) in the assessment of lymphedema. The Sozo device produces an L-Dex score in 30 seconds by passing a small, painless electrical current through the limb. The amount of interstitial fluid is inversely proportional to the resistance in the circuit. As lymphedema develops, the amount of fluid will increase, making it easier for the signal to travel through the extremity. The L-Dex score represents the difference in extracellular fluid volume in the diseased limb compared to an unaffected limb. We obtain L- Dex scores at baseline at each postoperative visit to monitor changes to lymphedema. The L-dex score may be the most sensitive test to detect lymphedema in the earliest stages, even before symptoms become apparent.[17]

Multidisciplinary Management of Lymphatic Diseases

Prior to surgical workup, our patients undergo medical and therapeutic optimization of their lymphedema symptoms as surgical results are optimized when combined with therapy. Decongestive treatment, performed by our Certified Lymphedema Therapists (CLTs), is commonly recommended for patients with ISL stages I-II lymphedema. Our CLTs are specifically trained in manual lymphatic drainage to manually move lymph fluid away from the obstructed portion of the limb towards the center of the body. Concurrently, multilayer low-stretch bandages are applied to the limb to prevent refilling of the evacuated fluid. Our therapists work with patients to develop specific exercise regiments to restore flexibility and strength which improves lymphatic drainage through muscle contraction. Patients are encouraged to use a lymphatic drainage pump which forces excess lymph fluid out of the affected limb and into the central body circulation. We work with patients to establish a well-balanced diet and control body weight for symptom management.

Surgical Treatment

Historically, lymphatic surgery was reserved for the most severe cases. However, over the past several decades, "supermicrosurgery" on lymphatic vessels has allowed for the development of techniques to treat lymphedema in the early stages.[3] Surgical management of lymphedema is divided into

physiologic procedures and debulking or reductive procedures. Both procedures aim to restore lymphatic flow. Physiologic procedures rewire the lymphatic system to restore lymphatic flow and improve the clearance of excess lymphatic fluid. Excisional procedures focus on removing diseased tissue. Physiologic procedures are indicated for early stages of lymphedema; these procedures restore anterograde flow of lymphatic fluid. Lymphovenous anastomosis (LVA) and vascularized lymph node transplant (VLNT) are common physiologic procedures. Debulking procedures are indicated in later stages of lymphedema; these procedures remove fibro-fatty tissue. A brief surgical guide of the procedures we offer is provided in Figure 3.

Lymphovenous anastomosis was originally pioneered in 1952 by Sherman and colleagues and subsequently modified by Koshima, who introduced supermicrosurgical LVA which utilizes lymphatics and venules less than 0.8mm in diameter.[11] This operative technique is a bypass operation that redirects the flow of lymphatic fluid into the venous circulation.[2] The lymphatic channel is connected directly to the venous system for venous drainage, bypassing the area of obstruction. This procedure is indicated for patients who still have functionality of the lymphatic system as demonstrated by ICG lymphography. Flow of lymphatic fluid is only partially obstructed. ICG is used to visualize the flow of dye from the distal extremity toward the trunk. Using a near-infrared camera, the course of functioning lymphatic vessels is traced by following uptake of the dye and correlated with the findings of MRL. ICG and MRL is used to visualize the most functional lymphatic channels and these are chosen for anastomoses. Once optimal vessels are identified, short transverse incisions are planned over the marked channels. Isosulfan blue dye is injected subcutaneously for improved visualization of the lymphatic during anastomosis. Once a lymphatic is identified, a subdermal venule of similar caliber is chosen (between 0.3mm and 0.8 mm in diameter).[11] The anastomosis between the lymphatic and vein is created end-to-end or end-to-side using 11-0 or 12-0 nylon suture.[2] Once the anastomosis has been created, patency can be assessed by visualizing the prompt, anterograde flow of blue-stained fluid across the suture line. Increased pressure in the lymphatic vessel forces fluid into the venous system. Increasing the number of LVAs created maximizes symptom relief.[2] This procedure carries high therapeutic benefits for patients with ISL stage I-II lymphedema with minimal morbidity. It is an outpatient procedure that utilizes minimal incisions and absent blood loss.

For patients with a more advanced stage of disease (ISL stages II-III), vascularized lymph node transfer (VLNT) is recommended. During this procedure, healthy lymph nodes, along with their vascular supply, are transferred to the affected area. Care is taken to maintain vascularity of the lymph nodes for greater improvement of edema and better lymphatic function. The newly transplanted lymph nodes act as a sponge to absorb lymphatic fluid and direct it into the vascular system. These lymph nodes secrete growth factors (VEGF) that stimulate the generation of new lymphatic pathways and channels at the site of disease.[3] Vascularized lymph node transfer is performed for patients who have suffered from damage to the lymph node basins secondary to lymphadenectomy or radiation therapy.[2] As a result, patients have complete blockage of lymphatic fluid at the site of insult.

Vascularized lymph node transfer typically utilizes groin, thoracic, submental and supraclavicular node, though recently mesenteric lymph node transfer and omental transfer has been reported.[11] Most commonly, supraclavicular lymph nodes based off the transverse cervical artery and vein and the superficial inguinal lymph nodes supplied by the superficial circumflex iliac artery are used.[2] Recently, Dayan introduced reverse lymphatic mapping to aid in the identification of donor nodes from the groin and axilla that are expandable and whose harvest will not cause subsequent lymphedema at the donor-site.[18] This involves injecting technitium into the web spaces of the hand or foot and identifying nodes using the gamma probe.[3,11] Furthermore, technical modifications for lymph node placement have evolved to improve post-operative outcomes. Since upper extremity lymphedema occurs as a result of previous surgery to the axilla with or without radiation, wide excision of scar tissue, to

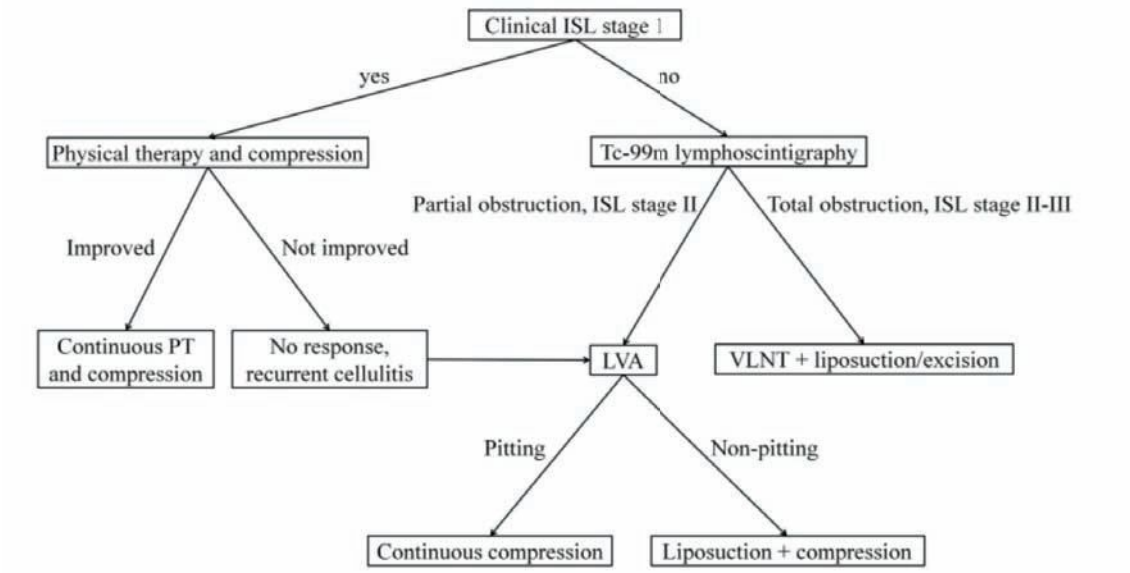


Figure 4: Washington University in St. Louis Lymphedema Surgery Algorithm ISL, International Society of Lymphology; LVA, lymphovenous anastomosis; PT, physical therapy; VLNT, vascularized lymph node transfer

prevent impingement on surrounding vasculature, is advocated. This will create optimal conditions for lymphangiogenesis and aid in creating a patent connection between the nodes and the recipient bed, such as the thoracodorsal artery.[11]

For lymphedema of the lower extremity, the ankle and the groin are the most common recipient sites. As in the axilla, it is important to remove scar tissue in the groin caused by previous surgery and radiation. The superficial circumflex iliac vessels are used for the anastomosis. When lymphedema occurs distal to the groin, the ankle is the optimal recipient site due to its dependent position. Gravitational forces pull fluid into the ankle, so lymph nodes in this region can facilitate drainage. When the ankle is used for anastomosis the anterior tibialis or dorsalis pedis arteries are often used.[11] For optimal surgical outcomes, when performing, VLNT flap inset, minimal tension should be used.[11]

VLNT is an effective procedure for patients with total occlusion of lymph channels based on lymphoscintigraphy; ISL stage II lymphedema, history of cellulitis; and for patients who have failed 12 months of conservative therapy.[11] For these patients, results have shown up to 30-60% reduction of excess volume when compared with the unaffected limb.[2,11] In a systematic review that captured 305 patients, almost 50% of patients did not require postoperative compression garments.[3]

Finally, for patients with severe lymphedema, ISL stage III, excisional treatment is recommended. Excisional treatment can be performed with liposuction, during which tissue is removed by vacuum aspiration. Liposuction for the treatment of lymphedema is most useful in addressing large adipose tissue deposits and volume excess of upwards of 600 ml. Liposuction results in immediate reduction in volume and lymphatic pressure of the extremity and improved lymphatic flow. All patients must wear a compressive garment immediately after the procedure and are encouraged to wear compression garments indefinitely. One study has found that liposuction achieved an average excess volume reduction of 96.6% and patients report an immediate improvement in well-being and quality of life.[3,19]

The Charles procedure is performed at our institution for patients with elephantiasis and significant fibrosis of the extremities. This procedure involves the radical excision of skin and subcutaneous tissue down to muscle fascia or underlying epimysium which is subsequently covered by skin grafts. This is an ablative procedure that disrupts remaining lymphatic function and results in ulceration, hyperkeratosis of overlying skin.[2,3] Due to the risk of complications, this approach is reserved for very severe cases that are not amenable to therapy or any other approach.

Patients stay in the Intensive Care Unit postoperatively.

Surgical modifications have evolved to combine the procedures mentioned above. For patients with BCRL it is possible to perform LVA at the time of microvascular free tissue breast reconstruction. If a lymph node transfer is required, we recommend performing this in a subsequent procedure such that the breast reconstruction is complete and the thoracodorsal vessels can be used for the VLNT without concern.[2] In our practice, the senior author of this report has experience harvesting lower abdominal flaps with the attached inguinal lymph nodes for the treatment of lymphedema among patients undergoing concurrent delayed breast reconstruction. The thoracodorsal vessels are used as recipients in the axilla.[11]

Conclusion

Our state-of-the-art multidisciplinary lymphedema treatment program offers conservative, medical, and therapeutic management. Our partners in therapy are crucial for baseline lymphedema measurements, preoperative optimization, postoperative therapy, and limb volume surveillance. We have developed an imaging protocol that utilizes MRI lymphangiography to stage lymphedema and guide surgical planning. ICG is used for intraoperative lymph channel identification. Patients with ISL stage I-II lymphedema are offered LVA, and patients with more advanced stages of disease are offered VLNT. Our surgical algorithm is provided in Figure 4. Improving the quality of life for patients with lymphedema is central to our goal. Clinical and basic science research focused on the pathophysiology of lymphedema propels our mission forward. Though conservative management with therapy is our first-line treatment, surgical management offers an exciting and innovative way to approach an oftentimes difficult and recalcitrant problem.

References

1. Chang DW, Suami H, Skoracki R. A Prospective Analysis of 100 Consecutive Lymphovenous Bypass Cases for Treatment of Extremity Lymphedema. Plast Reconstr Surg. 2013;132(5):1305-1314. doi:10.1097/prs.0b013e3182a4d626
2. Kung TA, Champaneria MC, Maki JH, Neligan PC. Current Concepts in the Surgical Management of Lymphedema. Plast Reconstr Surg. 2017;139(4):1003e-1013e. doi:10.1097/prs.0000000000003218
3. Kokosis G, Darrach H, Sacks JM. Lymphedema. In: Cameron J, Cameron A. Current Surgical Therapy. 13th Ed. Elsevier; 2019: 1097-1101.
4. Abdelfattah U, Jaimez PM, Clavero JA, Bellantonio V, Pons G, Masia J. Correlation between superficial and deep lymphatic systems using magnetic resonance lymphangiography in breast cancer-related lymphedema: clinical implications. J Plastic Reconstr Aesthetic Surg. 2019;73(6):1018-1024. doi:10.1016/j.bjps.2019.11.053
5. Schaverien MV, Coroneos CJ. Surgical Treatment of Lymphedema. Plast Reconstr Surg. 2019;144(3):738-758. doi:10.1097/prs.0000000000005993
6. Neligan PC, Kung TA, Maki JH. MR lymphangiography in the treatment of lymphedema. J Surg Oncol. 2017;115(1):18-22. doi:10.1002/jso.24337
7. Johnson AR, Fleishman A, Tran BNN, et al. Developing a Lymphatic Surgery Program: A First-Year Review. Plast Reconstr Surg. 2019;144(6):975e-985e. doi:10.1097/prs.0000000000006223
8. Dean LT, Moss SL, Ransome Y, et al. "It still affects our economic situation": long-term economic burden of breast cancer and lymphedema. Support Care Cancer. 2019;27(5):1697-1708. doi:10.1007/s00520-018-4418-4
9. Darrach H, Yesantharao PS, Persing S, et al. Surgical versus Nonsurgical Management of Postmastectomy Lymphedema: A Prospective Quality of Life Investigation. J Reconstr Microsurg. 2020;36(08):606-615. doi:10.1055/s-0040-1713667
10. Akita S, Mitsukawa N, Kazama T, et al. Comparison of lymphoscintigraphy and indocyanine green lymphography for the diagnosis of extremity lymphoedema. J Plastic Reconstr Aesthetic Surg. 2013;66(6):792-798. doi:10.1016/j.bjps.2013.02.023
11. Chang DW, Masia J, Garza R, et al. Lymphedema: Surgical and Medical Therapy. Plast Reconstr Surg. 2016;138(3S):209S-218S. doi:10.1097/prs.0000000000002683
12. Notohamiprodjo M, Weiss M, Baumeister RG, Sommer WH, Helck A, Crispin A, Reiser MF, Herrmann KA. MR lymphangiography at 3.0 T: correlation with lymphoscintigraphy. Radiology. 2012 Jul;264(1):78-87. doi: 10.1148/radiol.12110229. Epub 2012 Apr 20. PMID: 22523325.
13. Liu N, Zhang Y. Magnetic Resonance Lymphangiography for the Study of Lymphatic System in Lymphedema. J Reconstr Microsurg. 2014;32(01):066-071. doi:10.1055/s-0034-1384213
14. Bae JS, Yoo R-E, Choi SH, et al. Evaluation of lymphedema in upper extremities by MR lymphangiography: Comparison with lymphoscintigraphy. Magn Reson Imaging. 2018;49:63-70. doi:10.1016/j.mri.2017.12.024
15. Chang DW, Suami H, Skoracki R. A Prospective Analysis of 100 Consecutive Lymphovenous Bypass Cases for Treatment of Extremity Lymphedema. Plast Reconstr Surg. 2013;132(5):1305-1314. doi:10.1097/prs.0b013e3182a4d626
16. Akita S, Nakamura R, Yamamoto N, et al. Early Detection of Lymphatic Disorder and Treatment for Lymphedema following Breast Cancer. Plast Reconstr Surg. 2016;138(2):192e-202e. doi:10.1097/prs.0000000000002337
17. L-Dex Score. Impedimed website. Updated 2020. Accessed November 10,2020. https://www.impedimed.com/healthcare/l-dex-score/
18. Dayan JH, Dayan E, Smith ML. Reverse Lymphatic Mapping. Plast Reconstr Surg. 2015;135(1):277-285. doi:10.1097/prs.0000000000000822
19. Carl H, Walia G, Bello R, et al. Systematic Review of the Surgical Treatment of Extremity Lymphedema. J Reconstr Microsurg. 2017;33(06):412-425. doi:10.1055/s-0037-1599100

Disclosure

None reported.

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Translating Technique into Outcomes in Amputation Surgeries

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Multiple technical considerations are available to improve long-term outcomes for amputees.



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Abstract

The department of surgery at Washington University is putting increased emphasis on outcomes for amputees. This multidisciplinary effort begins with choosing the correct surgery and incorporating the latest technical advances in amputation surgery.

Introduction

There are two million amputees in the United States. Projections estimate there will be 3.6 million amputees by 2050 due to the rise of peripheral vascular disease and diabetes mellitus.[1,2] Despite the 10.6 billion total cost of amputation and postoperative management, surgical amputations often have suboptimal results.[3] Wound complications and deep tissue infections are common, often requiring revisionary procedures or costly, morbid re-amputations. Amputees have a hospital readmission rate of 19.5 times per person-year with associated hospital stays of 71.2 days per person-year.[3] This significantly impacts amputees' quality of life, ability to perform ADLs, and profoundly affects longevity. Mortality associated with a major amputation ranges from 15-20% in the first 30 days and approaches 50% over the first five years.[3,4,5] A thoughtful approach to amputations in the context of a larger limb preservation effort can create meaningful differences in long-term quality of life for amputees. At Washington University, incorporation of the latest technical developments in amputation surgery form the initial step in a broader institutional outcomes-oriented approach to amputee care. This article will introduce the modern technical innovations that have been demonstrated to improve clinical outcomes in amputation surgeries.[6]

Transfemoral Amputation

Transfemoral amputations disrupt normal muscle balance between abducting/adducting and flexion/extension muscle groups; leading to 65% greater energy expenditure when ambulating compared to non-amputees. Following transfemoral amputation, residual limb length, orientation of the femur, muscular reattachment, and muscular atrophy impact prosthetic fit and mobility Transfemoral amputees have 65% greater energy expenditure when ambulating compared to non-amputees. Surgeons aim to restore an energy efficient gait by maintaining the biological, anatomical alignment of the femur.[8]

Before the 1980s, transfemoral amputations sacrificed the adductor magnus and sectioned the hamstring muscles.[7,8,9,10] Resting tension and motor power were lost since the adductor magnus has the greatest moment arm, giving it the best

mechanical advantage.[9] The loss of adduction causes unopposed abduction and a thigh flexion—abduction deformity.[7,8] The anatomical and mechanical axes of the femur become discordant—destabilizing the femur. As a result, the patient lurches sideways with each step. Muscle dis-insertion causes 40-60% of the remaining muscle bulk to atrophy—making prosthetic fit and control difficult.[8,10]

To address the energy demands imposed by a lurching gait and address the problems with prosthetic fit, transfemoral amputation evolved to a medial-based flap with preservation of the adductor magnus and myodesis of the adductor to the distal femur.[7,9] Maintaining insertion of the adductor magnus at the linea aspera, will maximize the power and stability of the remaining muscles.[8] The adductor magnus is ideal for myodesis because it is innervated by both the sciatic and obturator nerves, so it functions in both adduction and extension at the pelvis. Adductor myodesis improves femoral position; soft tissue padding for the distal femur; balanced gait mechanics; gait efficiency, and improved prosthetic fit.[8,10]

Medially-based myofasciocutaneous flaps off the obturator artery are preferred because the obturator artery is rarely affected by peripheral vascular disease. The femur is transected proximal to the knee joint; the sartorius, gracilis, and medial hamstrings are transected and included in the muscle anchorage.[8,10] The sciatic nerve is dissected, but is not ligated to decrease neuroma formation.[10] The adductor magnus is myodesed to the lateral cortex of the femur. Adductor myodesis is traditionally performed using Krackow sutures, but recently fiber tape was found to be an easy, quick, and strong alternative.[7] The quadriceps muscle is reattached to the posterior femur and the hamstrings are anchored to the adductor magnus posteriorly.[8,10]

Surgeons aim to create the longest possible residual limb to provide the longest lever arm for transfers, sitting, and increased walking velocity.[9,11,12] Greater length preservation will decrease gait asymmetry and pelvic tilt. Shorter residual limbs result in muscular atrophy, increased trunk excursion, and increased pelvic motion caused by muscular imbalance.[11,12]

Osseointegration

Osseointegration was developed in the 1990s in response to persistent challenges related to the socket-limb interface.[13,14,15,16,17] Traditionally, a prosthetic limb is attached to the patient's residual limb using a custom designed socket, but 25-33% of patients experience chronic wounds, pinching, perspiration issues, skin irritation, and pain.[13,18] Osseointegration is the direct fixation of an artificial implant into living bone. The implant can withstand normal weight bearing and loading pressures. Offloading the soft tissue surrounding the residual limb, decreases pressure sore and wound formation. Attaching the prosthetic directly into the bone improves osseoperceptive sensory feedback and prosthetic control.[13,16-18]

The Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) Implant System was developed by Branemark et al. in 1999.[17] The FDA-approved OPRA system includes three main parts: an implanted fixture, an abutment, and abutment screw. Performed in two stages, the first operation implants the fixture intramedullary into the bone stump to provide rotational stability. After a six-month healing period, anterior and posterior muscles are sutured to the periosteum and subcutaneous fat is removed proximal to the skin opening. The final, critical step of the operation is the formation of a tight seal around the distal bone graft.[13] Thin, hair follicle free, immobile skin should encircle the abutment to limit soft tissue redundancy and provide vascularized soft tissue coverage at the implant bone interface.[17] Recently, a single stage approach for osseointegration has been developed.[13,17]

The principle concern regarding osseointegrated implants is the risk of bone or soft tissue infection requiring subsequent reconstruction.[13,18] Superficial infections, requiring oral antibiotics, have a 18-63% incidence,[18] while deep infections are rare. Most authors believe that because the incidence of deep tissue infection is low, it weighs favorably against the common risks of hyperhidrosis, ulcerations, and bullous disease associated with socket prostheses.[18] Furthermore, using titanium-coated implants decreases bacterial biofilm formation, limiting periprosthetic joint infection.[19,20] Creating a well-vascularized, multilayered soft tissue closure and a tight seal around the stoma decreases irritation, inflammation, infection, and, subsequently, closure complications at soft tissue implant interface. Plastic surgery expertise may further decrease soft tissue complications.[13]

Following osseointegration, patients report improved physical functioning, decreased pain, improved prosthetic use, improved prosthetic control, increased walking ability, increased social interactions, increased independence, and improved health related quality of life.[13,18,21,22] Using the OPRA system, prosthetics may be driven by implanted electrodes

passed through the femur which creates a bidirectional interface for intuitive prosthetic control via sensory feedback from epimysial and nerve cuff electrodes.[14,17] Washington University has recently been approved as a pilot center for use of the OPRA device in the United States.

Transtibial Amputation

Transtibial amputation has historically been performed using the Burgess technique. Previously well described, the Burgess technique involves cutting both the tibia and fibula, but the fibula is cut at a more proximal level.[23] The proximal tibiofibular joint is undisturbed.[24] A long posterior myocutaneous flap is sutured over the end of the residual tibia, followed by myodesis of the gastrocneumius tendon to the proximal tibial periosteum.[23,25,26]

Disruption of the interosseous membrane between the tibia and the fibula results in residual limb instability. The fibula is unable to participate in load transfer, so with prolonged weight bearing, the fibula becomes angulated toward the tibia and results in a conical, pointed residual limb that causes soft tissue breakdown.[8] Janos Ertl developed the osteomyoplastic amputation to address the discordant motions of the tibia and fibula after disarticulation.[8,24-27] Ertl described the creation of an osteoperiosteal tube by elevating tibial periosteum and affixing it to the residual fibula. This osteoperiosteal sleeve was sutured at the ends of the tibia and fibula and filled with bone graft. This sealed the medullary canal and formed a solid bony synostosis between the tibia and fibula which created a stable platform and increased surface area for load transfer.[8,25-27] The myodesis recreates physiological muscle tension and stabilizes the surface area available for prosthetic fitting.[27] Sealing the medullary canal restores normal intramedullary pressure to the tibia and improves circulation to the stump.[27] The Ertl procedure is also performed for transtibial amputees with residual limb pain due to an unstable fibula.[6,27]

Pinto and Harris modified this procedure by creating a vascularized fibular strut with or without the osteoperiosteal sleeve. Their technique utilizes a 4.5 cm fragment of autogenous fibula that maintains its blood supply via connection to adjacent musculature.[28] The fibular strut is fixated across the distal aspect of the remaining tibia and fibula. All of their patients developed solid synostosis of the strut which was radiographically and clinically evident by the stable fibula and decreased pain with weight bearing.[29]

Currently, the most common "Ertl" transtibial amputation involves the use of a long posterior myocutaneous flap. The residual tibia length is 10-15 cm for optimal prosthetic fit. The fibula is divided 4 cm distal to the tibia; after removal of the distal leg, one centimeter of the fibula is rotated medially and fixated between the distal tibia and fibula with Kirschner wire or headless screw fixation.[8,29,30] The fibular strut can be supplemented with a vascularized periosteal sleeve which is created by raising periosteum off of the anterior surface of the distal tibia.[8,27-29] The periosteum is taken with the cortical bone to maintains its vascular supply—creating a vascularized sleeve. Autogenous bone graft may be placed on the bone bridge or within the osteoperiosteal sleeve.[8,27] The osseous surface is covered with myodesed posterior musculature, Achilles tendon, anterior tibial, and peroneal musculature.[8,27,30,31]

The Ertl amputation remains controversial. Opponents argue that the risks associated with longer operative and tourniquet times are not outweighed by the supposed benefits. The wound complication rates and physical function scores are equivalent to the standard procedure.[25,31] Inclusion of the bone bridge increases the surgical revision rate, implant removal, screw fixation problems, and neuroma formation.[26,27,30,31,32] Advocates argue that the increased surface area of the weight bearing region is better able to dissipate force. This results in less pain, improved ambulation, and more prosthetic options.[26,27,33] A higher proportion of U.S. service members who had the Ertl procedure were able to return to active duty.[25-27] However, among vascular patients, only one case series found improved ambulation rates.[27,31] We conclude: younger, more active individuals, and U.S. military personnel who seek to return to active duty may benefit from the osteomyoplastic bone bridge reconstruction while older patients, with medical comorbidities, may not experience additional functional gains and should be screened with caution.

Osseointegration for Transtibial Amputees

Osseointegration to improve prosthetic use, mobility, ambulation, and quality of life among transfemoral amputees has been described.[6,13-22,34] Osseointegration is not widely performed for transtibial amputees, but a recent cohort of nine transtibial amputees who underwent osseointegration reported increased mobility, increased walking ability, and increased prosthetic use.[35] Even among patients with peripheral vascular disease, historically a

contraindication for osseointegration, all patients were able to walk unassisted one year postoperatively and reported improved quality of life.[34,35]

Agonist-Antagonist Myoneural Interface

MIT's Center for Extreme Bionics developed a new construct aimed at improving myoelectric prosthetic control among amputees: the agonist-antagonist myoneural interface (AMI).[6,36,37,38] Recent studies have shown that the dynamic relationships within agonist-antagonist muscle pairs are fundamental to natural sensations of joint movement.[35,36] In a traditional amputation, residual muscles are arranged isometrically to provide maximum padding for the prosthetic socket. Eliminating the dynamic relationships between agonist-antagonist pairs prevents muscle spindles and golgi tendon organs from communicating proprioceptive information to the CNS.[26] The AMI construct consists of an agonist and antagonist muscle tendon surgically connected in series: when the agonist contracts, the antagonist is stretched.[36-38] Thus, mechanoreceptors in both muscles communicate the position, speed, and torque of the joint.[36-38]

A tendon harvested from the tarsal tunnel mechanically links the two muscles that compose the AMI. The tarsal tunnels are fixated to the tibia and act as a pulley such that force produced in one muscle causes stretch in the other muscle.[36,38] When provided with a bionic limb consisting of powered ankle and subtalar joints electrically connected to the two AMIs, patients are able to move the bionic limb by contracting the AMI muscles associated with the intended motion.[36] The AMI controlling the subtalar joint is composed of the tibialis posterior and the peroneus longus muscles; this AMI is responsible for prosthetic inversion and eversion movements. The AMI controlling the bionic ankle joint is composed of the lateral gastrocnemius muscle and tibialis anterior muscles; this AMI is responsible for prosthetic plantar flexion and dorsiflexion. Since each muscle within the AMI is harvested with its own nerve, the AMI acts as a bidirectional interface between the nerve and bionic prosthetic. Implanted electrodes interface with sensors within the bionic limb to generate a movement command for the motors within the prosthetic.[6,36]

This surgical procedure is now described as the "Ewing Amputation" which incorporates the two AMIs described into the transtibial residuum. Patients who have undergone the Ewing Amputation have improved stability, improved motion path efficiency, improved gait symmetry, natural reflexive behavior during stair ambulation, and improved performance on torque control tasks when compared to traditional transtibial amputees.[36,38] None of the patients experienced muscle atrophy of the residual limb. This may be because the AMI creates nonisometric fixation of muscles which allows for concentric, eccentric and isometric muscular contraction. As a result of increased muscle loading, muscle mass increases.[36,38]

Knee Disarticulation

The knee disarticulation (KD) amputation is disproportionately underutilized due to concerns surrounding wound healing complications, issues with prosthetic fit, and concern about a bulbous stump.[39,40] Many surgeons worry that the long flaps necessary to close the incision over the femoral condyles will cause wound healing complications.[41] However, the metabolic cost of walking is greater for proximal amputations due to the additional weight of two prosthetic joints.[42] Especially among patients with PVD, self-selected walking speed and cadence decrease with proximal amputations, while oxygen consumption increases. Thus, the KD is an energy efficient alternative to transfemoral amputation.[42,43]

The end-weight bearing stump produced by the KD allows for direct load transfer which is the physiologic method of weight bearing produced by the 30 bones of the foot.[9] The weight bearing surface in a KD is the knee joint, which is less stiff and has greater surface area than the osseous stump produced by a transfemoral or transtibial amputation. In a knee disarticulation, the direct transfer prosthetic socket only needs to suspend the prosthesis; in a transosseous amputation the surface area of the bone is small so the bone must be "unweighted" by a socket that distributes the force over the entire surface of the residual bone. Distributing force over a larger surface area is protective against soft tissue breakdown.[8,9]

The surgical technique utilizes a long posterior myofasciocutaneous flap incorporating the gastrocnemius muscle bellies to improve blood supply and padding to the distal stump.[40,42,44] The patellar tendon is removed, and the posterior fat pad is excised. The knee joint capsule and collateral ligaments are divided circumferentially. The cruciate ligaments are released from their attachments; the medial and lateral hamstring tendons are divided; and the popliteal vessels are clamped, divided, and ligated while the perforating vessels remain intact. The tibial and peroneal nerves are

drawn distally, cut, and allowed to retract into the soft tissue to prevent neuroma formation.[42] Muscles that cross the knee joint remain intact and are sutured to the distal end of the stump. The patellar tendon is sutured to the cruciate ligaments and the medial and lateral hamstring tendons are sewn to the knee joint capsule. The iliotibial band is sutured to the lateral aspect of the capsule to improve abduction and hip extension through the gluteus maximus.[42] For optimal wound healing, blood supply to the gastrocnemius is preserved by protecting the medial and lateral sural branches of the popliteal artery, and perforators between the gastrocnemius and overlying skin.[44,45]

Mazet and Hennessy designed a technique to reduce the bulkiness of the KD stump by trimming the medial, lateral and posterior condyles and adding a patellectomy to make a conical distal stump.[41,45] Flaring of the condyles usually results in a bulbous stump which makes donning a prosthetic difficult; by trimming the condyles and discarding the patella, bulbousness is decreased, so shorter tissue flaps are needed to close the incision, improving wound healing.[45,46] Further refined by Burgess, who removed 1.5 cm of the distal end and raised the prosthetic knee joint, cosmetic appearance of the limb is improved because the center of the prosthetic knee joint is brought closer to the level of the contralateral knee.[40,42,43,47]

Attinger modified this technique by using a dorsal flap. Instead of discarding the patella, the patella is advanced to cover the end-weight bearing surface of the femur such that the posterior surface of the patella is in direct contact with the distal end of the femur.[40] The quadriceps tendon is sewn over the cruciate ligament, and the hamstring muscles are myodesed to the quadriceps tendon. Preserving the patella is beneficial for weight bearing during transfers and knee ambulation for patients who are not prosthetic candidates.[40]

Knee disarticulations preserve adductor muscle insertion which improves motor control; maintains the anatomical alignment of the femur; and decreases muscle atrophy.[46,49] Balancing the flexors and extensors within the residual limb decreases the risk of developing hip flexion contractures.[40,41,43,44,48] Patients use prosthetics earlier, and walk sooner.[46,47] The longer lever arm improves walking stability, prosthesis control, and increases proprioception.[40,41,43,44,45,49] For non-ambulatory patients, the longer lever arm of knee disarticulation provides easier sitting balance in a wheelchair, trunk stability, mobility in bed, and ease of transfers, while decreasing the risk of developing ulceration and contractures.[40,41,44,45,50,51,52]

Using these techniques, patients with PVD have 60-84% primary healing rates, 8-9% revision rate, 0-21% re-amputation rate, and ambulation rates upwards of 75%.[40,43,44,45,49,50] The conically-shaped stump allows the patient to use a vacuum suction prosthesis that does not need to be removed each time the patient goes to the bathroom. This restores independence to amputees.[40,41,43,46,47,50] By combining the posterior myocutaneous flap and the Mazet technique up to 81% of patients ambulate.[40,43,44,45]

Conclusion

Multiple technical considerations are available to improve long term outcomes for amputees. A thoughtful approach to level of amputation should be taken, incorporating through-joint amputations when feasible to improve direct weight-bearing and independence with transfers. Newer developments such as osseointegration and agonist-antagonist myoneural interface are now being offered at Washington University, and are poised to improve the ease of use and quality of prosthetic ambulation.

References

1. Ziegler-Graham K, MacKenzie EJ, Ephraim PL, Travison TG, Brookmeyer R. Estimating the prevalence of limb loss in the United States: 2005 to 2050. Arch Phys Med Rehab. 2008;89(3):422-429. doi:10.1016/j.apmr.2007.11.005
2. Neville RF, Kayssi A. Development of a Limb-Preservation Program. Blood Purificat. 2017;43(1-3):218-225. doi:10.1159/000452746
3. Galmer AM, Selim SM, Giri J, Lau JF, Weinberg MD. Building a Critical Limb Ischemia Program. Curr Treat Options Cardiovasc Medicine. 2016;18(8):50. doi:10.1007/s11936-016-0476-4
4. Dillingham TR, Pezzin LE. Rehabilitation Setting and Associated Mortality and Medical Stability Among Persons With Amputations. Arch Phys Med Rehab. 2008;89(6):1038-1045. doi:10.1016/j.apmr.2007.11.034
5. Fan KL, DeLia D, Black CK, et al. Who, What, Where: Demographics, Severity of Presentation, and Location of Treatment Drive Delivery of Diabetic Limb Reconstructive Services within the National Inpatient Sample. Plastic Reconstr Surg. 2020;145(6):1516-1527. doi:10.1097/prs.0000000000006843
6. Herr HM, Clites TR, Srinivasan S, et al. Reinventing Extremity Amputation in the Era of Functional Limb Restoration. Ann Surg. 2020;Publish Ahead of Print. doi:10.1097/sla.0000000000003895
7. Hsu AR. Transfemoral Amputation Adductor Myodesis Using FiberTape and Knotless Anchors. Foot Ankle Int. 2018;39(7):874-879. doi:10.1177/1071100718776041
8. Pinzur MS, Gottschalk F, Pinto MAG de S, Smith DG. Controversies in lower extremity amputation. Instr Course Lect. 2007;57:663-672.
9. Pinzur MS. Outcomes-Oriented Amputation Surgery. Plast Reconstr Surg. 2011;127:241S-247S. doi:10.1097/prs.0b013e318200a409
10.Gottschalk F. The importance of soft tissue stabilization in trans-femoral amputation: English version. Der Orthopäde. 2015;45(S1):1-4. doi:10.1007/s00132-015-3098-8
11. Bell JC, Wolf EJ, Schnall BL, Tis JE, Tis LL, Potter BK. Transfemoral amputations: the effect of residual limb length and orientation on gait analysis outcome measures. J Bone Jt Surg Am Volume. 2013;95(5):408-414. doi:10.2106/jbjs.k.01446
12. Bell JC, Wolf EJ, Schnall BL, Tis JE, Potter BK. Transfemoral amputations: is there an effect of residual limb length and orientation on energy expenditure? Clin Orthop Relat R. 2014;472(10):3055-3061. doi:10.1007/s11999-014-3630-x

13. Marano AA, Modiri O, Rozbruch SR, Otterburn DM. Soft Tissue Contouring at the Time of Osseointegrated Implant Reconstruction for Lower Extremity Amputation. Ann Plas Surg. 2020;85(S1):S33-S36. doi:10.1097/sap.0000000000002329
14. Brånemark R, Berlin O, Hagberg K, Bergh P, Gunterberg B, Rydevik B. A novel osseointegrated percutaneous prosthetic system for the treatment of patients with transfemoral amputation: A prospective study of 51 patients. Bone Jt J. 2014;96-B(1):106-113. doi:10.1302/0301-620x.96b1.31905
15. Hagberg K, Hansson E, Brånemark R. Outcome of Percutaneous Osseointegrated Prostheses for Patients With Unilateral Transfemoral Amputation at Two-Year Follow-Up. Arch Phys Med Rehab. 2014;95(11):2120-2127. doi:10.1016/j.apmr.2014.07.009
16. Hagberg K, Jahani S-AG, Kulbacka-Ortiz K, Thomsen P, Malchau H, Reinholdt C. A 15-year follow-up of transfemoral amputees with bone-anchored transcutaneous prostheses: mechanical complications and patient-reported outcomes. Bone Jt J. 2020;102-B(1):55-63. doi:10.1302/0301-620x.102b1.bjj-2019-0611.r1
17. Li Y, Brånemark R. Osseointegrated prostheses for rehabilitation following amputation : The pioneering Swedish model. Der Unfallchirurg. 2017;120(4):285-292. doi:10.1007/s00113-017-0331-4
18. Gerzina C, Potter E, Haleem AM, Dabash S. The future of the amputees with osseointegration: A systematic review of literature. J Clin Orthop Trauma. 2020;11(Suppl 1):S142-S148. doi:10.1016/j.jcot.2019.05.025
19. Raphel J, Holodniy M, Goodman SB, Heilshorn SC. Multifunctional coatings to simultaneously promote osseointegration and prevent infection of orthopaedic implants. Biomaterials. 2016;84:301-314. doi:10.1016/j.biomaterials.2016.01.016
20. Juhnke D-L, Beck JP, Jeyapalina S, Aschoff HH. Fifteen years of experience with Integral-Leg-Prosthesis: Cohort study of artificial limb attachment system. J Rehabil Res Dev. 2015;52(4):407-420. doi:10.1682/jrrd.2014.11.0280
21. Leijendekkers RA, Hinte G van, Frölke JP, et al. Functional performance and safety of bone-anchored prostheses in persons with a transfemoral or transtibial amputation: a prospective one-year follow-up cohort study. Clin Rehabil. 2018;33(3):450-464. doi:10.1177/0269215518815215
22. Lundberg M, Hagberg K, Bullington J. My prosthesis as a part of me: a qualitative analysis of living with an osseointegrated prosthetic limb. Prosthet Orthot Int. 2011;35(2):207-214. doi:10.1177/0309364611409795
23. Burgess EM, Romano RL, Zettl JH, Schrock RD. Amputations of the leg for peripheral vascular insufficiency. J Bone Jt Surg Am Volume. 1971;53(5):874-890.
24. Plucknette BF, Krueger CA, Rivera JC, Wenke JC. Combat-related bridge synostosis versus traditional transtibial amputation: comparison of military-specific outcomes. Strategies Trauma Limb Reconstr Online. 2015;11(1):5-11. doi:10.1007/s11751-015-0240-4
25. Gwinn DE, Keeling J, Froehner JW, McGuigan FX, Andersen R. Perioperative differences between bone bridging and non-bone bridging transtibial amputations for wartime lower extremity trauma. Foot Ankle Int. 2008;29(8):787-793. doi:10.3113/fai.2008.0787
26. Bosse MJ, Morshed S, Reider L, et al. Transtibial Amputation Outcomes Study (TAOS): Comparing Transtibial Amputation With and Without a Tibiofibular Synostosis (Ertl) Procedure. J Orthop Trauma. 2017;31(NA;):S63-S69. doi:10.1097/bot.0000000000000791
27. Taylor BC, Poka A. Osteomyoplastic Transtibial Amputation: The Ertl Technique. J Am Acad Orthop Surg. 2016;24(4):259-265. doi:10.5435/jaaos-d-15-00026
28. Pinto MAGS, Harris WW. Fibular segment bone bridging in trans-tibial amputation. Prosthet Orthot Int. 2004;28(3):220-224. doi:10.3109/03093640409167753
29. Brown BJ, Iorio ML, Hill L, Carlisle B, Attinger CE. Below-Knee Amputation with a Vascularized Fibular Graft and Headless Compression Screw. Plast Reconstr Surg. 2013;131(2):323-327. doi:10.1097/prs.0b013e3182778615
30. Brown BJ, Iorio ML, Hill L, et al. Ertl Below-Knee Amputation Using a Vascularized Fibular Strut in a Nontrauma Elderly Population: A Case Series. Ann Plas Surg. 2014;73(2):196-201. doi:10.1097/sap.0b013e318273f740
31. Kahle JT, Highsmith MJ, Kenney J, Ruth T, Lunseth PA, Ertl J. The effectiveness of the bone bridge transtibial amputation technique: A systematic review of high-quality evidence. Prosthet Orthot Int. 2017;41(3):219-226. doi:10.1177/0309364616679318
32. Tintle LSM, Keeling CJJ, Forsberg LJA, Shawen LSB, Andersen LRC, Potter MBK. Operative Complications of Combat-Related Transtibial Amputations: A Comparison of the Modified Burgess and Modified Ertl Tibiofibular Synostosis Techniques. J Bone Jt Surgery-american Volume. 2011;93(11):1016-1021. doi:10.2106/jbjs.j.01038
33. Ferris AE, Christiansen CL, Heise GD, Hahn D, Smith JD. Ertl and Non-Ertl amputees exhibit functional biomechanical differences during the sit-to-stand task. Clin Biomech. 2017;44:1-6. doi:10.1016/j.clinbiomech.2017.02.010
34. Atallah R, Li JJ, Lu W, Leijendekkers R, Frölke JP, Muderis MA. Osseointegrated Transtibial Implants in Patients with Peripheral Vascular Disease: A Multicenter Case Series of 5 Patients with 1-Year Follow-up. J Bone Jt Surg Am Volume. 2017;99(18):1516-1523. doi:10.2106/jbjs.16.01295
35. Leijendekkers RA, Hinte G van, Frölke JP, et al. Functional performance and safety of bone-anchored prostheses in persons with a transfemoral or transtibial amputation: a prospective one-year follow-up cohort study. Clin Rehabil. 2018;33(3):450-464. doi:10.1177/0269215518815215
36. Clites TR, Carty MJ, Ullauri JB, et al. Proprioception from a neurally controlled lower-extremity prosthesis. Sci Transl Med. 2018;10(443):eaap8373. doi:10.1126/scitranslmed.aap8373
37. Clites TR, Carty MJ, Srinivasan SS, Talbot SG, Brånemark R, Herr HM. Caprine Models of the Agonist-Antagonist Myoneural Interface Implemented at the Above- and Below-Knee Amputation Levels. Plast Reconstr Surg. 2019;144(2):218e-229e. doi:10.1097/prs.0000000000005864
38. Clites TR, Herr HM, Srinivasan SS, Zorzos AN, Carty MJ. The Ewing Amputation: The First Human Implementation of the Agonist-Antagonist Myoneural Interface. Plastic Reconstr Surg - Global Open. 2018;6(11):e1997. doi:10.1097/gox.0000000000001997
39. Murakami T, Murray K. Outcomes of knee disarticulation and the influence of surgical techniques in dysvascular patients: A systematic review. Prosthet Orthot Int. 2015;40(4):423-435. doi:10.1177/0309364615574163
40. Albino FP, Seidel R, Brown BJ, Crone CG, Attinger CE. Through knee amputation: technique modifications and surgical outcomes. Archives Plastic Surg. 2014;41(5):562-570. doi:10.5999/aps.2014.41.5.562
41. Cull DL, Taylor SM, Hamontree SE, et al. A reappraisal of a modified through-knee amputation in patients with peripheral vascular disease. Am J Surg. 2001;182(1):44-48. doi:10.1016/s0002-9610(01)00663-8
42. Bowker JH, Giovanni TPS, Pinzur MS. North American Experience with Knee Disarticulation with Use of a Posterior Myofasciocutaneous Flap: Healing Rate and Functional Results in Seventy-seven Patients*. J Bone Jt Surgery-american Volume. 2000;82(11):1571-1574. doi:10.2106/00004623-200011000-00009
43. Pinzur MS, Gold J, Schwartz D, Gross N. Energy demands for walking in dysvascular amputees as related to the level of amputation. Orthopedics. 1992;15(9):1033-1036; discussion 1036-7.
44. Kock H-J, Friederichs J, Ouchmaev A, Hillmeier J, Gumppenberg S von. Long-term Results of Through-knee Amputation with Dorsal Musculocutaneous Flap in Patients with End-stage Arterial Occlusive Disease. World J Surg. 2004;28(8):801-806. doi:10.1007/s00268-004-7311-x
45. Mazet R, Hennessy CA. Knee Disarticulation: A New Technique And a New Knee-Joint Mechanism. J Bone Jt Surg. 1966;48(1):126-139. doi:10.2106/00004623-196648010-00013
46. Mazet R, Schmitter ED, Chupurdia R. Disarticulation of the knee. A follow-up report. J Bone Jt Surg. 1978;60(5):675-678. doi:10.2106/00004623-197860050-00015
47. Burgess EM. Disarticulation of the Knee: A Modified Technique. Arch Surg-chicago. 1977;112(10):1250-1255. doi:10.1001/archsurg.1977.01370100104023
48. Nellis N, Water JMVD. Through-the-knee amputation: an improved technique. Am Surg. 2002;68(5):466-469.
49. Morse BC, Cull DL, Kalbaugh C, Cass AL, Taylor SM. Through-knee amputation in patients with peripheral arterial disease: A review of 50 cases. J Vasc Surg. 2008;48(3):638-643. doi:10.1016/j.jvs.2008.04.018
50. Duis KT, Bosmans JC, Voesten HGJ, Geertzen JHB, Dijkstra PU. Knee disarticulation: survival, wound healing and ambulation. A historic cohort study. Prosthet Orthot Int. 2009;33(1):52-60. doi:10.1080/03093640802557020
51. Albers GHR, Eijken JW v d, Bras J. Through knee amputation with gastrocnemius musculocutaneous flap: 6 cases of tibial osteosarcoma followed for 3 (1-6) years. Acta Orthop Scand. 1994;65(1):67-70. doi:10.3109/17453679408993721
52. Ayoub MM, Solis MM, Rogers JJ, Dalton ML. Thru-knee amputation: the operation of choice for non-ambulatory patients. Am Surg. 1993;59(9):619-623.

Disclosure

None reported. **MM**

Vascularized Bone Flaps for Carpal Reconstruction

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Recent advances in the field of vascularized bone transfer have expanded our treatment options such that the carpal preservation is now available to most patients.



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Abstract

Within the field of hand and upper extremity surgery, reconstruction of the bony carpus remains a perplexing task and is a field undergoing rapid evolution. Among the eight bones of the carpus, the scaphoid and lunate are most frequently affected by traumatic and avascular processes which render their articular surfaces degenerated and painful. These conditions include scaphoid waist fracture, scaphoid proximal pole fracture, and Kienböck's disease of the lunate. While traditional salvage operations with limited functional outcomes have historically been employed for management of these unsolved problems, advances in microsurgical understanding and capability are changing the treatment algorithm at our center. This paradigm shift centers in large part around the introduction of new techniques for vascularized bone and cartilage transfer for carpal reconstruction.

Vascularized Bone

Vascularized free tissue transfer is a fundamental technique in the armamentarium of a plastic and reconstructive surgeon. While the majority of free tissue transfers aim to bring muscle and or skin from areas of excess to areas of reconstructive need (i.e. in breast reconstruction), clinical situations occasionally arise wherein the transfer of vascularized bone and/or cartilage is required. The most common indication for vascularized bone transfer is mandibular reconstruction after traumatic injury or tumor extirpation. The fibula free flap has long been used for this purpose and others, and this is a reliable tool for reconstruction of large bones. [1]

Though it is well understood that many challenges limiting the success of carpal reconstruction are related to insufficient bony vascularity, traditional bone flaps liked the fibula are far too large and potentially morbid to be useful for carpal reconstruction. Pedicled bone flaps based upon small vessels supplying segments of the distal radius have been applied to the task of carpal reconstruction with some success.[2] However, these are limited with respect to reach, size, structural integrity, reliability of blood supply. Furthermore, these local bone flaps cannot provide vascularized articular cartilage which is a key component that will be discussed in detail below.

Recently, a novel class of small vascularized bone free flaps has been introduced. This dyad of bone and osteochondral flaps are based upon the descending geniculate vessels which supply the medial femoral condyle and medial femoral trochlea. Utilization of this versatile



Figure 1. Scaphoid waist non-union visualized on a CT scan.

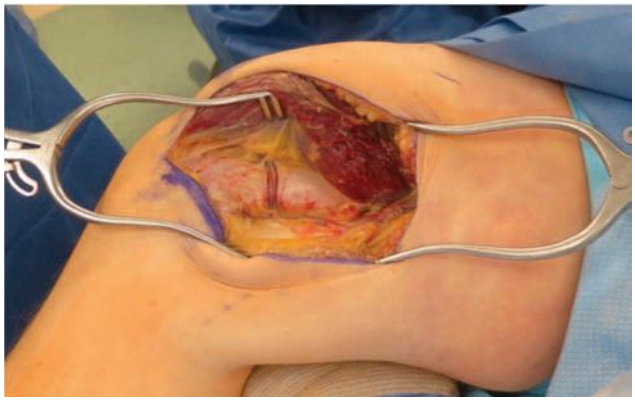


Figure 2. The descending geniculate artery can be seen running parallel to the femur, and then climbing up onto the medial femoral condyle where it provides blood flow to local bone and cartilage.

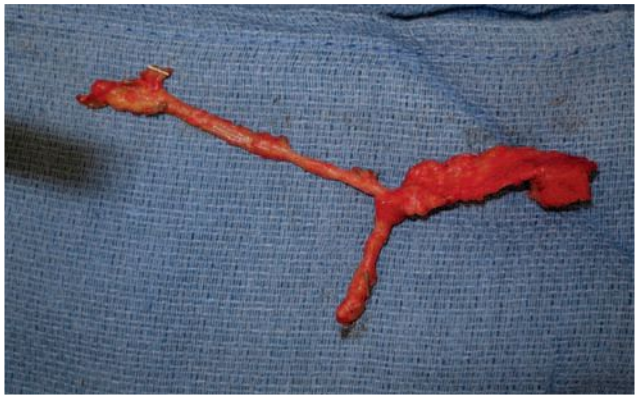


Figure 3. A medial femoral condyle bone flap has been harvested based upon its descending geniculate pedicle, and is ready for inset into the scaphoid and vascular anastomosis.

donor site for vascularized bone free flaps has resulted in expansion of our ability to bring vascularized bone and cartilage to the carpus for the purpose of articular and extra-articular bony reconstruction. This advanced microsurgical approach to reconstruction of the carpus has revolutionized the treatment of challenging scaphoid fractures and Kienböck's disease. Is the objective of this article to outline these recent advances and current treatment options.

Scaphoid Waist Non-Union:

The scaphoid is the most commonly fractured bone in the carpus and the waist is the most common anatomic location for fracture to occur. In many cases, non-operative management in a cast or prompt open reduction and internal fixation leads to fracture union and favorable patient outcomes. However not infrequently, scaphoid waist fractures fail to heal after operative or non-operative management (Figure 1). Left untreated, scaphoid waist non-union may lead to pain and rapidly progressive arthritis and loss of wrist function. Risk factors for this unfavorable outcome include fracture displacement, delayed treatment, and smoking.[3]

The traditional first line of treatment for scaphoid waist non-union is open reduction and infernal fixation of the fracture (which represent a second surgery for patients who were initially treated operatively) with non-vascularized cancellous or corticocancellous bone grafting.[4] In many cases, this is successful, but still there are some patients who again go on to non-union. Recalcitrant scaphoid waist non-union despite sound surgical treatment may be multifactorial, but current thinking is that reduced vascularity of the proximal pole leads to difficulty with incorporation of non-vascularized bone graft. For this reason, vascularized bone free flaps, which bring new and exuberant blood supply to the fracture site, have gained in popularity.

While different sources of vascularized bone have been described for the treatment of scaphoid waist non-unions, we favor the medial femoral condyle donor site. Through a modest incision on the medial side of the knee, we are

able to access the medial femoral condyle without disrupting the joint or nearby musculotendinous units. The dominant periosteal vascular supply to the medial femoral condyle is through the descending geniculate artery, which is dissected back to its origin from the superficial femoral artery (Figure 2). After isolating this vascular pedicle, its branches are followed onto the medial femoral condyle, where a small portion of bone supplied by these vessels is harvested using an osteotome.[5] While large amounts of bone are available for harvest,[6] a small 1cm x 1cm x 1 cm cube of vascularized bone is sufficient for treatment of the scaphoid waist (Figure 3). This bone and its vascular pedicle are brought from the knee to the wrist where the bone is used to fill the non-articular defect in the scaphoid waist, and the artery and vein are microsurgically anastamosed to the radial vessels to provide bony perfusion.

A growing body of literature suggests that MFC bone flap reconstruction of recalcitrant scaphoid non-unions has a high rate of success[7] even in cases which have been refractory to other treatment. Clinical union is expected approximately 8-12 weeks after surgery, and after this point patients undergo a course of therapy focused upon regaining range of motion. Perhaps even more importantly, clinical studies have found that morbidity related to the knee donor site is exceptionally uncommon. Most patients return to unrestricted ambulation on the first post-operative day.[8]



Figure 4: Proximal pole scaphoid non-union after an unsuccessful attempt at primary fixation with a headless compression screw. The fragment is very small and is not suitable for salvage. Instead, proximal pole reconstruction with a medial femoral trochlea free flap is indicated.

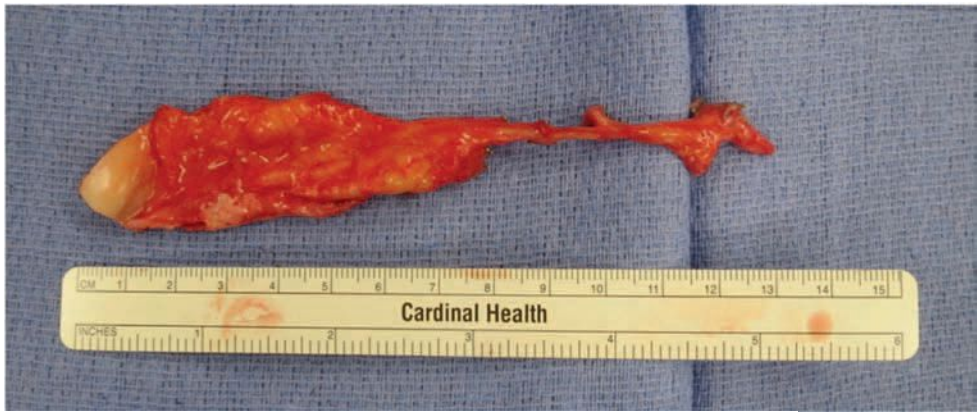


Figure 5: The medial femoral trochlea osteochondral free flap can be used for reconstruction of the proximal scaphoid or lunate.

Proximal Pole Scaphoid Non-Union:

When scaphoid fractures occur within the proximal pole which abuts the radius, the reconstructive challenge is even greater. Because of the scaphoid's retrograde blood supply, fractures in this location are at an elevated risk for non-union compared to waist fractures. In cases of extreme hypovascularity, the ischemic proximal pole not only fails to heal, but may undergo avascular necrosis and fragmentation (Figure 4). While this avascular segment indeed represents only a small portion of the scaphoid, it includes the critical articular surface which is transfers loads across the wrist and onto the radial platform.



Figure 6: The proximal scaphoid has been replaced by a medial femoral trochlea osteochondral free flap which is fixated to the distal fragment using a headless compression screw.



Figure 7: Coronal plate MRI of this patient with advances Kienbock's Disease demonstrates an avascular lunate with collapse.

Small, fragmented, and/or necrotic proximal pole fractures are particularly problematic because in many cases the proximal fragment is unsalvageable. Because the MFC bone flap does not carry the cartilage necessary for proximal pole reconstruction, it is not a suitable solution for this fracture pattern. Fortunately, in addition to supplying the medial femoral condyle, the descending geniculate vessels also send a transverse branch to the medial femoral trochlea (MFT). The trochlea is the superomedial extent of the patellofemoral articular surface, and it has been shown to have minimal involvement in weight bearing. This articular segment can be harvested as a small osteochondral free flap which is very similar in shape to the native scaphoid proximal pole (Figure 5). Rather than bridging two fractured segments of the scaphoid at the waist (like the MFC), this MFT free flap is used to completely replace the unsalvageable proximal pole with healthy vascularized bone and cartilage (Figure 6).[9]

Results of MFT free flap reconstruction of the scaphoid proximal pole demonstrate reliable radiographic union and excellent objective and subjective patient reported upper and lower extremity function.[10] Using this reconstructive technique, we are now able to reconstruct the scaphoid and preserve normal carpal anatomy in even the most challenging of fracture patterns.

Kienböck's Disease

Kienböck's disease is an idiopathic avascular necrosis of the proximal portion of the lunate which results in avascular necrosis and ultimately articular collapse (Figure 7). While we don't know exactly why Kienbocks' disease occurs, it has been observed that this condition is more common in patients with ulnar negative variance. This is likely due to a concentration of the carpal biomechanical load upon the radiocarpal joint, with little contribution of the ulnocarpal articulation.

A variety of carpus-preserving techniques have been described for the treatment of early Kienböck's disease prior to collapse of the lunate's proximal articular surface. However, once the proximal portion of the lunate has collapsed, wrist salvage with proximal row carpectomy or limited intercarpal fusion has previously been indicated. While these operations perform reasonably well in older and



Figure 8: CT Scan of the wrist demonstrating a reconstructed lunate bone after medial femoral trochlea flap transfer.

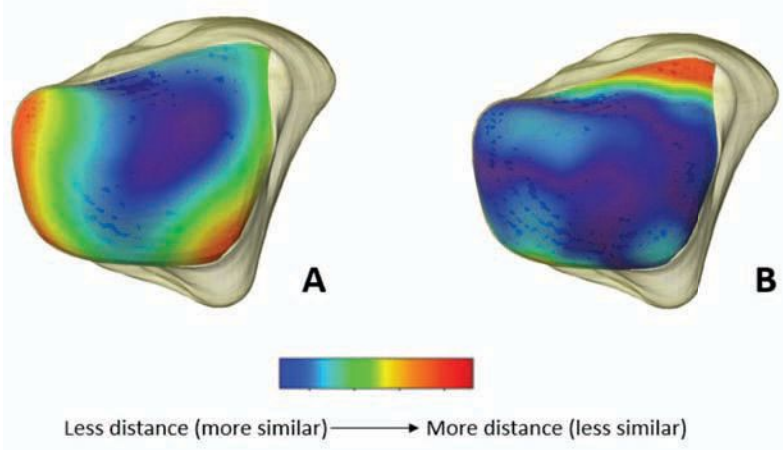


Figure 9: The proximal capitate (A) and the MFT flap (B) have been digitally overlaid upon the native lunate to generate a heat map of local intersurface distances. Given the more favorable correspondence seen between the MFT and lunate, MFT reconstruction may offer a morphologic advantage over proximal row carpectomy in this patient.

lower demand patients, they may fail to offer the function and durability desired in a younger and/or higher demand patient.[11-14]

As an alternative to wrist salvage in these high demand patients with proximal lunate articular collapse, the MFT flap (originally described for scaphoid reconstruction) has been adapted for proximal lunate reconstruction.[15] Rather than excise the damaged lunate, its distal articular surface abutting the capitate is preserved and the proximal segment is replaced with vascularized bone and cartilage which closely mimics the shape of the native lunate (Figure 8).

Like the scenarios described above, survival and union of this transferred osteochondral segment is routine. This reliability is attributable to the microvascular anastomosis, which provides blood flow to the transferred tissue. While this procedure is still relatively new, medium term objective and subjective patient reported outcomes have been encouraging,[16] and donor site morbidity has been found to be low.[17]

Sharpening the Cutting Edge: An Unconventional Collaboration to Advance Carpal Articular Reconstruction

Given the relatively novelty of vascularized osteochondral free flap reconstruction of the carpus, articular reconstruction of the proximal scaphoid and lunate has become the focus of a successful interdisciplinary research effort at our institution. The central question being addressed in this endeavor is exactly how well the MFT osteochondral free flap mimics the native scaphoid and lunate articular surfaces it is meant to reconstruct.

Previous surgical studies of this issue have used rudimentary 2-dimensional methods to describe intersurface correspondence.[18,19] Because the carpal and femoral articular surfaces are complex 3-dimensional surfaces, these methods are insufficient and a new approach is warranted. To this end, our group (led by myself and Dr. Amelia Van Handel) has leveraged the incredible range of expertise residing on the Washington University campus and formed a collaboration with Drs. Kari Allen and Leigha Lynch from the department of anatomy and neuroscience. While these researchers usually focus on the evolution of primate brain size and skull shape using medical imaging and 3-dimensional morphometric methods, we found that their expertise in quantities 3D modeling of complex surfaces could be applied to carpal articular reconstruction. Over the course of two years, this team of unlikely

collaborators has developed a protocol for quantitative assessment of different surgical options for carpal articular reconstruction (Figure 9). At this point we are able to use MRI data to quantitatively assess carpal and femoral articular morphology to assess and compare the suitability of an individual's anatomy for MFT or other reconstructive techniques. In the future, we hope to validate and apply this technique to provide precision and individualized patient counseling and surgical planning.

Conclusion

Recalcitrant scaphoid waist fractures, proximal pole scaphoid fractures with an unsalvageable articular fragment, and advanced Kienböck's disease in the young patient are among the most difficult problems facing hand surgeons today. Recent advances in the field of vascularized bone transfer have expanded our treatment options such the carpal preservation is now available to most patients. Specifically, the MFC and MFT free flaps based upon the descending geniculate vessels provide small, flexible, and expandable sources of vascularized bone and cartilage which are suitable for use in the bony carpus. While these procedures are relatively new, mid-term outcomes and our own institutional experience have been encouraging.

References

1. Bayne CO, Bishop AT, Shin AY. Technique of harvest of the free vascularized fibula. Tech Hand Up Extrem Surg. 2014;18(4):181-188. doi:10.1097/BTH.0000000000000064.
2. Zaidemberg C, Siebert JW, Angrigiani C. A new vascularized bone graft for scaphoid nonunion. YJHSU. 1991;16(3):474-478.
3. Schuind F, Moungondo F, Kazzi El W. Prognostic factors in the treatment of carpal scaphoid non-unions. Eur J Orthop Surg Traumatol. 2016;27(1):3-9. doi:10.1007/s00590-016-1886-4.
4. Braga-Silva J, Peruchi FM, Moschen GM, Gehlen D, Padoin AV. A comparison of the use of distal radius vascularised bone graft and non-vascularised iliac crest bone graft in the treatment of non-union of scaphoid fractures. 2008;33(5):636-640. doi:10.1177/1753193408090400.
5. Jones DB Jr., Moran SL, Bishop AT, Shin AY. Free-Vascularized Medial Femoral Condyle Bone Transfer in the Treatment of Scaphoid Nonunions. Plastic and Reconstructive Surgery. 2010;125(4):1176-1184. doi:10.1097/PRS.0b013e3181d1808c.
6. Iorio ML, Masden DL, Higgins JP. The Limits of Medial Femoral Condyle Corticoperiosteal Flaps. YJHSU. August 2011:1-5. doi:10.1016/j.jhsa.2011.07.015.
7. Larson AN, Bishop AT, Shin AY. Free medial femoral condyle bone grafting for scaphoid nonunions with humpback deformity and proximal pole avascular necrosis. Tech Hand Up Extrem Surg. 2007;11(4):246-258. doi:10.1097/bth.0b013e3180cab17c.
8. Mehio G, Morsy M, Cayci C, et al. Donor Site Morbidity and Functional Status Following Medial Femoral Condyle Flap Harvest. Plastic and Reconstructive Surgery. August 2018:1-28. doi:10.1097/PRS.0000000000004886.
9. Bürger HK, Windhofer C, Gaggl AJ, Higgins JP. Vascularized Medial Femoral Trochlea Osteocartilaginous Flap Reconstruction of Proximal Pole Scaphoid Nonunions. YJHSU. 2013;38(4):690-700. doi:10.1016/j.jhsa.2013.01.036.
10. Pet MA, Assi PE, Yousaf IS, Giladi AM, Higgins JP. Outcomes of the Medial Femoral Trochlea Osteochondral Free Flap for Proximal Scaphoid Reconstruction. The Journal of Hand Surgery. 2020;45(4):317–326.e3. doi:10.1016/j.jhsa.2019.08.008.
11. Croog AS, Stern PJ. Proximal Row Carpectomy for Advanced Kienböck's Disease: Average 10-Year Follow-Up. The Journal of Hand Surgery. 2008;33(7):1122-1130. doi:10.1016/j.jhsa.2008.02.031.
12. Chim H, Moran S. Long-Term Outcomes of Proximal Row Carpectomy: A Systematic Review of the Literature. Jnl Wrist Surg. 2012;01(02):141-148. doi:10.1055/s-0032-1329547.
13. Wall LB, DiDonna ML, Kiefhaber TR, Stern PJ. Proximal Row Carpectomy: Minimum 20-Year Follow-Up. YJHSU. 2013;38(8):1498-1504. doi:10.1016/j.jhsa.2013.04.028.
14. Wagner ER, Werthel J-D, Elhassan BT, Moran SL. Proximal Row Carpectomy and 4-Corner Arthrodesis in Patients Younger Than Age 45 Years. The Journal of Hand Surgery. 2017;42(6):428-435. doi:10.1016/j.jhsa.2017.03.015.
15. Bürger HK, Windhofer C, Gaggl AJ, Higgins JP. Vascularized medial femoral trochlea osteochondral flap reconstruction of advanced Kienböck disease. The Journal of Hand Surgery. 2014;39(7):1313-1322. doi:10.1016/j.jhsa.2014.03.040.
16. Pet MA, Assi PE, Giladi AM, Higgins JP. Preliminary Clinical, Radiographic, and Patient-Reported Outcomes of the Medial Femoral Trochlea Osteochondral Free Flap for Lunate Reconstruction in Advanced Kienböck Disease. The Journal of Hand Surgery. March 2020:1-8. doi:10.1016/j.jhsa.2019.12.008.
17. Windhofer C, Wong VW, Larcher L, Paryavi E, Bürger HK, Higgins JP. Knee Donor Site Morbidity Following Harvest of Medial Femoral Trochlea Osteochondral Flaps for Carpal Reconstruction. The Journal of Hand Surgery. 2016;41(5):610-614.e611. doi:10.1016/j.jhsa.2016.01.015.
18. Hugon S, Koninckx A, Barbier O. Vascularized osteochondral graft from the medial femoral trochlea: anatomical study and clinical perspectives. Surg Radiol Anat. 2010;32(9):817-825. doi:10.1007/s00276-010-0629-1.
19. Hawkins-Rivers S, Budoff JE, Ismaily SK, Noble PC, Haddad J. MRI Study of the Capitate, Lunate, and Lunate Fossa With Relevance to Proximal Row Carpectomy. The Journal of Hand Surgery. 2008;33(6):841-849. doi:10.1016/j.jhsa.2008.02.021.

Disclosure

None reported.

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Advances and Innovations in Breast Microsurgery

by Rachel A. Anolik, MD & Justin M. Sacks, MD, MBA

Washington University in St. Louis School of Medicine

Washington University in St. Louis is committed to constantly re-evaluating and improving our technique to stay at the forefront of our specialty, while optimizing outcomes for our patients.



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History of Breast Microsurgery

In order to appreciate how far we have come in terms of the evolution of breast reconstruction it is important to take a look back into our past. We owe our current innovations to the foundation that was laid by those who came before us. One such pioneer was Stuart Milton, MD, who in the 1960s described reconstruction techniques using "random pattern" flaps. These flaps were limited to a length to width ratio of 1.5:1.[1] In the early 1970s he found that flaps with much more area could be harvested when a blood vessel was included. These have come to be known as "axial pattern" pedicled flaps.[2] This pedicle flap concept lead to an important advancement in breast reconstruction. In 1982, Hartrampf performed the first pedicled flap for breast reconstruction, known as the transverse rectus abdominus myocutaneous (TRAM) flap.[3] This became one of the most common autologous tissue options for breast reconstruction performed for decades. The next step in evolution was the development of the free flap for breast reconstruction. The concept of a free flap was first described in 1973 by Taylor and Daniel. They described the transfer of autologous tissue to a distant site based on anastomosing small vessels.[4] Holmstrom then expanded upon this work and in 1979 reported what he called a free abdominoplasty flap, which was essentially a free TRAM flap.[5]

Perforator Surgery

The technique of microsurgery was first described in the 1970s and initially consisted mainly of the transfer of bulky myocutaneous flaps. Attempts have since that time been made to reduce muscle bulk and limit morbidity as the field of microsurgery has advanced. Early muscle sparing techniques included the split latissimus flap by Elliott[6] and the partial rectus abdominus muscle flap by Feller.[7] The first example of true perforator surgery was by Koshima for head and neck reconstruction in which the flap was based off of a paraumbilical perforating vessel from the deep inferior epigastric artery system. Allen and Treece built upon this work and performed the first deep inferior epigastric artery perforator (DIEP) flap for breast reconstruction in 1992.[8] The recipient vessels are most often the internal mammary artery (IMA) and vein (IMV) between the second and third rib. The DIEP flap was able to provide

the same soft tissue reconstruction as the TRAM flap while reducing morbidity, pain, and shortening recovery time.

Abdominally Based Free Tissue Transfer

The abdomen is the ideal donor site for breast reconstruction. Most women have excess adiposity suitable for breast reconstruction. The donor site scar is similar to an abdominoplasty and is overall well accepted. The skin and soft tissue of the abdomen is soft and pliable and can be easily molded into a breast. The DIEP flap is based on the deep inferior epigastric system which has a medial and lateral row of perforating vessels which penetrate the rectus muscle and supply blood and fat. This flap is able to be performed without sacrificing muscle or fascia, by splitting the rectus abdominus muscle in the direction of its fibers. A flap approximately 12cm in height and 21-24cm in width may be harvested from each hemiabdomen. Sensory nerves to the skin run with the perforators and may be dissected with the flap in order to provide sensation. Flaps are inset with the thinner lateral aspect superiorly oriented and the thicker medial aspect inset inferiorly. This may be folded on itself for increased projection. The long pedicle of the DIEP flap allows for ease of inset, with most often a contralateral flap allowing for the ideal orientation when IM recipient vessels are chosen. An alternative option to the DIEP flap is the superficial inferior epigastric artery (SIEA) flap. As the superficial cuts are made through the skin during a DIEP flap dissection, the SIEA vessels are encountered and evaluated. If these vessels are adequate, an SIEA flap is often raised. The SIEA should be >1mm at the level of the anterior superior iliac spine (ASIS) and should have a palpable pulse. There is often an inverse relationship between the SIEA and DIEP vessels in terms of perfusion of the abdominal wall. The SIEA flap is advantageous in that it completely preserves the abdominal wall avoiding the need to even split the rectus fascia and muscle. However, there are increased rates of fat necrosis, likely due to lateral positioning of the pedicle on the flap.[9] The major complications of abdominally based free tissue transfer are rare, with total flap loss approximately 1-2%. This is usually related to kinking of the pedicle, as problems with the vein are eight times more likely than the artery. Fat necrosis due to inadequate perfusion of fat is approximately 13%, abdominal wall seroma 5% and hernia <1%.[10] The SIEA and DIEP flaps can be safely and reliably performed by a trained microvascular surgeon.

Non-Abdominally Based Free Tissue Transfer

Although the DIEP flap has become the gold standard for microsurgical breast reconstruction, some patients are not candidates for this flap and so alternative techniques must be offered. Contraindications would include, but are not limited to, patients who have previously had an abdominoplasty, patients who are too thin or those who prefer another donor site. Thigh-based flaps are often our second choice donor site. There is some reluctance to use a thigh-based flap due to limited volume, issues with wound healing, sensory loss and the potential for lymphedema. Several options including the profundal artery perforator (PAP) flap, lateral thigh perforator (LTP) flap, transverse upper gracilis (TUG), or diagonal upper gracilis (DUG) flap. Of these options, the DUG flap is the author's preferred choice for several reasons. In contrast to the other thigh-based flaps, this flap is relatively straight forward to dissect, maximizes volume of the thigh flap, and minimizes donor site morbidity. The flap was originally described by Dayan. It is elevated along langers lines of the thigh, which increases volume while minimizing tension of the closure. This also helps to decreased wound healing issues. The positioning of the skin paddle at the posterior border of the adductor longus avoids the femoral triangle minimizing the risk of lymphedema, which is a dreaded complication. The distal third of the skin paddle is more reliable as the orientation is more posterior and more closely follows the angiosome.[11]

Immediate Lymphatic Reconstruction in Breast Cancer Treatment

As treatments for locally advanced and metastatic breast cancer have improved patient survival, we have seen the sequelae of some of those treatments. Disruption of the lymphatic system after sentinel lymph node biopsy (SLNB), axillary lymph node dissection (ALND), and radiation can lead to upper

extremity lymphedema. The incidence of lymphedema after SLNB is 6-13% and after ALND is 13-65%.[12] These rates are significantly increased when combined with radiation therapy. The main symptoms include limb swelling, heaviness, tingling, and discomfort. This can also have a significant psychological, functional and even financial burden on patients. Many hours are spent on physical therapy and in compression garments and many health care dollars are spent on devices to aid in decongestive therapy. The emerging field of lymphatic surgery is beginning to ease that burden. Current established strategies focus on either debulking or physiologic procedures. Debulking procedures aim to remove the fibrofatty deposition caused by the vicious cycle of lymph stasis, which leads to inflammation which then increases the deposition of fibrofatty tissue, which then further disrupts the lymphatic system increasing lymph stasis. Physiologic procedures re-route lymphatic fluid. Utilizing laser angiography, the lymphatic channels may be mapped intraoperatively in order to facilitate lymphovenous bypass (LVB). LVB anastomoses a normal distal lymphatic channel into a nearby vein to redirect lymph fluid into the venous system and bypass a known blockage. Another physiologic strategy is a vascularized lymph node transfer (VLNT), which brings lymphatic tissue on a vascular pedicle and aims to establish new lymphatic connections. The preferred donor sites of the authors include the omentum and the supraclavicular lymph nodes. While these surgeries may provide some improvement for patients already suffering from lymphedema, ideally we could prevent patients from developing the disease. Immediate lymphatic reconstruction aims to do just that. Lymphatic microsurgical preventive healing approach, known as LYMPHA, was first described by Boccardo et al from Italy in 2009.[12] The authors injected methylene blue dye into the upper extremity and found draining lymphatic channels in the axilla at the time of ALND. Following the oncologic resection, they reconnected those lymphatics to branches of the axillary vein to maintain lymphatic drainage of the arm. A year later only 4% developed lymphedema, compared to 6-13% of patients after SLNB or 13-65% of patients after ALND as previously discussed. These results have been extremely promising and several groups across the United States now have prospective trials collecting data on outcomes after immediate lymphatic reconstruction.

Conclusion

At Washington University in St. Louis, we offer comprehensive breast cancer reconstruction with a multidisciplinary team approach. Our fellowship trained surgeons are able to provide patients with the full spectrum of reconstructive options, whether it be implant-based or autologous tissue reconstruction, from a variety of donor sites and immediate lymphatic reconstruction at the time of axillary lymph node dissection. We are also participating in cutting edge research and building a database of outcomes following lymphatic surgery in order to contribute to the growing body of literature. We are committed to constantly re-evaluating and improving our technique to stay at the forefront of our specialty, while optimizing outcomes for our patients.

References

1. Milton, S.H., Pedicled skin-flaps: the fallacy of the length: width ratio. Br J Surg, 1970. 57(7): p. 502-8.
2. Milton, S.H., Experimental studies on island flaps. 1. The surviving length. Plast Reconstr Surg, 1971. 48(6): p. 574-8.
3. Hartrampf, C.R., M. Scheflan, and P.W. Black, Breast reconstruction with a transverse abdominal island flap. Plast Reconstr Surg, 1982. 69(2): p. 216-25.
4. Taylor, G.I. and R.K. Daniel, The free flap: composite tissue transfer by vascular anastomosis. Aust N Z J Surg, 1973. 43(1): p. 1-3.
5. Holmstrom, H., The free abdominoplasty flap and its use in breast reconstruction. An experimental study and clinical case report. Scand J Plast Reconstr Surg, 1979. 13(3): p. 423-27.
6. Elliott, L.F., B. Raffel, and J. Wade, Segmental latissimus dorsi free flap: clinical applications. Ann Plast Surg, 1989. 23(3): p. 231-8.
7. Feller, A.M., Free TRAM. Results and abdominal wall function. Clin Plast Surg, 1994. 21(2): p. 223-32.
8. Allen, R.J. and P. Treece, Deep inferior epigastric perforator flap for breast reconstruction. Ann Plast Surg, 1994. 32(1): p. 32-8.
9. Granzow, J.W., et al., Breast reconstruction with the deep inferior epigastric perforator flap: history and an update on current technique. J Plast Reconstr Aesthet Surg, 2006. 59(6): p. 571-9.
10. Gill, P.S., et al., A 10-year retrospective review of 758 DIEP flaps for breast reconstruction. Plast Reconstr Surg, 2004. 113(4): p. 1153-60.
11. Dayan, J.H. and R.J. Allen, Jr., Lower Extremity Free Flaps for Breast Reconstruction. Plast Reconstr Surg, 2017. 140(5S Advances in Breast Reconstruction): p. 77S-86S.
12. Boccardo, F., et al., Lymphedema microsurgical preventive healing approach: a new technique for primary prevention of arm lymphedema after mastectomy. Ann Surg Oncol, 2009. 16(3): p. 703-8.

Disclosures

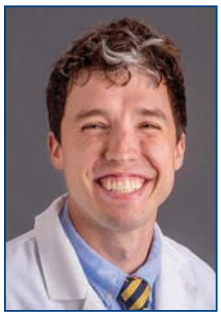
None reported. **MM**

Review on the Myopia Pandemic: Epidemiology, Risk Factors, and Prevention

by James R. Landreneau, MD, Nathan P. Hesemann, MD & Maggie A. Cardonell, MD

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Preventative therapies for myopia progression are aimed at screening at-risk patients at a young age in order to halt axial growth, in return reducing one's degree of myopia.



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Abstract

Nearsightedness, or myopia, is becoming more prevalent worldwide. The eye experiences dynamic growth throughout adolescence, but the etiopathogenesis of myopia progression is not fully understood. Myopia is associated with several pathologic eye conditions, leading to irreversible vision loss. Treatment for preventing myopia progression is reliant on effective screening and initiating treatment early in life. This article will review risk factors for myopia progression and discuss treatment strategies that are most effective in halting its spread.

Background

One of the more staggering trends in ophthalmic care has been the rapid global rise of myopia, also called nearsightedness.[1] The prevalence of myopia exceeds 28% globally, and there are projections that approximately half of the world's population, or five billion people, will have some degree of myopia by 2050.[2] With the increase of myopia worldwide, it is concerning that an estimated 10% of the world's population, or more than 700 million people, do not receive adequate therapy.[3] Treatment options for myopia include spectacle correction, contact lenses, or refractive surgery to correct a patient's refractive error and improve distance vision.

Individuals who are myopic, especially those who are highly myopic with a spherical equivalent of -6.00D or more, have more than just the need for spectacle correction as they may also have chronic pathologic visual changes that include retinal detachment, myopic macular degeneration, glaucoma, amblyopia, and early-onset cataract. Highly myopic individuals are 20 times more likely to have a retinal detachment in their lifetime than an emmetropic individual.[6] Pathologic myopia, defined as having high myopia with irreversible retinal atrophy, affects approximately 1% of Caucasians and 1-3% of Asians.[4] An increased emphasis on slowing myopic progression with effective childhood screening has been adopted by clinicians in primary care, pediatrics, and ophthalmology.[5] Understanding the risk factors for myopia progression and the mechanisms controlling the eye's axial growth are key to developing therapies for myopia.

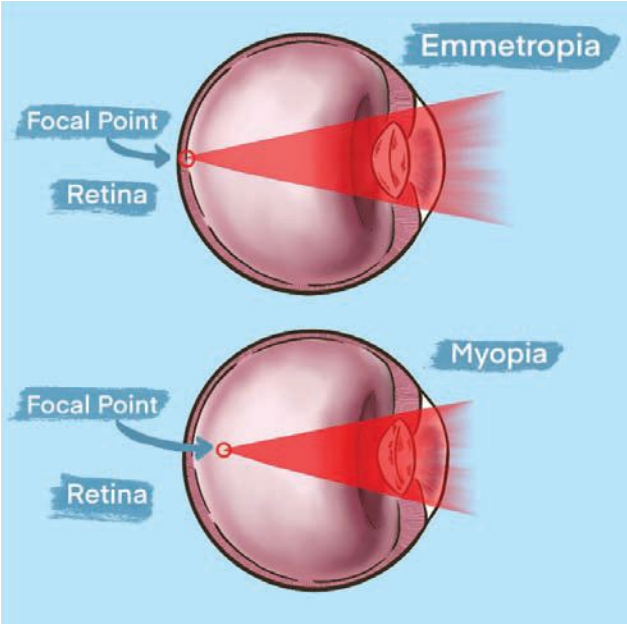


Figure 1. Emmetropia versus myopia. When viewing an object at distance, an emmetropic eye is able to focus a clear image on the retinal surface. In myopic eyes, the image is focused in front of the retinal surface.

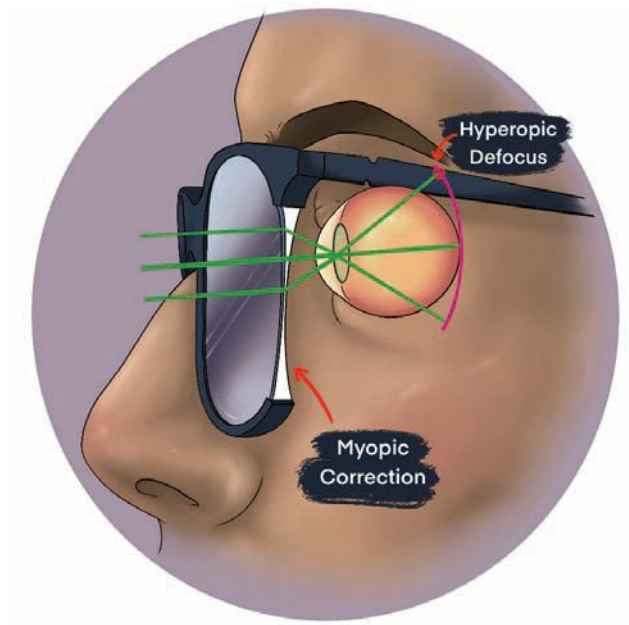


Figure 2. Myopic correction creating hyperopic defocus in the mid-peripheral retina. Hyperopic defocus is theorized as a primary driver for myopic progression.

The Goal of Emmetropization?

An eye that is focused clearly in the distance (20 feet or >) without correction is said to be emmetropic, and the regulatory process that achieves this goal is called emmetropization. In early development, the globe commonly grows spherically in all directions prior to beginning axial elongation with respect to the corneal and retinal axis.[6] The eye experiences dynamic growth throughout childhood and early adulthood. Myopia results in a visual focus landing in front of the retina, caused by either refractive or axial changes to the eye. A schematic showing the differences in focal points between emmetropia and myopia is shown in Figure 1.

This overshoot in eye power or growth, influenced by both environmental stimuli and genetic factors, is referred to as "myopization."[7] Refractive myopia is defined as having abnormally strong dioptric (D) power leading to a misplaced focused image in front of the retina. Axial myopia, the more common cause of myopia, also leads to a focused image in front of the retina due to excessive length of the eye. Therefore, the majority of preventative myopia therapy targets slowing the eye's axial growth during development.

There is evidence to support that myopia represents a dysregulated state influenced by external visual cues. Traditional negative-lens spectacle correction for myopia, has been shown to significantly alter ocular growth and refractive power in children.[8] When myopia correction is given to a patient, the eye's focal point at distance is adjusted more posteriorly in order to land onto the retinal surface and provide clarity for distance viewing. This myopic correction of the central retina incidentally creates hyperopic defocus in mid-peripheral retina with a focal point lying behind the retina as shown in Figure 2.

Hyperopic defocus in the mid-peripheral retina driven by negative lens-induced myopia in turn leads to posterior scleral remodeling, choroidal thinning, and eye lengthening. The mid-peripheral retina has been studied as one of the important locations for the visually-guided growth of the eye based on peripheral defocus leading to axial elongation in animal models.[9] The mechanisms by which the mid-peripheral retina modulates axial growth is incompletely understood. Treatment strategies aimed at creating myopic defocus at the mid-peripheral retina, meaning to have the eye's focal point rest in front of the retina, have proven successful in reducing myopic progression.[5,9,23,37-42,45-46] A comparison of hyperopic defocus versus myopic defocus is shown in Figure 3.

In addition to hyperopic peripheral defocus, other

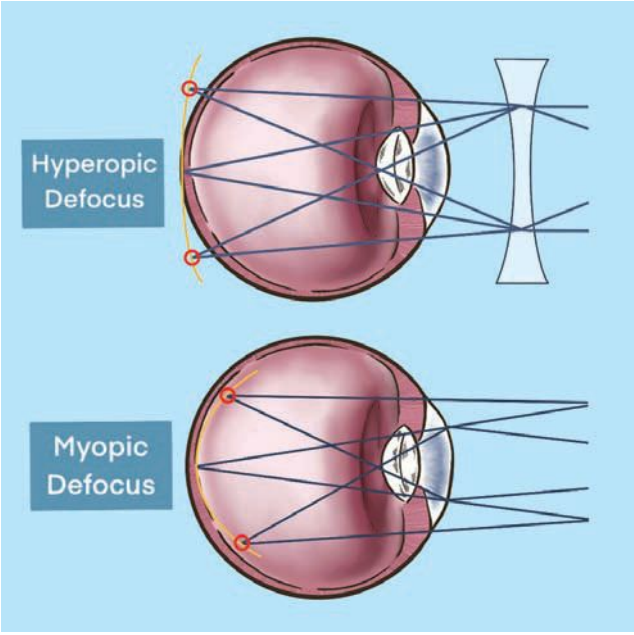


Figure 3. Hyperopic defocus versus myopia defocus. Hyperopic defocus with focal point resting behind mid-peripheral retina versus myopic defocus with focal point resting in front of mid-peripheral retina.

risk factors contributing to increased axial elongation include genetic factors, less outdoor time, weakened accommodation, and increased amount of near work.[10]

Risk factors

Age

Younger age at onset of myopia is the highest independent risk factor for myopia progression. Patients who have at least -1.25D of myopia, particularly if they are aged 6-7 years old, are at higher risk for faster progression when compared to older children.[11] The COMET study involved 426 ethnically diverse children with a baseline myopic spherical equivalent of -1.25D to -4.50D.[12] In this study, the mean age of myopia stabilization was 15.61 years. At the time of stabilization, the average amount of myopia was -4.87D. Children who showed myopic progression at age six to seven, had on average 1.70D more myopia at stabilization than children who showed similar progression starting at age eight and older. The vast majority of study participants (96%) received myopia stabilization by age 24.[12] The age to initiate treatment for myopia progression is still unknown, although the results of the COMET study helped show that starting preventative myopic therapy at a younger age may be advantageous. There are currently ongoing studies exploring the treatment of pre-myopic children with known risk factors for myopic progression in early childhood.[13]

Ethnicity

The prevalence of myopia worldwide varies greatly based on regional and ethnic differences. The prevalence of myopia exceeds 80% in some regions in East Asia, and there is a two-times higher prevalence of myopia in East Asians than in Caucasians of similar age.[14] In comparison, the estimated prevalence of myopia in studied African populations in 2020 <10%.[2] In the COMET study, the African American participant cohort had an earlier average age of myopia stabilization (13.82 years) and consequently the least amount of myopia at stabilization (-4.36D) when compared to other ethnic groups.[14]

Environmental Factors

Increased amount of time spent outdoors has been shown to be protective against the development of incident myopia.[15] Animal studies suggest ultraviolet light may inhibit axial elongation by stabilizing the sclera.[16] In a recent meta-analysis review of 25 papers investigating the relationship between outdoor time and myopia, it was shown that increased outdoor time was protective in the incidence of myopia but not effective in slowing the progression of myopia in eyes who were already myopic. Based on the study's dose-response analysis, spending 76 minutes a day outdoors resulted in a 50% incidence reduction of myopia when compared to control eyes.[17]

The association between near work and incidence of juvenile-onset myopia has been under investigation for several years. The CLEERE longitudinal study compared visual activities between emmetropic and incident myopic subjects.[18] This study concluded that there were little differences in the amount of near work between both groups before myopia onset. Following myopia onset, it was hypothesized that myopic patients adopted more near-work activities based off of their refractive error.[18] A meta-analysis of 27 studies found that more time spent doing near work increased an individual's odds of myopia. Specifically, the odds of myopia increased 2% for every one diopter-hour more near work performed each week.[19]

Parental Myopia

Several studies have investigated the association between parental myopia and their child's risk for developing myopia.[20-21, 22] A recent meta-analysis of 16 studies reviewing the link between parental myopia and juvenile myopia reported a statistically significant increased risk of myopia in children having one myopic parent (OR = 1.87) and two myopic parents (OR = 2.40).[23] Environmental influences, such as children adopting behavioral traits similar to their myopic parents, have been evaluated as additional risk factors for myopic development. Several genetic loci have been linked to ocular axial elongation.[24] The complex interaction between an individual's genes and behavioral habits with the patient's risk factor for myopic progression requires further investigation.

Preventative Therapies

Preventative therapy for myopia progression currently has three aims: to screen patients with risk factors for myopia progression, to stabilize myopic progression, and to provide optical correction for healthy visual development. There are both medical and optical therapies available which meet that preventative goal, while surgical options for myopia control remain under investigation. In recent literature, scleral crosslinking using topical riboflavin and UV-A light have shown promising results in reducing axial elongation in animal models.[25] Posterior scleral contraction surgery with scleral grafts have successfully reduced myopic and axial length progression in limited human studies.[26] The COMET study proposed that using progressive addition bifocal lenses (PALs) in children could help reduce myopic progression by treating high accommodative lag seen in myopic patients with near-vision tasks.[12] Unfortunately, myopic progression in the PAL-treated group was only reduced by a non-significant 0.20D when compared to single-vision corrective lens (control group) over a 3-year span.[27] Despite the insignificant reduction in myopic progression, the COMET study proved that optical therapies can aid in controlling axial growth. The following contemporary medical and optical treatments have shown superiority in controlling myopic progression.

Atropine Ophthalmic Drops

Atropine reduces accommodation and increases pupillary diameter. In early studies theorizing the link between accommodation and myopia, low concentration atropine was used to determine if blocking accommodation could help control myopic progression.[28] Several experimental trials have since shown that there is a non-accommodative mechanism in the control of myopia and the mechanism of action of atropine is poorly understood.[29-30] Despite this lack of clarity about how atropine therapy works, comparative studies exploring treatment options in controlling myopic progression have proven the efficacy and superiority of atropine versus other alternative treatments.[31] In the ATOM trials, various low-dose concentrations of topical atropine proved to be beneficial in slowing axial elongation and myopia progression in Asian children with early-onset myopia.[32-33] The ATOM1 studied the effect of 1% atropine, while the ATOM2 study stratified treated subjects into receiving 0.01%, 0.1%, and 0.5%. In the initial two-year treatment period in the ATOM2 study, higher concentrations of atropine were more effective in controlling myopia progression, with an average progression of -0.49D, -0.38D, and -0.30D in the 0.01%, 0.1%, and 0.5% concentration groups, respectively. In the following one-year washout period there was less rebound myopic progression in the 0.01% atropine cohort.[34] Further studies have shown using 0.01% atropine proved more effective in slowing myopic progression, prevented less rebound myopia after cessation of treatment, and reduced visual side effects.[35]

The more recent LAMP study compared lower atropine concentrations of 0.01%, 0.025%, and 0.05% on myopia progression.[36] Using a similar patient demographic as the ATOM study, the LAMP study found that the 0.05% atropine was doubly more efficacious as 0.01% atropine, showing -1.12D, -0.85D, and -0.55D of myopic progression in a two-year treatment period in the 0.01%, 0.025%, and 0.05% concentration groups, respectively.

Side-effects for atropine therapy include, but are not limited to, photophobia, poor near visual acuity, increased pupillary diameter, and headache.[37] Adverse effects to atropine therapy are concentration-dependent. For example, the incidence of photophobia is reported as 6.3% in 0.01% atropine therapy as compared to 43.1% in doses greater than 0.5%.[38] There may be additional side-effects of long-term administration of antimuscarinic agents on ocular tissue that have not been reported.[39] The side-effect profile

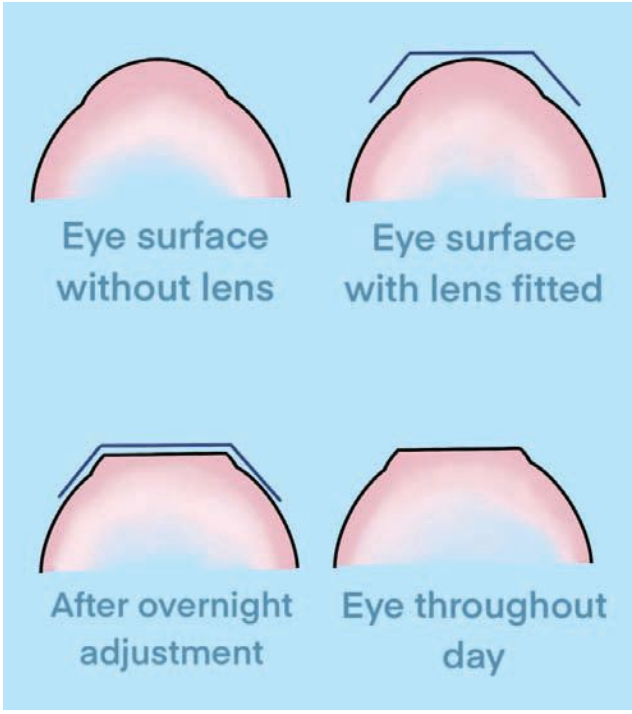


Figure 4. Orthokeratology remodeling. Orthokeratology RGP lens temporary remodeling of the corneal epithelium. The base curve of the central cornea is flattened, leading to a reduction in corneal power. This change allows for a transient reduction in myopia for the user.

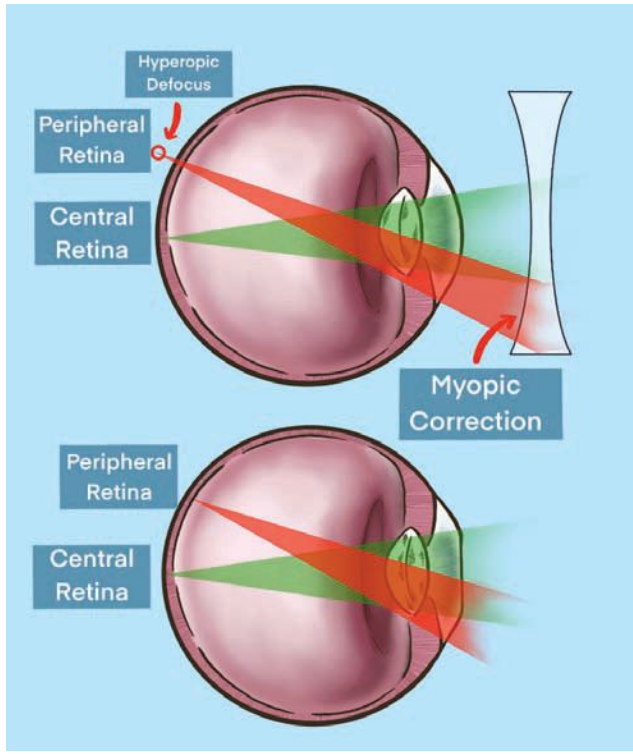


Figure 5. Traditional myopic correction versus orthokeratology correction. Traditional negative-lens myopia correction stimulating hyperopic defocus (top eye) versus Orthokeratology-treated eye reducing hyperopic peripheral defocus (bottom eye).

of atropine should be considered when monitoring compliance to atropine therapy in treated patients.

Orthokeratology

Orthokeratology is the use of an overnight rigid gas permeable (RGP) contact lens for the treatment of low- to moderate-myopia. During overnight wear remodeling of the corneal epithelial surface into a flatter, more oblate and less powerful refractive surface occurs and creates a transient reduction in myopia during the day that lasts until the cornea returns to its natural shape. Following central corneal flattening the focal point of the eye is shifted onto the retinal surface. Orthokeratology corneal remodeling is shown in Figure 4.

Case studies investigating children with myopia who wore an orthokeratology lens in one eye with no correction in the fellow eye showed axial length reduction in the treated eyes when compared to control eyes.[40-41] The ROMIO study enrolled 102 myopic patients aged 6 to 10 years to be in orthokeratology lenses or single-vision glasses for a two-year study period.[42] On average, the orthokeratology-treated group had slower increase in axial elongation by approximately 43% compared to the single vision-glasses group. A recent meta-analysis reviewing 13 prospective randomized clinical trials found that orthokeratology was effective in reducing axial elongation, on average, by 50% over a two-year period.[43] In addition to temporarily flattening the central cornea, orthokeratology also changes the peripheral refractive status of the cornea resulting in less hyperopic defocus of the peripheral retina. This is hypothesized to be a tool in helping control myopic progression as shown in Figure 5.

The rate of rebound myopia and axial elongation after discontinuation of orthokeratology treatment is underreported in orthokeratology literature.[44]

The safety profile of orthokeratology is reassuring; however, the risk of microbial keratitis with overnight wear or improper handling leading to contamination of a contact lens in children can be visually devastating.[45] There is a higher risk of corneal infection with

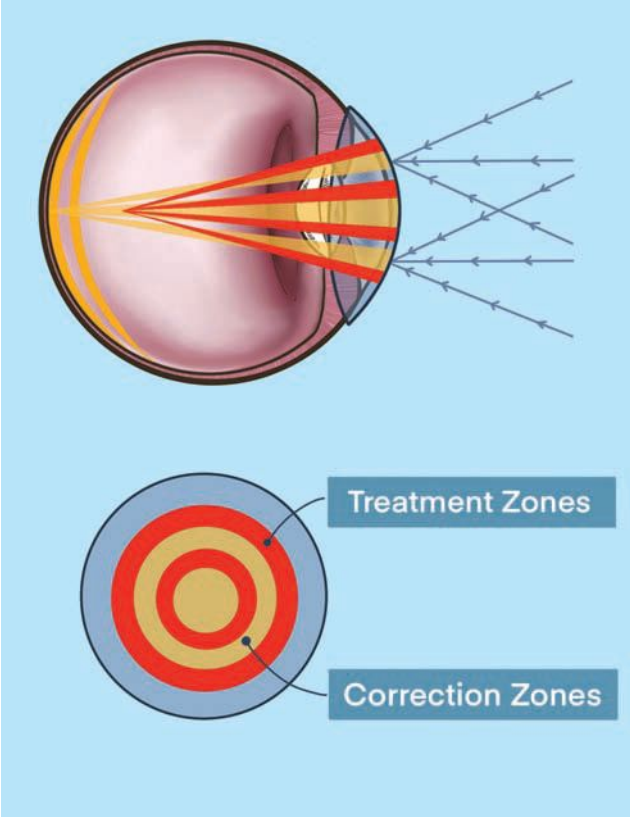


Figure 6. MiSight dual-focus optical design. The correction zones (yellow) allow for clear distance viewing for myopia. The treatment zones (red) have higher add-powers to stimulate myopic defocus.

orthokeratology-wear with improper lens or hand hygiene, using expired contact solution, and exposure to a nonsterile solution.[46] Other possible adverse effects of orthokeratology include contact lens irritation, dry eye, and corneal epithelial iron deposition.

Contact Lenses (MiSight)

Over the past decade, multifocal, aspheric optics, and bifocal contact lenses have all shown modest potential in the treatment for myopia.[47] In 2019, the FDA approved MiSight as the first contact lens available in the treatment for myopia progression.[48] The MiSight lens design has "dual-focus optics" in which there is are two zones of myopia correction for all gaze positions and two neighboring concentric treatment zones to eliminate peripheral hyperopic defocus.[49] This novel lens design ensures for proper distance visual acuity and normal accommodation for near work in the central corrective zone while simultaneously eliminating hyperopic defocus with plus-powered peripheral rings in the peripheral

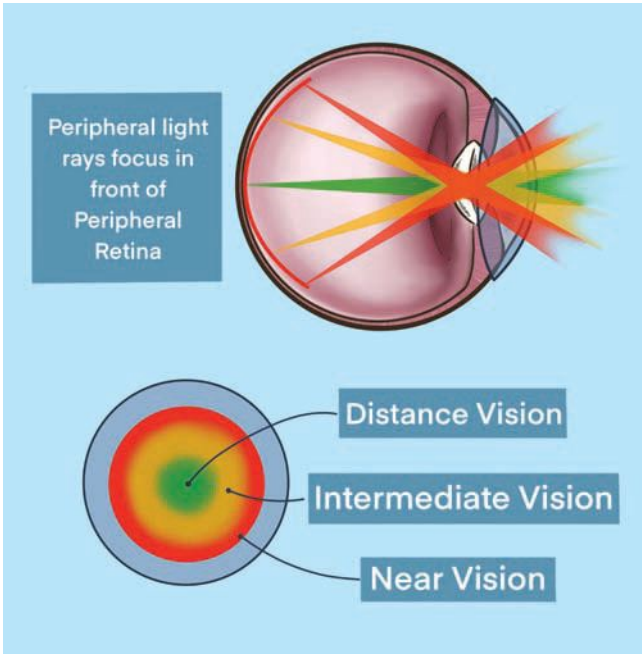


Figure 7. Multifocal concentric ring contact lens design. Central vision correction followed by concentric rings helping with intermediate- and near-vision.

corrective zone. The MiSight design and optical schematic is shown in Figure 6.

In comparison to other soft contact lenses, including bifocal contact lenses, used in the treatment for myopia control, MiSight has shown superiority in slowing myopic progression and slowing axial elongation. In a three-year randomized double-masked clinical trial comparing the MiSight lens to control lens, MiSight showed less myopic progression by 0.40D, 0.54D, and 0.73D at 12 months, 24 months, and 36 months, respectively.[50] Additionally, there was an average of 0.32mm less axial elongation in the MiSight treated group.

Similar risks apply to MiSight treatment for preventing myopia as orthokeratology lenses, including microbial keratitis and noncompliance with lens maintenance or usage. The preliminary safety profile of MiSight lenses is encouraging and further long-term studies are needed to determine the viability of this treatment for myopia control.[44]

Multifocal Contact Lenses

There are several multifocal contact lens designs, each engineered to provide a spectrum of clear vision for both near- and distance-vision tasks. With the multifocal concentric ring design, the center circle

of the lens provides distance clarity with neighboring concentric rings offering intermediate and near clarity in a stepwise fashion dependent on the add-power of the respective lens. An example of this contact lens design is shown in Figure 7.

Recently, the BLINK trial aimed to determine whether soft concentric multifocal contact lenses can slow myopic progression in children and whether the strength of the add-power in the multifocal lens was of importance.[51] Similar to MiSight, the central tenet in the BLINK study was using peripheral add-power in the multifocal lens to reduce hyperopic defocus to control axial growth. Over a 3-year investigative period using an ethnically diverse American study population, high add-power (+2.50D) slowed myopic progression by 0.45D and reduced axial length by 0.23mm compared to single-vision contact lenses (control group).

Conclusions

Several pathologic eye conditions are associated with myopia, many of which are related to the eye's dysregulated axial lengthening. Preventative therapies for myopia progression are aimed at screening at-risk patients at a young age in order to halt axial growth, in return reducing one's degree of myopia.

Successful treatments for reducing myopia progression have targeted reducing the amount of hyperopic defocus, in which light focused behind the peripheral retina. This article described therapeutic regimens – orthokeratology, atropine ophthalmic drops, multifocal contact lenses, and dual-focus optical contact lenses – which are commonly used and have shown success in treating myopia progression.

Understanding myopia and selecting patients who are at high-risk for myopic progression for treatment is a shared responsibility by primary care providers, opticians, and ophthalmologists. As we continue to move forward with newer treatments and more sophisticated screening, there is hope for a reduction, or reversal, of this optical pandemic.

Editor's Addendum

As the Journal went to press another article was published about myopia during the pandemic. It found major increases in children age 6 to 13 years during COVID-19 "owing to substantially decreased time spent outdoors and increased screen time at home." Interested readers are referred to: Wang J et al. Progression of Myopia in School-Aged Children After COVID-19 Home Confinement. JAMA Ophthalmol. 2021:139(3):293-300

Reference

1. Foster PJ, Jiang Y. Epidemiology of myopia. Eye (Lond). 2014;28(2):202-208.
2. Holden BA, Fricke TR, Wilson DA, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016;123(5):1036-1042.
3. Fricke TR, Holden BA, Wilson DA, et al. Global cost of correcting vision impairment from uncorrected refractive error. Bull World Health Organ. 2012;90(10):728-738.
4. Dhakal R, Goud A, Narayanan R, Verkicharla PK. Patterns of posterior ocular complications in myopic eyes of Indian population. Sci Rep. 2018;8(1):13700.
5. Jonas DE, Amick HR, Wallace IF, et al. Vision Screening in Children Aged 6 Months to 5 Years: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2017;318(9):845-858.
6. Wu PC, Chuang MN, Choi J, et al. Update in myopia and treatment strategy of atropine use in myopia control. Eye (Lond). 2019;33(1):3-13.
7. Wallman J, Winawer J. Homeostasis of eye growth and the question of myopia [published correction appears in Neuron. 2012 Apr 12;74(1):207]. Neuron. 2004;43(4):447-468.
8. Smith EL 3rd. Optical treatment strategies to slow myopia progression: effects of the visual extent of the optical treatment zone. Exp Eye Res. 2013;114:77-88.
9. Moore KE, Benoit JS, Berntsen DA. Spherical Soft Contact Lens Designs and Peripheral Defocus in Myopic Eyes. Optom Vis Sci. 2017;94(3):370-379.
10. Hou W, Norton TT, Hyman L, Gwiazda J; COMET Group. Axial Elongation in Myopic Children and its Association With Myopia Progression in the Correction of Myopia Evaluation Trial. Eye Contact Lens. 2018;44(4):248-259.
11. Hyman L, Gwiazda J, Hussein M, et al. Relationship of age, sex, and ethnicity with myopia progression and axial elongation in the correction of myopia evaluation trial. Arch Ophthalmol. 2005;123(7):977-987.
12. COMET Group. Myopia stabilization and associated factors among participants in the Correction of Myopia Evaluation Trial (COMET). Invest Ophthalmol Vis Sci. 2013;54(13):7871-7884.
13. Chia, A et al.. The Use of Atropine 0.01% in the Prevention and Control of Myopia (ATOM3). https://clinicaltrials.gov/ct2/show/NCT03140358.
14. Rudnicka AR, Kapetanakis VV, Wathern AK, et al. Global variations and time trends in the prevalence of childhood myopia, a systematic review and quantitative meta-analysis: implications for aetiology and early prevention. Br J Ophthalmol. 2016;100(7):882-890.
15. Sherwin JC, Reacher MH, Keogh RH, Khawaja AP, Mackey DA, Foster PJ. The association between time spent outdoors and myopia in children and adolescents: a systematic review and meta-analysis. Ophthalmology. 2012;119(10):2141-2151.
16. Li X, Wu M, Zhang L, Liu H, Zhang L, He J. Riboflavin and ultraviolet A irradiation for the prevention of progressive myopia in a guinea pig model. Exp Eye Res. 2017;165:1-6.
17. Xiong S, Sankaridurg P, Naduvilath T, et al. Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review. Acta Ophthalmol. 2017;95(6):551-566.
18. Jones-Jordan LA, Mitchell GL, Cotter SA, et al. Visual activity before and after the onset of juvenile myopia. Invest Ophthalmol Vis Sci. 2011;52(3):1841-1850.
19. Huang HM, Chang DS, Wu PC. The Association between Near Work Activities and Myopia in Children-A Systematic Review and Meta-Analysis. PLoS One. 2015;10(10):e0140419.
20. Jones-Jordan LA, Sinnott LT, Manny RE, et al. Early childhood refractive error and parental history of myopia as predictors of myopia. Invest Ophthalmol Vis Sci. 2010;51(1):115-121.
21. Pacella R, McLellan J, Grice K, Del Bono EA, Wiggs JL, Gwiazda JE. Role of genetic factors in the etiology of juvenile-onset myopia based on a longitudinal study of refractive error. Optom Vis Sci. 1999;76(6):381-386.
22. Kurtz D, Hyman L, Gwiazda JE, et al. Role of parental myopia in the progression of myopia and its interaction with treatment in COMET children. Invest Ophthalmol Vis Sci. 2007;48(2):562-570.
23. Zhang X, Qu X, Zhou X. Association between parental myopia and the risk of myopia in a child. Exp Ther Med. 2015;9(6):2420-2428.

BOOK REVIEW

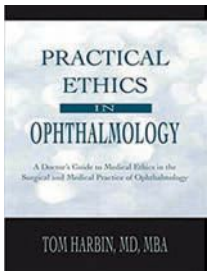
Practical Ethics in Ophthalmology

Pond Reads Press
ISBN: 978-1643438429

by Tom Harbin, MD, MBA

Reviewed by John C. Hagan, III, MD, FAAO, FACS, Ophthalmologist

The Oath of Hippocrates is no longer an adequate lodestar for the Ophthalmologist Eye MD. Even the most honest and ethical physician must face complex, nuanced situations where reference to this short, easy to read book will be useful. In such situations the patient, the physician and society will all benefit. I would like to see this book distributed by Departments of Ophthalmology to all their students, residents, fellows, and faculty. Of course the irony of this subject is that the ophthalmologists that need it the most (unnecessary surgery, fraudulent billing, practicing under the influence of alcohol-drugs, sexual abuse of staff-patients, etc.) will never consider serious perusal of this important new text. There is much conflation with general medical ethics and physicians in other branches of medicine would find this succinct book valuable as well. As with his other best-selling book, *Waking Up Blind: Lawsuits Over Eye Surgery* (Langdon Street Press, 2009), Dr. Harbin's focus on ethics will make us better physicians-ophthalmologists and improve the quality of care we render. **MM**



24. Wojciechowski R. Nature and nurture: the complex genetics of myopia and refractive error. Clin Genet. 2011;79(4):301-320.
25. Dotan A, Kremer I, Livnat T, Zigler A, Weinberger D, Bourla D. Scleral cross-linking using riboflavin and ultraviolet-a radiation for prevention of progressive myopia in a rabbit model. Exp Eye Res. 2014;127:190-195.
26. Su Y, Pan A, Wu Y, Zhu S, Zheng L, Xue A. The efficacy of posterior scleral contraction in controlling high myopia in young people. Am J Transl Res. 2018;10(11):3628-3634
27. Gwiazda J, Hyman L, Hussein M, et al. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. Invest Ophthalmol Vis Sci. 2003;44(4):1492-1500.
28. Donders F. On the Anomalies of accommodation and refraction of the eye. London: The New Sydenham Society; 1864.
29. Raviola E, Wiesel TN. Neural control of eye growth and experimental myopia in primates. Ciba Found Symp. 1990;155:22-44.
30. McBrien NA, Moghaddam HO, New R, Williams LR. Experimental myopia in a diurnal mammal (Sciurus carolinensis) with no accommodative ability. J Physiol. 1993;469:427-441.
31. Huang J, Wen D, Wang Q, et al. Efficacy Comparison of 16 Interventions for Myopia Control in Children: A Network Meta-analysis. Ophthalmology. 2016;123(4):697-708.
32. Chua WH, Balakrishnan V, Chan YH, et al. Atropine for the treatment of childhood myopia. Ophthalmology. 2006;113(12):2285-2291.
33. Chia A, Chua WH, Cheung YB, et al. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). Ophthalmology. 2012;119(2):347-354.
34. Chia A, Chua WH, Wen L, Fong A, Goon YY, Tan D. Atropine for the treatment of childhood myopia: changes after stopping atropine 0.01%, 0.1% and 0.5%. Am J Ophthalmol. 2014;157(2):451-457.e1.
35. Chia A, Lu QS, Tan D. Five-Year Clinical Trial on Atropine for the Treatment of Myopia 2: Myopia Control with Atropine 0.01% Eyedrops. Ophthalmology. 2016;123(2):391-399.
36. Yam JC, Li FF, Zhang X, et al. Two-Year Clinical Trial of the Low-Concentration Atropine for Myopia Progression (LAMP) Study: Phase 2 Report. Ophthalmology. 2020;127(7):910-919.
37. Tan D, Tay SA, Loh KL, Chia A. Topical Atropine in the Control of Myopia. Asia Pac J Ophthalmol (Phila). 2016;5(6):424-428.
38. Gong Q, Janowski M, Luo M, et al. Efficacy and Adverse Effects of Atropine in Childhood Myopia: A Meta-analysis. JAMA Ophthalmol. 2017;135(6):624-630.
39. Anstice NS, Phillips JR. Effect of dual-focus soft contact lens wear on axial myopia progression in children. Ophthalmology. 2011;118(6):1152-1161.
40. Cheung SW, Cho P, Fan D. Asymmetrical increase in axial length in the two eyes of a monocular orthokeratology patient. Optom Vis Sci. 2004;81(9):653-656.
41. Cho P, Cheung SW, Edwards M. The longitudinal orthokeratology research in children (LORIC) in Hong Kong: a pilot study on refractive changes and myopic control. Curr Eye Res. 2005;30(1):71-80.
42. Cho P, Cheung SW. Retardation of myopia in Orthokeratology (ROMIO) study: a 2-year randomized clinical trial. Invest Ophthalmol Vis Sci. 2012;53(11):7077-7085.
43. VanderVeen DK, Kraker RT, Pineles SL, et al. Use of Orthokeratology for the Prevention of Myopic Progression in Children: A Report by the American Academy of Ophthalmology. Ophthalmology. 2019;126(4):623-636.
44. Swarbrick HA, Alharbi A, Watt K, Lum E, Kang P. Myopia control during orthokeratology lens wear in children using a novel study design. Ophthalmology. 2015;122(3):620-630.
45. Liu YM, Xie P. The Safety of Orthokeratology--A Systematic Review. Eye Contact Lens. 2016;42(1):35-42.
46. Jun J, Zhiwen B, Feifu W, Lili L, Fan L. Level of Compliance in Orthokeratology. Eye Contact Lens. 2018;44(5):330-334.
47. Walline JJ, Gaume Giannoni A, Sinnott LT, et al. A Randomized Trial of Soft Multifocal Contact Lenses for Myopia Control: Baseline Data and Methods. Optom Vis Sci. 2017;94(9):856-866.
48. FDA approves first contact lens indicated to slow the progression of nearsightedness in children. (2019). Retrieved from https://www.fda.gov/news-events/press-announcements/fda-approves-first-contact-lens-indicated-slow-progression-nearsightedness-children.
49. Ruiz-Pomeda A, Pérez-Sánchez B, Valls I, Prieto-Garrido FL, Gutiérrez-Ortega R, Villa-Collar C. MiSight Assessment Study Spain (MASS). A 2-year randomized clinical trial. Graefes Arch Clin Exp Ophthalmol.
50. Chamberlain P, Peixoto-de-Matos SC, Logan NS, Ngo C, Jones D, Young G. A 3-year Randomized Clinical Trial of MiSight Lenses for Myopia Control. Optom Vis Sci. 2019;96(8):556-567.
51. Walline JJ, Walker MK, Mutti DO, et al. Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children: The BLINK Randomized Clinical Trial. JAMA. 2020;324(6):571-580.

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Disclosure

None reported. **MM**

DIETS & HEALTH MINISERIES

Fasting Off "The COVID-19"

by Sean Mccalmon, DO, Suguni Loku Galappaththy, MD, Sheetal Bulchandani, MD & Peminda K. Cabandugama, MD

UMKC School of Medicine

Intermittent fasting not only provides a cost effective method of losing weight, it also has long lasting health benefits.



Sean Mccalmon, DO, is an Endocrinology Fellow at the University of Missouri-Kansas City. **Suguni Loku Galappaththy, MD**, and **Sheetal Bulchandani MD**, are Internal Medicine Residents at the University of Missouri-Kansas City. Peminda K. Cabandugama, MD, (above), is an Assistant Professor of Internal Medicine and Faculty Member of the Endocrinology Fellowship Program at the University of Missouri-Kansas City, Kansas City, Missouri, and is the Vice President of the Midwest Obesity Society.

Abstract

The SARS-CoV-2 outbreak has led to an increase in sedentary lifestyles compounded with the loss of access to public exercise facilities and limited fresh grocery supply. With the multitude of possible diet options available, how do you choose one that works with your lifestyle, financial means, and ultimately proves to be most effective? In this article, we review the medical benefits and challenges of several different types of fasting diets that can be adopted by the general public.

Introduction

The socioeconomic fallout of the SARS-CoV-2 outbreak led to over 20 million Americans unemployed at one point and millions of others under months-long social distancing or quarantine measures.[8] This change has led to an increase in sedentary lifestyles compounded with the loss of access to public exercise facilities and limited fresh grocery supply. Secondary effects of quarantine such as weight gain, higher A1c levels, increased insulin resistance and loss of daily activities lead to lifestyle changes which result in clinically significant exacerbations of chronic conditions.

Obesity, diabetes and the sequelae of these conditions have long been at the forefront of medical care in the U.S. The COVID-19 pandemic left many Americans at home, engaging in unhealthy lifestyle habits, and resulted in the weight gain that is now colloquially referred to as "the COVID-19". This is in reference to an average 19-pound weight gain—a setback which erodes the milestones healthcare has gained on chronic inflammatory conditions.

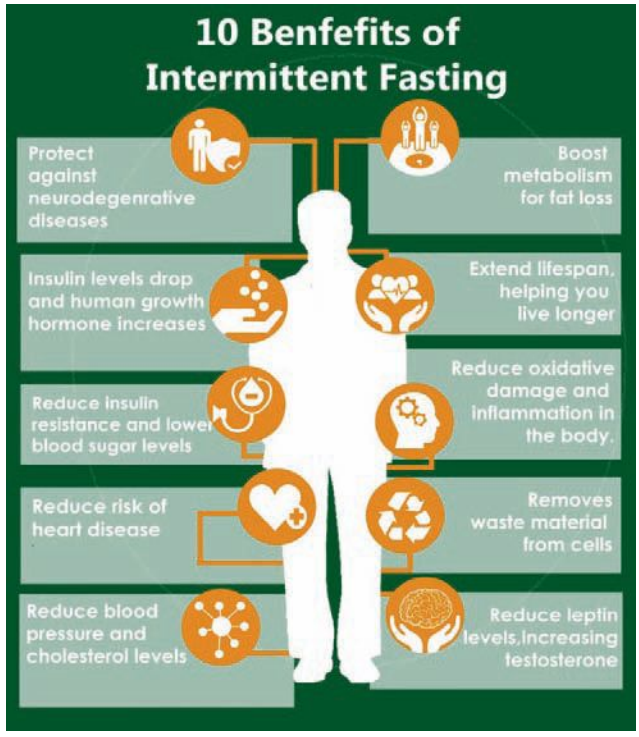
Prior to this pandemic, the United States was embroiled in a battle with the epidemic of obesity. Trends from 2017-2018 showed roughly 45% of middle-aged adults and 40% of adults in their 20s classified as obese showing an overall worsening trajectory toward a majority-obese population in the United States.[3] Overall mortality increases by 30% for every 5 kg/m^2 of Body Mass Index (BMI) above 25 kg/m.[2] Obesity has multiple complications with an effect on nearly every organ system ranging from depression, cardiovascular disease, chronic obstructive pulmonary disease, dyslipidemia, diabetes mellitus, urinary incontinence, degenerative joint disease, and various types of cancer, to name a few. [13]

With the multitude of possible diet options available, how do you choose one that works with your lifestyle, financial means, and ultimately proves to be most effective? Some may choose specific dietary changes such as the popular Keto Diet, which includes foods high in fat and protein and low in carbohydrates. Another feasible alternative would

be the Mediterranean Diet, which includes mostly vegetables, fish, nuts, and grains with poultry products in moderation, while rarely eating beef products, processed foods, and sugary drinks. With U.S. data showing acute worsening of eating and lifestyle habits, we postulate that a cultural shift toward differing styles of fasting could spark a collective movement toward weight loss after quarantine.

In this article, we review the medical benefits and challenges of several different types of fasting diets that can easily be adopted by the general public. Some of these may be attempted without the need for significant clinical guidance or feedback to reach maximal efficacy. However, we always encourage patients to confer with their healthcare provider before starting any new diets.

A special note should be made at this point that with all of the fasting diets; it is recommended to avoid processed foods, breads, pastas, white rice, and excess fats. Additionally, pregnant or breastfeeding women, children, and teenagers should avoid aggressive fasting strategies.



Why Would You Fast?

Intermittent fasting not only provides a cost-effective method of losing weight, it also has long lasting health benefits. Several dietary interventions have shown to improve cardiovascular risk involving limiting calorie intake during a given period. Participants have seen improvements in weight, blood pressure, and insulin sensitivity. Intermittent fasting is similar to caloric restriction, with the subtle caveat that it focuses on the timing of consumption of the meals. The Oxidative Stress Hypothesis is the theory that decreased energy intake causes mitochondria to produce fewer free radicals.[4] Multiple studies have shown that obese patients undergoing intermittent fasting techniques have resulted with lower levels of inflammation markers and higher levels of antioxidants.[12]

Types of Fasts

The Circadian Rhythm Fast

The Circadian Rhythm hypothesis involves timing of fasting allowing for optimization of organ systems. Eating later in the day is associated with higher postprandial glucose levels which have been shown to increase the risk of diabetes mellitus. Fasting regimens that allow eating during the middle of the day had better weight loss with less adipose, better glucose control, lower lipid levels and decreased inflammation. Conversely, time restriction that only allows late afternoon or evening intake (after 4:00 p.m.) saw no improvement and worsening glucose control, blood pressure, and lipid levels.[4] One small study found that in just 10 days of circadian misalignment (described as 12 hours out of phase from habitual eating and sleeping times), subjects had decreased leptin (17%), increased blood glucose (6%) despite increased insulin levels (22%).[5] This study drew parallels to jet lag and shift work.

The 16:8 Fast

One popular strategy of intermittent fasting is known as the 16:8 Method, implying 16 hours of the day is dedicated towards fasting while restricting food consumption to an eight-hour window. There are no specific food recommendations or restrictions during the eight-hour feeding window, however, it is recommended that within this window three healthy meals are consumed.[9] When applied to a normal working schedule, it can be achieved with an eating window between 9:00 a.m. to 5:00 p.m. For most people, this simply means eating dinner earlier in the day.

Time-restricted eating offers a method to lower energy intake without the tedious necessity of counting calories. One study, published in *Nutrition and Healthy Aging*, examined 23 obese participants who were allowed to eat during a restricted time interval of 10:00 a.m. to 6:00 p.m. for 12 weeks. Weight loss, as well as other parameters of metabolism were recorded and compared to a no intervention control group. The time restricted group saw decreases in body weight by 3%, and systolic blood pressure by 7 mmHg.[2] Another study involving 34 males were randomly assigned to time restricted feeding versus normal diet while undergoing resistance training regimen. The time-restricted group ate three meals at 1:00 p.m., 4:00 p.m., and 8:00 p.m. The normal diet group consumed their meals at 8:00 a.m., 1:00 p.m., and 8:00 p.m. Meals were composed of the same macronutrients for each group. Exercise consisted of three weekly sessions involving resistance training of different muscle groups for each session. After eight weeks, the time-restricted group saw a decrease in fat mass of 16.4% versus 2.8% in the normal diet group. There was similar fat-free mass maintenance among both groups.[10]

The 5:2 Fast

If fasting every day seems too daunting, the 5:2 Diet may be an appropriate strategy. With this intermittent fasting strategy, participants spend five days of the week eating regularly while restricting intake to 500 calories two days of the week.[7] This diet is appealing in that it does not involve an actual fast, and it can be spread throughout the week. For example, restricting calories on Monday and Thursday, or Wednesday and Saturday. Again, it is recommended that the five regular eating days include healthy foods. Reducing caloric intake to just 25% on fasting days can be achieved by eating three smaller meals, small breakfast and late lunch, or one single meal. It is recommended to consume foods high in fiber and protein in order to stay satisfied on fasting days. This method is intended for people interested in a less restrictive diet plan such as people who might feel lightheaded or fatigued with fasting.

A study published in the *International Journal of Obesity* compared 25% energy restriction in the form of intermittent or continuous. The study was conducted with 107 obese (BMI 30.6 kg/m^2) premenopausal women over the course of six months. The 25% intermittent-restriction group consumed 2710 KJ/d on two days per week, while the 25% continuous restriction group consumed 6276 KJ/day on seven days per week. The intermittent group saw weight loss of 6.4 Kg and the continuous group saw weight loss of 5.6 Kg. The study concluded that intermittent-energy restriction is as effective as continuous energy restriction with respect to weight loss, as well as insulin resistance.[6]

The Alternate Day Fast

For the more advanced intermittent fasting participants, fasting every other day during a full 24 hour period is an option. This is not recommended for beginning fasters due to the level of difficulty with compliance. A study published in *Obesity Society* involving Alternate Day Fasting randomized 64 participants into four different groups for 12 weeks. The four groups included Alternate Day Fasting, Exercise, Alternate Day Fasting and Exercise, and a control group. The combination group saw the most weight loss of 6 Kg with retained lean mass. The Alternate Day Fasting group saw weight loss of 3 Kg, and the exercise alone group only lost 1 Kg. LDL cholesterol decreased 12% and HDL increased 18% from baseline in the combination group.[11]

The Ramadan Fast

During the height of COVID-19, the religious fasting holiday of Ramadan was also occurring. Ramadan consists of fasting ~15 hours (dawn to sunset) per day for ~30 days straight. Studies have shown that the mortality of COVID-19 is due in part to a systemic hyper-inflammatory cytokine storm with increased IL-6, TNF-a, IL-1, IL-10. Multiple studies have shown that these proinflammatory cytokines are significantly reduced in men and women during Ramadan compared to before and after Ramadan.[1] One study in particular, involved 12 healthy males who underwent diurnal intermittent fasting during Ramadan and plasma levels of cytokines were recorded at baseline, fasting outside of Ramadan and during Ramadan. In this study, levels of IL-1B and IL-6 were significantly lower during fasting whether it was outside of Ramadan or during the social parameters of Ramadan.[14]

Conclusion

With obesity rates continuing to rise, and the restrictions placed by the COVID-19 pandemic

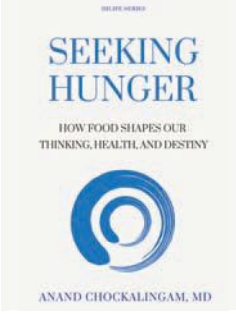
BOOK REVIEW

Seeking Hunger

by Anand Chockalingam, MD

HiLife Series
ISBN: 979-8574028438

Hunger has threatened, driven, and shaped our existence since the beginning of human history. However, our fast-paced society and modern culture have altered our relationship with food and hunger. While consumerism and urbanization have created new priorities and values for humankind, they have left us with little time to introspect and connect to our body.



In this short book, you will journey through humankind's relationship with hunger through the ages. You will understand how to relate to hunger on your terms to secure a lifetime of health and energy. Hunger is an invaluable life experience, and you will see why hunger is fundamental and natural to humans. In *Seeking Hunger*, you will discover the reason why we need hunger to live a full life.

This is the first book in the HiLifeJourney series to better health and a meaningful life. HiLifeJourney combines mindfulness, Siddha Yoga, and positive psychology with the latest cardiology research for holistic wellness.

Author Prof. Anand Chockalingam, MD, is a cardiologist at the University of Missouri, Columbia, and MSMA member. From his research into stress cardiomyopathy, mental health, and heart failure, he pioneered a self-inquiry-based program called 'Heartful Living' for cardiac patients with hypertension, diabetes, obesity, and heart failure.

Since 2015, this program has helped thousands of people world over discover lasting health, reduce their need for medication, and feel decades younger. It has helped doctors to become resilient, students to become confident, and individuals to improve their mindset and health. **MM**

limiting physical activity, it only makes sense that people are snacking more, showing an increase in the rates of depression, and gaining weight. With gym closures being a feature of the lockdowns, we recommend finding an at-home body weight exercise routine. Similarly, with restaurants not being open, we would recommend focusing on a healthier diet at home. These practices along with well-studied intermittent fasting strategies as outlined above are likely to lead to sustained weight loss in a cost-efficient manner; both facets that are currently necessary during the current global pandemic.

References

1. Mo'ez A-Islam, E. (2020). Ramadan intermittent fasting and immunity: An important topic in the era of COVID-19. Retrieved October 03, 2020, from http://www.thoracicmedicine.org/article.asp?issn=1817-1737;year=2020;volume=15;issue=3;spage=125;epage=133;aulast=Faris#ft10
2. Gabel, K. (2018, June 15). Effects of 8-hour time restricted feeding on body weight and metabolic disease risk factors in obese adults: A pilot study. Retrieved October 01, 2020, from https://content.iospress.com/download/nutrition-and-healthy-aging/nha170036?id=nutrition-and-healthy-aging%2Fnha170036
3. Hales, C. (2020, February). Prevalence of Obesity and Severe Obesity Among Adults: United States, 2017–2018. Retrieved September 30, 2020, from https://www.cdc.gov/nchs/products/databriefs/db360.htm
4. Dong, T. (2020, August 10). Intermittent Fasting: A Heart Healthy Dietary Pattern? Retrieved October 01, 2020, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7415631/
5. Scheer, F. (2009, March 17). Adverse metabolic and cardiovascular consequences of circadian misalignment. Retrieved October 03, 2020, from https://pubmed.ncbi.nlm.nih.gov/19255424/
6. Harvie, M. (2011, May). The effects of intermittent or continuous energy restriction on weight loss and metabolic disease risk markers: A randomized trial in young overweight women. Retrieved October 03, 2020, from https://pubmed.ncbi.nlm.nih.gov/20921964/
7. Diet Review: Intermittent Fasting for Weight Loss. (2019, May 22). Retrieved October 03, 2020, from https://www.hsph.harvard.edu/nutritionsource/healthy-weight/diet-reviews/intermittent-fasting/
8. Bureau of Labor Statistics, U.S. Department of Labor, The Economics Daily, Unemployment rate rises to record high 14.7 percent in April 2020 on the Internet at https://www.bls.gov/opub/ted/2020/unemployment-rate-rises-to-record-high-14-point-7-percent-in-april-2020.htm (visited September 27, 2020).
9. Olsen, N. (2020, January 17). A guide to 16:8 intermittent fasting. Retrieved October 03, 2020, from https://www.medicalnewstoday.com/articles/327398
10. Moro, T. (2016). Effects of eight weeks of time-restricted feeding (16/8) on basal metabolism, maximal strength, body composition, inflammation, and cardiovascular risk factors in resistance-trained males. Retrieved October 01, 2020, from https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-016-1044-0
11. Bhutani, S. (2013, May 29). Alternate day fasting and endurance exercise combine to reduce body weight and favorably alter plasma lipids in obese humans. Retrieved September 29, 2020, from https://pubmed.ncbi.nlm.nih.gov/23408502/
12. Johnson, J. (2007, December 14). Alternate day calorie restriction improves clinical findings and reduces markers of oxidative stress and inflammation in overweight adults with moderate asthma. Retrieved October 01, 2020, from https://pubmed.ncbi.nlm.nih.gov/17291990/
13. Obesity is a disease that can impact more than your patients' weight. (2020, February). Retrieved October 03, 2020, from https://www.rethinkobesity.com/impact-of-obesity/associated-risks-of-obesity.html
14. Almeneessier, A. (2019, December 10). The effects of diurnal intermittent fasting on proinflammatory cytokine levels while controlling for sleep/wake pattern, meal composition and energy expenditure. Retrieved October 03, 2020, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6903761/

Disclosure

None reported. **MM**

Tracheotomy Outcomes in the Medical Intensive Care Unit

by Arya W. Namin, MD, Brian P. Kinealy, MD, Brette C. Harding, MD, Mohammed M. Alnijoumi, MD & Laura M. Dooley, MD

Placing a tracheostomy can allow for less sedation and agitation, enhanced ability to produce speech, ability to take oral nutrition, increased patient comfort, ability to be transferred out of the ICU, and ease of replacement of tracheostomy tube.



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Abstract

This is a retrospective chart review of 161 MICU patients who underwent tracheotomy by the Otolaryngology service at the University of Missouri Hospital from April 2015 through March 2018. The objectives of this study were to describe long term outcomes of patients who underwent tracheotomy, and identify any clinical variables associated with these outcomes. One-year mortality was 37% (50/161), and on multivariate analysis only age (p=0.001) was associated with mortality.

Introduction

Mechanical ventilation for patients with acute respiratory failure in the intensive care unit (ICU) is delivered via endotracheal tube (ETT) or tracheostomy tube. In addition to pulmonary toilet, airway obstruction, and the need for secure surgical airway, indications for tracheotomy include anticipated prolonged ventilation or ventilatory problems. Patients requiring prolonged mechanical ventilation commonly are candidates for tracheostomy, a safe and routine surgical procedure, especially when performed on an elective basis.[1] While the surgical procedure itself is considered safe, inpatient mortality rates remain high after tracheostomy, on the order of 28 to 39%.[2–5] Other groups have shown that post-ICU mortality was increased in patients with a tracheostomy, although this may be due to confounding comorbidities that prevented decannulation and increased those patients' risk for death at baseline.[4,5]

Although data regarding the impact of tracheostomy on mortality remains conflicted, the idea that tracheostomy improves patient quality of life is well-supported. Compared to intubation, tracheostomy is associated with increased patient comfort, increased ease of tube replacement and suctioning, and the ability to transfer the patient from the ICU. Patient speech, mobility, and swallowing are enhanced following tracheostomy.[6] Tracheostomy is associated with a decrease in sedation time (from seven to one hour per day) with no increase in agitation.[7]

Tracheotomy is the most commonly performed operation in critically-ill patients, and approximately two-thirds of all tracheostomies performed are on critically-ill patients requiring mechanical ventilation in the ICU.[8-10] Describing outcomes such as inpatient decannulation, discharge disposition, and one-year mortality as well as identifying any clinical variables associated with these outcomes will allow

Table 1. Comorbidities, Clinical features, and Clinical Outcomes by Body Mass Index Category

	BMI <30	BMI 30-40	BMI > 40	P value
N	66	46	49	
Age	56.7	60.8	57.1	P=0.261
Sex				
Female	33 (50)	26 (57)	34 (69)	P=0.112
Male	33 (50)	20 (43)	15 (31)	
Technique				
Open	56 (85)	38 (83)	48 (98)	P=0.037*
Percutaneous	10 (15)	8 (17)	1 (2)	
Comorbidities				
T2DM	17 (26)	13 (28)	34 (69)	P<0.001*
Hypertension	36 (55)	32 (70)	35 (71)	P=0.114
Heart Failure	6 (9)	12 (26)	14 (29)	P=0.016*
CAD	18 (27)	19 (41)	16 (33)	P=0.298
PH	0 (0)	2 (4)	4 (8)	P=0.071
COPD	29 (44)	23 (50)	25 (51)	P=0.709
CKD	8 (12)	7 (15)	7 (78)	P=0.885
OSA	2 (3)	6 (13)	19 (39)	P<0.001*
APACHE II	16.7	16.9	16.9	P=0.990
Inpatient Decannulation	17 (26)	7 (15)	12 (24)	P=0.417
Disposition				
Home	18 (27)	6 (13)	13 (27)	P=0.097
Facility	32 (48)	32 (70)	27 (55)	
One Year Mortality	27 (41)	16 (35)	16 (33)	P=0.631

*Indicates statistical significance. Abbreviations: BMI, body mass index; T2DM, type 2 diabetes mellitus; CAD, coronary artery disease; PH, pulmonary hypertension; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; OSA, obstructive sleep apnea; APACHE II, Acute Physiology and Chronic Health Evaluation II.

for better preoperative counseling when discussing these difficult decisions. Additionally, as outcomes are becoming more intensely scrutinized by third-party payers, published data describing the outcomes of these patients is important. The objectives of this study are to report inpatient mortality and one-year mortality after tracheotomy in the medical intensive care unit (MICU) patient, and to identify any clinical features associated with one-year mortality. Additionally, outcomes regarding ventilator liberation, tracheotomy decannulation, and disposition are reported.

Methods

This study was approved by the University of Missouri Institutional Review Board. This is a case series with chart review of all MICU patients who underwent tracheotomy by the Otolaryngology service at the University of Missouri Hospital from April 2015 through March 2018. The operative notes, clinical notes, laboratory data, and vital signs were reviewed. Demographic, clinical, and follow-up data were collected. Percutaneous versus open technique and BMI were recorded. The world health organization has defined three subclasses of obesity: obese class 1 (BMI 30.00 – 34.99 kg/ m^2), obese class 2 (BMI 35.00 – 39.99 kg/ m^2), and obese class 3 (BMI ≥ 40.00 kg/ m^2).[11] For study purposes patients were classified as not obese (BMI < 30.00 kg/ m^2), class 1 or 2 obesity (BMI 30.00 – 39.99 kg/ m^2), and class 3 obesity (BMI ≥ 40.00 kg/ m^2). The presence or absence of the following medical comorbidities were recorded: type 2 diabetes mellitus (T2DM), hypertension, heart failure, coronary artery disease, pulmonary hypertension, chronic obstructive pulmonary disease, chronic kidney disease, and obstructive sleep apnea. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated for each patient.[12] The study outcome measures were time from tracheotomy to liberation from ventilator, capping tracheotomy, decannulation, MICU discharge, hospital discharge, duration of hospital admission, duration of MICU admission, discharge disposition, and one-year mortality.

Statistical Analysis

Mean age and APACHE II score were compared across BMI groups using analysis of variance. Sex, surgical technique, comorbidities, inpatient decannulation, disposition, and one-year mortality were compared across BMI groups using the Pearson

Table 2. Time in Days for Inpatient Care Transition Milestones

	BMI <30	BMI 30-40	BMI >40	P value
Tracheotomy to ventilator liberation	15.4	16.0	13.9	P=0.842
Tracheotomy to capping	21.0	24.2	25.9	P=0.481
Tracheotomy to decannulation	35.5	48.6	44.67	P=0.506
Tracheotomy to MICU discharge	13.7	17.1	16.2	P=0.415
Tracheotomy to hospital discharge	27.9	30.3	30.0	P=0.835
Hospital admission duration	41.1	43.2	42.0	P=0.896
MICU admission duration	26.8	30.0	28.2	P=0.574

Chi-Square test. Time from tracheotomy to liberation from ventilator, capping tracheotomy, decannulation, MICU discharge, hospital discharge, duration of hospital admission, and duration of MICU admission were compared across BMI groups using analysis of variance. Multivariable logistic regression was used to analyze the association of age, tracheotomy technique, BMI category, APACHE II score, and gender with one-year mortality. The statistical analysis was completed with IBM SPSS Statistics Version 25 (SPSS, Inc, and IBM Company, Armonk, New York, USA).

Results

A total of 161 MICU patients underwent tracheotomy during the study period. The mean age of patients included in the study was 58 years (range: 20 – 83 years). The study population was 58% (93/161) female and 42% (68/161) male. The mean BMI of patients included in the study was 35.2 kg/ m^2 (range: 15 – 89 kg/ m^2). Forty-one percent (66/161) of patients were not obese, 28.6% (46/161) were class 1 or 2 obese, and 30.4% (49/161) were class 3 obese (Table 1). Twelve percent (19/161) were done using a percutaneous technique, and those patients who were not obese were significantly more likely to undergo a tracheotomy using this technique (p=0.037). Sixty-nine percent (34/49) of patients with class 3 obesity had T2DM, while 26% (17/66) of non-obese patients had T2DM (p< 0.001). Twenty-nine percent (14/49) of class 3 obese patients had heart failure, while 9% (6/66) non-obese patients had heart failure (p=0.016). Thirty-nine percent (19/49) of class 3 obese patients had obstructive sleep apnea, which 3% (2/66) non-obese patients had obstructive sleep apnea (p< 0.001). Inpatient decannulation rates for non-obese, class 1 and 2 obese, and class three obese patients were 26% (17/66), 15% (7/46), and 24% (12/49); respectively (p=0.417). Discharge disposition to facility for non-obese, class 1 and 2 obese, and class three obese patients was 48% (32/66), 70% (32/46), and 55% (27/49); respectively (p=0.097). The overall inpatient mortality rate was 15% (24/161). The overall one-year mortality rate was 37% (59/161). One-year mortality for non-obese, class 1 and 2 obese, and class three obese patients was 41% (27/66), 35% (16/46), and 33% (16/49); respectively (p=0.631). Of the 59 patients who died during the first year after tracheotomy, the range in days from tracheotomy to mortality was 14 – 358 days, with an average of 98 days.

Time from tracheotomy to ventilator liberation for non-obese, class 1 and 2 obese, and class three obese patients was 15.4 days, 16.0 days, and 13.9 days; respectively (p=0.842) (Table 2). Time from tracheotomy to decannulation for non-obese, class 1 and 2 obese, and class three obese patients was 35.5 days, 48.6 days, and 44.7 days; respectively (p=0.506). Time from tracheotomy to hospital discharge for non-obese, class 1 and 2 obese, and class three obese patients was 27.9 days, 30.3 days, and 30.0 days; respectively (p=0.835). On multivariate analysis, only age was significantly associated with one-year mortality (p=0.001), while sex (p=0.127), surgical technique (p=0.764), BMI category (p=0.504), and APACHE II score (p=0.560) were not significantly associated with one-year mortality (Table 3).

Discussion

Treating patients in the ICU necessitates a complex decision-making process for all of those involved, including medical staff, patients, and their family members. Patients' intubated and sedated status, inability to effectively communicate or take oral nutrition, the need for mechanical ventilation, and the difficult decisions that need to be made about patient care all contribute to this process. Prolonged intubation can lead to further complications, such as laryngeal edema, subglottic stenosis, complications at the cuff site, tracheal bleeding, and injuries at the mouth or nose, making all of these factors mentioned intensified.[13] Additionally, ETT intubation can result

Table 3. Multivariable Binary Logistic Regression

Variable	Multivariate Analysis: Hazard Ratio (95% CI)	P Value
Age	1.05 (1.02-1.08)	P=0.001*
Sex		
Female	0.57 (0.28-1.71)	P=0.127
Male	Reference	
Technique		
Open	1.20 (0.37-3.85)	P=0.764
Percutaneous	Reference	
BMI Category		
<30	1.33 (0.58-3.08)	P=0.504
30-40	0.87 (0.35-2.17)	P=0.761
>40	Reference	
APACHE II	1.02 (0.96-1.08)	P=0.560

*Indicates statistical significance. Abbreviations: BMI, body mass index; APACHE II, Acute Physiology and Chronic Health Evaluation II.

in laryngeal ulceration which can evolve into posterior glottic stenosis, a very challenging disease to correct.[14]

While tracheostomy is a reliable tool to assist with improvement in outcomes for patients by decreasing their risk of development of these complications from ETT intubation, the clinical requirement of tracheostomy alone can predict that these patients have a high risk of mortality and palliative care discussions should be utilized.

Our study examines the outcomes of critically-ill patients in the MICU undergoing tracheostomy, specifically identifying inpatient mortality and one-year mortality rate. We found the inpatient and one-year mortality rate to be 15% and 37%, respectively, which is similar to previous studies.[15,16] Other than age, there were no significant risk factors identified to help stratify mortality risk of critically-ill patients undergoing tracheostomy.

It has been found in a randomized trial that two-year all-cause mortality was 51% in patients requiring prolonged mechanical ventilation who underwent early tracheostomy (within four days) and 53.7% in patients requiring prolonged mechanical ventilation who underwent late tracheostomy (after 10 days if still indicated).[17] In the late tracheostomy group, 53.7% of patients never underwent tracheostomy.[17] Evidence supports that risk for mortality is high in MICU patients requiring prolonged mechanical ventilation, regardless of whether the patient undergoes tracheotomy.[17] The inpatient and one-year mortality rates that we report in this current study can be discussed with the patient family during the preoperative discussion. As the rate of all-cause mortality in this patient population is high, a consideration of palliative care discussion with the patient and family is warranted, with a focus on patient goals of care and quality of life.

The mortality rate is high in all MICU patients requiring prolonged mechanical ventilation, and the mortality rates after tracheotomy in this patient population seen in this study and other published studies should not be interpreted as failure of the tracheotomy procedure. In fact, we would argue that the tracheotomy likely provided palliation to those patients who died. Studies have shown that critically-ill patients mechanically ventilated in the ICU experience frustration, anxiety, anger, fear, depersonalization, powerlessness, and a sense of futility when they have lost the ability to communicate via voicing. Additionally, these patients can experience depression and withdrawal from active participation in their medical care.[18] Placing a tracheostomy can allow for less sedation and agitation, enhanced ability to produce speech, ability to take oral nutrition, increased patient comfort, ability to be transferred out of the ICU, and ease of replacement of tracheostomy tube.[7]

There are many other important clinical outcomes asides from mortality to consider when examining tracheostomy outcomes in MICU patients. These include time to ventilator liberation, time to decannulation, MICU length of stay, hospital length of stay, and discharge disposition. These are important both for managing patient family expectations as well as health care resources (Table 2). On average the patients in this current study remained ventilator dependent for two weeks after the tracheotomy and remained tracheostomy dependent for about one month after the tracheotomy. The average MICU stay was approximately one month, and the average hospital stay was approximately 40 days (Table 2). It can also be discussed with family that less than 25% of patients will be decannulated prior to discharge, and more than 50% of the patients will be discharged to a facility. It is important to note that BMI was not significantly associated with these data points.

As outcomes are increasingly tracked and used as a marker for both reimbursement and quality, mortality rates after tracheostomy in specific patient

populations need to be reported in the literature. Additionally, reporting length of hospital stays, duration of tracheostomy dependence, and discharge disposition are important variables when analyzing utilization of health care resources. If there were strong clinical predictors of inpatient or one-year mortality, these clinical factors could be discussed with both the patients and their surrogate decision makers. However, both this current study and previous studies have found that there are few clinical features predictive of inpatient and one-year mortality.[19,20] As noted, the placement of tracheostomy is a significant portion of these patients' care that helps improve quality of life during critical illness and recovery. The lack of association between obesity and mortality both in this study and other studies is useful information when counseling patients and their surrogate decision makers.[19]

The management of MICU patients requires complex multidisciplinary care. At our institution, the Otolaryngology-Head and Neck Surgery and the Pulmonary Critical Care services began collaborating in order to offer percutaneous tracheostomy to appropriately selected patients. No difference in mortality was found between the open versus percutaneous techniques (Table 3). Additionally, no major short- or long-term complications were encountered in the patients who underwent percutaneous tracheotomy. MICU patients requiring prolonged mechanical ventilation have an average MICU stay of about one month and have a high inpatient and one-year mortality rate. Understanding and communicating these outcomes with patient's families can help the families make informed decisions during a difficult time.

Conclusions

The one-year mortality rate for MICU patients who underwent tracheotomy was 37% in this study. Age is significantly associated with one-year mortality, while sex, surgical technique, BMI, and APACHE II score are not significantly associated with one-year mortality. Communicating these outcomes with patient's families during the informed consent discussion can help the families make the best decision on behalf of the patient.

References

1. Chan T, Devaiah A. Tracheostomy in palliative care. Otolaryngol Clin North Am. 2009;42(1):133-141.
2. Frutos-Vivar F, Esteban A, Apezteguía C, et al. Outcome of mechanically ventilated patients who require a tracheostomy*: Crit Care Med. 2005;33(2):290-298.
3. Alain Combes, Luyt C-E, Nieszkowska A, Trouillet J-L, Gilbert C, Chastre J. Is tracheostomy associated with better outcomes for patients requiring long-term mechanical ventilation? Crit Care Med. 2007;35(3):802-807.
4. Clec'h C, Alberti C, Vincent F, et al. Tracheostomy does not improve the outcome of patients requiring prolonged mechanical ventilation: A propensity analysis. Crit Care Med. 2007;35(1):132-138.
5. Pandian V, Miller CR, Mirski MA, et al. Multidisciplinary Team Approach in the Management of Tracheostomy Patients. Otolaryngol Neck Surg. 2012;147(4):684-691.
6. Pandian V, Smith CP, Cole TK, et al. Optimizing Communication in Mechanically Ventilated Patients. J Med Speech-Lang Pathol. 2014;21(4):309-318.
7. Nieszkowska A, Combes A, Luyt C-E, et al. Impact of tracheotomy on sedative administration, sedation level, and comfort of mechanically ventilated intensive care unit patients*. Crit Care Med. 2005;33(11):2527.
8. Scurry WC, McGinn J. Operative Tracheotomy. Oper Tech Otolaryngol. 2007;18(2):85-89.
9. Zeitouni A, Kost K. Tracheostomy: a retrospective review of 281 cases. J Otolaryngol. 1994;23(1):61-66.
10. Goldenberg D, Golz A, Netzer A, Joachims HZ. Tracheotomy: changing indications and a review of 1130 cases. J Otolaryngol. 2002;31(4):211-215.
11. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organization technical report series. 2000;894:i-xii, 1-253.
12. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Critical care medicine. 1985;13(10):818-829.
13. Astrachan DI, Kirchner JC, Goodwin WJ. Prolonged intubation vs. tracheotomy: Complications, practical and psychological considerations. The Laryngoscope. 1988;98(11):1165-1169.
14. McWhorter A. Tracheotomy: timing and techniques. Curr Opin Otolaryngol Head Neck Surg. 2003;11:473-479.
15. Engoren M, Arslanian-Engoren C, Fenn-Buderer N. Hospital and Long-term Outcome After Tracheostomy for Respiratory Failure. Chest. 2004;125(1):220-227.
16. Kawakami D, Mima H, Shimozono T, et al. One-year mortality following tracheostomy in patients in the intensive care unit. Crit Care Med. 2018;46(1):527.
17. Young D, Harrison DA, Cuthbertson BH, Rowan K, TracMan Collaborators. Effect of early vs late tracheostomy placement on survival in patients receiving mechanical ventilation: the TracMan randomized trial. JAMA. 2013;309(20):2121-2129.
18. Freeman-Sanderson AL, Togher L, Elkins MR, Phipps PR. Quality of life improves with return of voice in tracheostomy patients in intensive care: An observational study. J Crit Care. 2016;33:186-191.
19. Byrd JK, Ranasinghe VJ, Day KE, Wolf BJ, Lentsch EJ. Predictors of Clinical Outcome After Tracheotomy in Critically Ill Obese Patients. The Laryngoscope. 2014;124(5):1118-1122.
20. Tong CCL, Kleinberger AJ, Paolino J, Altman KW. Tracheotomy Timing and Outcomes in the Critically Ill. Otolaryngol Neck Surg. 2012;147(1):44-51.

Disclosure

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