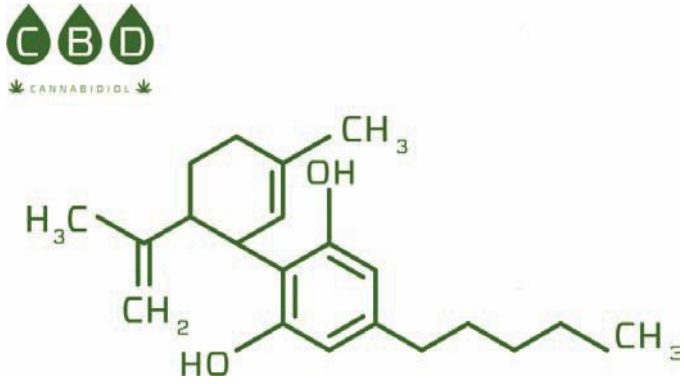
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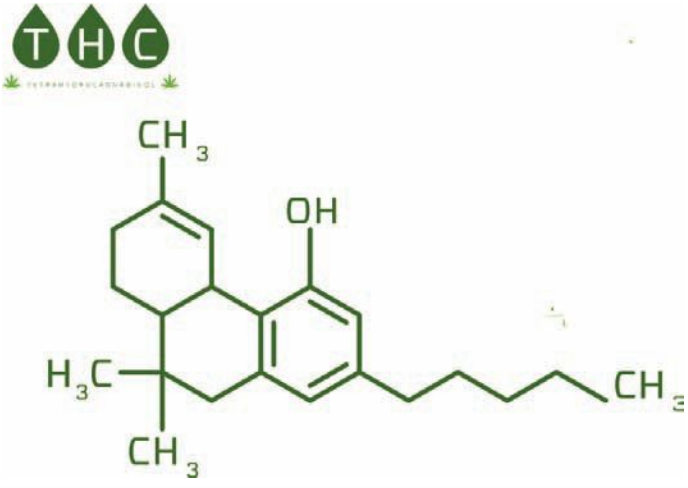
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National Cannabis Review: Are CBD & THC Valid Medicines?



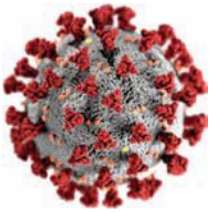




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Volume 117 | Number 5 | September/October 2020 **www.msma.org/missouri-medicine**

PRESIDENT'S FORUM

A Prescription for World Class Healthcare at Rock Bottom Cost!
by **George J. Hruza, MD** 392



NATIONAL CANNABIS REVIEW

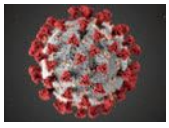
Medical Fraud, Mislabeling, Contamination: All Common in CBD Products
by David G. Evans, JD 394

Cannabis in Pregnancy and Lactation – A Review
by Joseph, Polcaro, DO
& Ivana M Vettraino, MD 400

Medicinal Marijuana, Stress, Anxiety, and Depression: *Primum non nocere*
by Mark Gold, MD 406

Book Review: Cannabis in Medicine: An Evidence-Based Approach
Edited by Kenneth Finn, MD
Reviewed by J. Michael Bostwick, MD 412

No Legal Recreational Marijuana in Missouri: We Have Enough Problems with Addiction!
by **John C. Hagan III, MD** 413



COVID-19 REPORT

COVID-19 Testing Tests Our Mettle
by Kathleen L. Hefferon, PhD, Justin R. St. Juliana, PhD & Henry I. Miller, MD 417

Mental Health on the Frontlines: Before, During, and After COVID-19
by **Simone A. Bernstein, MD** & **Jessica A. Gold, MD** 421

Break the Silence: Physician Suicide in the Time of COVID-19
by **Amanda M. Kingston, MD** 426

Send in the Army! Military Roles in the Pandemic
by **Charles W. Van Way, III, MD** 430

FROM YOUR ASSOCIATION

Annual Statement of Ownership 420
1 Picture = 1,000 Words 429
Correspondence 434
New Members 435
Missouri Medicine in the News 436
MMPAC Membership 437
New Member Spotlight 496

MEDICAL SCHOOL PERSPECTIVE

Transitioning Medical Education and Healthcare Delivery
by **Margaret Wilson, DO** 440

SCIENCE OF MEDICINE | FEATURE SERIES

ATSU A.T. Still University
FIRST IN WHOLE PERSON HEALTHCARE

Faculty Research Update - Presented by Kirksville College of Osteopathic Medicine, A.T. Still University, Kirksville, Missouri

Impact of the Single Accreditation System on Missouri Osteopathic Graduate Medical Education
by Richard J. LaBaere, II, DO & Kerrie J. Jordan, MS 444

Interprofessional Approach to Learning Vascular Access with Ultrasonography by Medical Students and Nurses
by Spencer Batten, MS, OMS IV, Vanessa Pazdernik, MS, Robert Schneider, DO & Tatyana Kondrashova, MD, PhD 450

Use of the Contralateral Knee as a Control in the Destabilization of Medial Meniscus Osteoarthritis Rat Model
by Michelle Hintz, MS, OMS IV, Taylor L. Ernest, MS, OMS VI & Peter Kondrashov, PhD 457

Development of Competency in Needle-Guided Procedures Through the Use of Soft-Embalmed Cadavers
by Tatyana Kondrashova, MD, PhD, Ryan Canaan, BS, OMS III, Brady Gunn, BS, OMS III, Vanessa Pazdernik, MS & Jeremy J. Houser, PhD 461

Anatomical and Radiographic Characterization of the Lateral Patellofemoral Ligament of the Knee
by Kevin Marberry, MD, Karl Boehm, DO, Fredrick Korpi, DO, Jane Johnson, MA & Peter Kondrashov, PhD 469

Educational Value of Ultrasonography Used as a Diagnostic Tool by Medical Students at a Student-Run Free Clinic
by Catherine Wlodarkiewicz, MA, OMS III, James Adams, DO & Tatyana Kondrashova, MD, PhD 475

SCIENCE OF MEDICINE | FEATURE REVIEW

Current Endovascular Treatment of Acute Ischemic Stroke
by **Kunal Bhatia, MD**, Sachin Bhagavan, MD, Navpreet Bains, DO, Brandi French, MD, Farhan Siddiq, MD, Camilo R. Gomez, MD & Adnan I. Qureshi, MD 480

SCIENCE OF MEDICINE

Sleep in the Elderly
by Prathusha Tatineny, MD, **Fariha Shafi, MD**, Ashraf Gohar, MD & **Abid Bhat, MD** 490

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A Prescription for World Class Healthcare at Rock Bottom Cost!

by George J. Hruza, MD

Imagine a country where the population has the second highest life expectancy at birth in the developed world at 85.2 years (U.S. 80.0 years), some of the lowest infant mortality rates at 2.4/1000 live births (U.S. 5.8) and the lowest maternal mortality rate in the world at 2.4 per 100,000 live births (U.S. 14.0). Now imagine that such world-beating health outcomes come at a fraction of the healthcare costs in the U.S. This country spends 4.2% of their (Gross National Product) GDP on healthcare compared to 18% of GDP in the U.S. in 2015. Even more reassuring is that all their citizens have access to affordable, high quality healthcare and physicians earn, after taxes, close to what their peers in the U.S. earn. This country has been rated by Bloomberg as the healthiest country in the world out of 145 that they analyzed.

Which country has achieved such incredible outcomes at such low cost? It is not Canada with its Medicare for all, often used as a potential model for the U.S. They attempt to control costs through limiting the supply of physicians and other healthcare services and price controls resulting in long waits for many procedures (GDP spending 10.4% on healthcare and rising). It is not Britain with its lauded NIH. They attempt to control costs by deciding which patients are deserving of various expensive services (GDP spending 9.9% and rising). The National Institute for Clinical Excellence (NICE) is the arbiter of whether a patient will receive a medical service. If it costs less than $25,600 per additional year of life, then the service is approved. If it costs more, then the patient is out of luck. The NIH also uses waitlists and price controls as another way to control costs. It is not even Sweden with its vaunted healthcare system (GDP spending 11.0%). The fatal flaw of these single payor systems is the promise of free healthcare. If a good or service is free, the demand for such a service will be unlimited and ultimately unsustainable leading to price controls, rationing, and the associated dislocations that come with that.

The country that has been able to achieve top healthcare outcomes at super low cost is Singapore. They have achieved this feat by applying techniques and principles developed in the U.S. (but not widely adopted here - yet). The flaw in our system is that the patient (first party) as the consumer is mostly insulated from the cost of the care they receive. The second party, the physician or other healthcare provider, collects most of their payment from the third party (insurer, HMO, PPO, Medicare, Medicaid, etc.). In this system, no one has a strong incentive to control costs. The patient wants the latest and greatest service irrespective of cost. The physician or other provider wants to get paid as much as possible for the service they provide, and the insurer makes a percentage of total premiums as profit (with the ACA, it is 20% for profit and overhead). If the cost of providing care increases to the insurer, they raise their premiums and end up with a higher dollar profit. In most markets, there is very high insurer market concentration resulting in very little to no competition that might keep premiums in check. The U.S. government, of course, keeps some control on costs through price controls (at least on physicians for the last 30 years; hospitals and pharmaceutical companies are not so constrained due to their much larger lobbying capacity). But history shows that price controls alone are not able to keep a lid on costs as there is an offsetting increase in volume of services.



George J. Hruza, MD, MBA, FAAD, FACMS, MSMA member since 1989, is the 2020-2021 President. He practices Dermatology in St. Louis, Missouri.

Offering something for free as an "entitlement" leads to a huge and, potentially infinite, increase in demand making such a model unsustainable in the long run.

What does Singapore do that we seem to be unable to do in the U.S.? Singapore took a free market approach to healthcare. There are two main components:

1. The patient, first party, is incentivized to shop for low cost, high quality healthcare by having some "skin in the game."

2. The physician and other providers of healthcare, second party, compete for the patient based on price and quality. All patients have health savings accounts (HSAs) linked with a high deductible insurance along with coinsurance and an out-of-pocket maximum. The HSA is funded through pretax contributions by the patient and used for paying out of pocket medical costs. Any money left over in the HSA belongs to the patient that can ultimately be used for retirement or even transferred to heirs upon death. Patients with low incomes receive subsidies, but they also have HSAs, where the balance is "their" money, not the government's. Proven preventive services get first dollar coverage. When such a plan was instituted in Indiana for their state employees, healthcare expenditures dropped by 35% vs. employees that stayed in the traditional HMO/PPO plans without adverse health outcomes. To get to the other half of the equation and achieve the dramatic savings seen in Singapore, everyone must be in such plans to introduce true competition into the healthcare market.

Last year, I needed an MRI of my knee and went to the nearby hospital imaging center to get it. My bill was zero as I had met my deductible. My insurance ended up paying the hospital $2,500 for the MRI. Early this year, my wife needed an MRI of her knee. At this point, we had not yet met our deductible, so we went to a free-standing imaging center where they did an equal quality MRI, but the total bill was only $500. As a physician, I understood the byzantine pricing system we have in the U.S. Most patients would not even know where to begin to do price comparisons and many with traditional insurance do not really care as their out-of-pocket cost will be the same wherever they get in network services. In Singapore, prices for all healthcare services are publicly posted and easily accessible to patients by law and, just like a carton of milk costing the same to all comers at Walmart, all patients getting a service from a specific physician or other healthcare provider gets the same price. There are no price controls, RVUs, fee schedules, or allowables. This approach injects competition into the market and spurs innovation to offer high quality services at the lowest possible cost. Many industries have been successful at this. There is no reason that healthcare cannot achieve the same. For drugs, there are no (Pharmacy Benefit Managers) PBMs. Prices of drugs are also posted for patients to be able to comparison shop. The third-party insurer does pay most of the bills, but is mostly a passive observer in the system. It is the patient that is in charge of where to spend their money. Individuals are far better at understanding what services have value to them and which do not.

We already have all the ingredients for a Singapore-type healthcare system. Here we refer to it as consumer-driven healthcare. HSAs combined with high deductible insurance plans and coinsurance are already available; employers could adopt them en masse without any additional legislation. These plans save money even when the employer puts money into the HSA for the employee. We still need price transparency, which the current administration has been pushing for.

Also, for this combination to put downward pressure on prices, we need almost all patients to be in such plans. The combination can get us to the 70-80% reduction in cost. Think about the cost and quality of myopia corrective surgery. Initially there was radial keratotomy. Now there is custom wavefront LASIK with better outcomes, far lower morbidity, and a cost that is 70% lower in inflation-adjusted terms. All this occurred due to true free market competition. Third party payors and PBMs should be removed from the pricing equation. Of course, there is the rub. Insurance companies, large integrated hospital systems, big pharma and PBMs have spent lavishly in Washington on lobbying to protect their monopoly power. Patients and taxpayers are left holding the bag. We should bring elements of the free market back to our healthcare system and empower patients, with the help of their physicians, to get back in the driver's seat and regain control over their healthcare.

Book Source

1. Sean Masaki Flynn: The Cure that Works: How to have the World's Best Healthcare – at a Quarter of the Price. Regnery Publishing, Washington, DC 2019, 276 pages.

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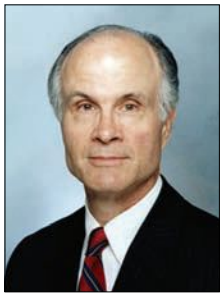
Medical Fraud, Mislabeling, Contamination: All Common in CBD Products

by David G. Evans, JD



Cannabidiol (CBD) is an oil derived from the cannabis plant. It is touted as a "wonder drug." Advertisements claim it is perfectly safe and legal and can be used for all that ails you or makes you uncomfortable mentally or physically. People are consuming it under the misapprehension that it is safe, however, CBD has negative side effects and may interfere with the functioning of other medications and may be contaminated.

Consumer demand for CBD has increased due to aggressive marketing and fraudulent health claims. In the rush to market CBD, there has been little consideration of the concerns that must be addressed before CBD is given full acceptance. This article will explore those concerns.



David G. Evans, JD, is a graduate of Westminster College in Fulton, Missouri, and Rutgers Law School. He is Senior Counsel for the Cannabis Industry Victims Educating Litigators (CIVEL). CIVEL educates lawyers on the legal rights of the victims of the marijuana industry. He was formerly a Research Scientist in the New Jersey Department of Health.

Is CBD Legal?

There are claims that CBD from hemp used as a medicine or food is always legal. This is not accurate. The Agriculture Improvement Act of 2018 changed federal law regarding the production and marketing of hemp. Hemp is defined as cannabis and its derivatives with extremely low (less than 0.3% a dry weight basis) concentration of the THC. These changes removed hemp from the federal Controlled Substances Act, which means that it will no longer be an illegal substance under federal law. However, Congress explicitly preserved the FDA's authority to regulate these products under the Federal Food, Drug, and Cosmetic Act and section 351 of the Public Health Service Act. These compounds are subject to the same requirements as FDA-regulated products containing any other substance regardless of the source of the substance. Cannabis products claiming in their marketing materials that they're intended for use in the diagnosis, cure, mitigation, treatment, or prevention of



diseases must go through the FDA drug approval process for human or animal use before they are legally marketed.[1]

As stated by the FDA Commissioner:

"Selling unapproved products with unsubstantiated therapeutic claims is not only a violation of the law, but also can put patients at risk, as these products have not been proven to be safe or effective. This deceptive marketing of unproven treatments raises significant public health concerns, as it may keep some patients from accessing appropriate, recognized therapies to treat serious and even fatal diseases."[2]

CBD products that are not approved by the FDA and are sold as medicines, or as food, or cosmetics are "black-market" and are illegally trafficked and sold. This includes those sold in reputable stores, restaurants, and other places that don't have FDA approval to do so. Black-market CBD products have not been evaluated by the FDA to determine if they are safe as foods or effective or safe for any medical use, and if safe, what the proper dosage would be. In addition, they are not administered with any federally approved medical protocols as are prescription drugs and there may be no warnings for how they interact with other drugs, or whether they have dangerous side effects.[3]

A pure form of CBD is approved by the FDA as a medicine for two rare seizure disorders. Its approval was based on well-controlled FDA clinical trials. This is a purified form of CBD in a reliable dosage form and a reproducible route of delivery. Since it is manufactured according to FDA standards by a reliable company that has followed the rules, we can assume it is free from adulterants and contaminants. Its side effects and other clinical data are publicly available. This type of data is not provided by the black-market CBD products.[4]

There are a number of papers discussing the pros and cons of CBD as a medicine that can be viewed on the National Library of Medicine website at www.nlm.nih.gov. Some studies, notwithstanding their many deficiencies, provide some support for the hypothesis that CBD may exert some beneficial effects, but is has yet to be proven to be both effective and safe. FDA quality studies with purified CBD are warranted. However, clinical data does not support some claimed uses of CBD for Parkinson's disease, schizophrenia, cancer palliation and treatment, chronic pain and spasticity, depression, anxiety disorder, insomnia, and inflammation. There is insufficient evidence to rate effectiveness of CBD for Bipolar disorder, Crohn's disease, diabetes, dystonia, Huntington's disease, multiple sclerosis (and its muscle spasms, tiredness, bladder control, the ability to move around, or well-being and quality of life), schizophrenia, nerve damage in the hands and feet (peripheral neuropathy) and other conditions.[5]

CBD Mislabeling and Contamination

Studies suggest that black-market CBD is not very reliable or safe. In 2020, the FDA did a study on products that claimed to have a specific amount of CBD and those claimed amounts were compared to the FDA testing results. Of the 102 products that indicated a specific amount of CBD, 18 products (18%) contained less than 80% of the amount of CBD indicated, 46 products (45%) contained CBD within 20 percent of the amount indicated, and 38 products (37%) contained more than 120 percent of the amount of CBD indicated. Of great concern is that 49% of the products tested contained THC.[6]

The *Journal of the American Medical Association* published a letter demonstrating the results of "undercover" purchases of CBD. Of 84 samples tested, THC was detected in 21%. There were other defects in the mislabeled products. Only 30.95% were accurately labeled. Accuracy of labeling depended on product type, with vaporization liquid most frequently mislabeled (87.50%) and oil most frequently labeled accurately (45.0 %). THC was detected (up to 6.43 mg/mL) in 18 of the 84 samples tested (21.43%).[7]

A Johns Hopkins researcher tested CBD products. Testing showed 44 products (59%) had detectible levels of CBD, but the average ratio of THC to CBD was 36-to-1. Only one product had a 1-to-1 ratio, which some research suggests is associated with fewer side effects and improved clinical benefit compared with higher ratios of THC to CBD. The testing indicated the edible cannabis products may have very little CBD.[8]

A study published by the National Institute of Health showed that products were mislabeled

with 26% containing less CBD than labeled and 43% containing more, indicating a high degree of variability and poor standardization of online products. Notably, the oil-based products were more likely to be accurate (45% compared to 25% for tincture and 12.5% for vaporization liquid) and had a smaller percentage of deviation. Oil based products also had a higher range of concentration. In addition to CBD mislabeling, THC was detected in 21% of samples. This study also notes that products containing THC could have sufficient enough concentrations to produce intoxication in children.[9]

In a recent federal lawsuit, the plaintiff bought CBD products relying on advertising that the products had "No Heavy Metals or Insecticides." The products failed laboratory testing for heavy metals, including copper, nickel, and lead and also for total yeast and mold. Lead can cause poisoning, speech, and language problems, neurologic toxicity, and reproductive problems. Mold can cause allergic and respiratory problems, and yeasts can cause infection in people with compromised immune systems.[10] On July 28, 2020, another CBD product was recalled due to lead contamination. The recall noted that acute lead poisoning could cause pain, muscle weakness, paresthesia, abdominal pain, nausea, vomiting, diarrhea, constipation, poor appetite, weight loss, symptoms associated with encephalitis, metallic taste in the mouth, shock, hemolysis, and kidney damage.[11]

False Medical Claims

Examples of false claims for CBD can be taken from FDA and Federal Trade Commission (FTC) warning letters to CBD companies. In order to make claims of treatment or medical use, products must obtain approval from the FDA after submitting their data. False claims include using CBD to treat: alcoholism, Alzheimer's disease, arthritis, autism, blood pressure and heart rate, cancer, chronic traumatic encephalopathy, cardiovascular disease, chemotherapy-induced hearing loss, colitis, concussions, depression, diabetes, leukemia, liver inflammation, lupus, Lyme disease, neurological damage, Parkinson's disease, stroke, schizophrenia, traumatic brain injury (TBI), and tumors.[12]

CBD Negative Side Effects and Drug Contraindications

There may be interactions between CBD and immunosuppressive drugs used in transplants or chemotherapy and with warfarin as there may be the potentiation of anticoagulant effects with marijuana, including CBD. CBD may interact with other medicines, including prescription and over-the-counter medicines, vitamins, herbal supplements, and any cannabis-based products. CBD may affect the way other medicines work, and other medicines may affect how CBD works.

CBD may decrease how fast the liver metabolizes the drug. This may possibly increase the effects and side effects. CBD may potentially interact in a negative way with anti-epileptic drugs such as: carbamazepine (Tegretol), phenytoin (Dilantin), phenobarbital (Luminal, Solfoton, Tedral), primidone (anti-seizure). Users should be cautious before taking CBD with: sedatives, herbs, and supplements that cause drowsiness, seizure medications, drugs that are broken down and changed by the liver. People should be cautious with using Brivaracetam (Briviact), Eslicarbazepine (Aptiom), and Everolimus (Zostress).[13] Consumers should not take CBD with Clobazam for seizures.[14] The use of CBD along with these drugs might increase the effects and side effects of the drugs.

Adverse Reactions

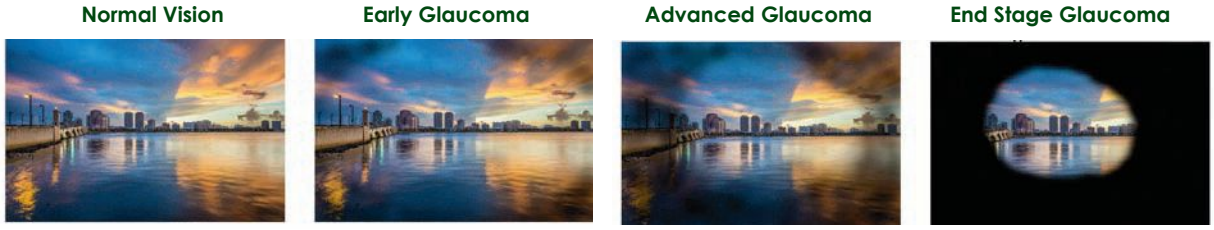
The adverse reactions to CBD include: hepatocellular injury, somnolence and sedation, suicidal behavior and ideation, hypersensitivity reactions–allergic reactions, negative interaction with anti-epilepsy drugs (such as Tegretol, Dilantin, luminal, Solfoton, Tedral, primidone), interactions with immunosuppressive drugs used in transplants or chemotherapy and with warfarin. CBD use can impair kidney function and cause anemia.[15] Black market CBD is generally sold without warnings about adverse reactions.

The side effects of CBD can include: drowsiness, decreased appetite, diarrhea, transaminase elevations, fatigue, feeling unwell (malaise), rash, difficulty sleeping (insomnia, disordered sleep, and poor-quality sleep), infections, somnolence, decreased appetite, diarrhea, and asthenia.[16]

Research shows that more than 40% of children with epilepsy who were given CBD orally had adverse events that included THC like symptoms. The research challenged the widely accepted premise that CBD is not intoxicating.[17]

Glaucoma Made Worse by Marijuana, THC, and CBD

by John C. Hagan III, Ophthalmologist Eye, MD



Source: https://www.graceandvision.com.au/eye-conditions/glaucoma/

Although glaucoma is a listed indication for issuing sham medical marijuana cards, the most recent evidence is that cannabis in either tetrahydrocannabinol (THC) or cannabidiol (CBD) are both harmful to the eye and have a deleterious effect on glaucoma.[1-5] CBD has been shown to increase intra-ocular pressure (IOP) the fundamental problem with most forms of glaucoma; while THC lowers IOP but the effect is transient and therapeutically worthless. Chronic cannabis use causes damage and loss of retina ganglion cells as does the disease glaucoma. Moreover, ganglion cells are central nervous system tissue, like the cells of the brain, and may serve as a surrogate marker for brain cell loss. This might account for neurological problems associated with heavy cannabis use such as memory loss, lethargy, and poor motivation, permanent IQ loss in youthful users, aggression, psychosis, etc. Half a century of research has found no benefit to any cannabis products in ophthalmology. Use of sham medical marijuana, CBD, or any form of cannabis is not recommended for glaucoma or any other eye condition by the American Academy of Ophthalmology or the Glaucoma Society. No physician should ever recommend cannabis use for any of the many forms of glaucoma.

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Glaucoma

A recent study suggests that CBD doesn't lower eye pressure but instead raises it. High eye pressure is the primary risk factor for glaucoma, a leading cause of blindness.[18] [Editor's Note: see sidebar.]

Warnings

Black Market CBD may be sold without warnings being provided. People should be warned about the known adverse reactions to CBD. People should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that CBD does not affect them adversely (e.g., impaired judgment, thinking, or motor skills). Use of CBD may increase the risk of suicidal thoughts and behavior. Hypersensitivity reactions can occur with use of CBD. It is not known if CBD is safe and effective in children under two years of age. FDA clinical trials of CBD did not include any patients aged above 55 years. CBD for elderly persons could be dangerous due to the greater frequency of decreased liver or cardiac function, and of concomitant disease or other drug therapy.[19]

Vehicle Operation

A recent FDA report states that CBD can cause sleepiness, sedation, and that may make operating a motor vehicle or machinery dangerous after consuming CBD products.[20]

CBD and Pregnancy

The FDA strongly advises that during pregnancy and while breastfeeding, women should not use CBD or THC. They may put themselves or their baby at serious risk by using these marijuana products. CBD products may also be contaminated with substances that may pose a risk to the fetus or breastfed baby such as pesticides, heavy metals, bacteria, and fungus. Studies in laboratory animals show male reproductive toxicity, including in the male offspring of CBD-treated pregnant females. This includes decrease in testicular size, inhibition of sperm development, and decreased testosterone.[21] The CDC also notes that marijuana use by a pregnant woman can have teratogenic effects causing birth defects.[22]

Drug Tests

CBD may affect drug test results. A truck driver lost his job when he tested positive for THC on a drug test after being told by the manufacturer that a CBD product had no THC.[23]

Recent CBD Lawsuits

There are many recent lawsuits filed against CBD manufacturers and more are on the way. They were filed after the FDA issued a series of warning letters that such products, unless approved by the FDA, are neither safe or effective for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and/or because they are intended to affect the structure or any function of the body. Some of the cases allege that the manufacturers' CBD products made false medical claims or were mislabeled as dietary supplements or there were false claims as to the amount of CBD present in the product. A California case claims that the company engaged in false and deceptive practices and that their products could not be sold legally. A Massachusetts case claimed that many of the defendant's products had significantly lower levels of CBD than advertised. A California case claimed that the defendant company made false claims that CBD could help the symptoms of autism and that could treat illnesses such as hepatitis, cancer, and Tourette syndrome. A New York case alleges false medical claims for marijuana and for violations of the federal securities laws. A Florida case alleged that CBD has "been touted as having numerous positive health effects." CBD has been used to treat conditions such as "anxiety, sleep disorders, and chronic pain." In selling the products with significantly less CBD, plaintiff claimed the Defendants "are cheating every consumer who buys the products by that amount." The Federal Trade Commission recently petitioned to enjoin a CBD company from disseminating false or unsubstantiated advertisement claims in connection sale of a product that purportedly treats, prevents or reduces the risk of COVID-19 and products that purportedly treat cancer.[24]

Government Bans on CBD Use

The federal Department of Transportation has issued a warning that CBD use can show up as a positive THC result on a drug test.[25] The U.S. military has banned the use of hemp/CBD products for military personnel.[26]

The Future of CBD and the FDA

The FDA is currently undertaking a large long-term study of black-market CBD products to understand the characteristics of CBD products in order to make informed decisions about how best to protect public health. The FDA will report again on the results from both the near and long-term studies when complete data sets are available.[27] On July 21, 2020, the FDA stated that in regard to CBD and other cannabinoids:

"The FDA believes the drug approval process represents the best way to ensure that safe and effective new medicines, including any drugs that contain cannabis or cannabis-derived compounds, are available to patients in need of appropriate medical therapy."[28]

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Cannabis use should be discouraged during pregnancy and lactation.

Cannabis in Pregnancy and Lactation – A Review

by Joseph, Polcaro, DO & Ivana M Vettraino, MD

Abstract

Cannabis (marijuana) is now legal for either medicinal use or recreational use in 33 states with more states considering legalization for medicinal and/or recreational use. More women planning pregnancy, pregnant, or breastfeeding will present with exposure to marijuana. A familiarity with the pharmacology and potential effects for pregnancy and lactation is important for the obstetrical care provider to permit optimal counseling for the gravida. This paper provides a pertinent review of cannabis for the obstetrical care provider. The literature available for review concludes that no amount of marijuana and associated product use in pregnancy and lactation is safe. Cannabis and associated product use has the potential for adverse maternal, fetal, and long-term childhood development and its use should be discouraged during pregnancy and lactation.

Introduction

Marijuana or cannabis is also known by many slang terms including weed, herb, pot, grass, bud, ganja, and Mary Jane. Cannabis has a long history with evidence of use for medicinal, spiritual, and recreational use dating at least 5000 years ago.[1,2] Historical texts show most ancient civilizations utilized cannabis for medicinal and spiritual properties.[3] Cannabis use as a medicinal has been reported in the United States during the 19th and early 20th centuries.[4] Medical marijuana was first described in the United States in 1850. The various modes of use include smoking, dabbing, eating, and most recently vaping.

As of June 2019, 11 states have adopted laws legalizing recreational use of marijuana. Another 22 states allow for the use of medical marijuana.[5] The federal government does not recognize cannabis as a legal drug. Cannabis is the most commonly used illegal drug in the United States of America (USA). Approximately 22.2 million individuals use marijuana each month. One in 10 individuals will become addicted if over the age of 18 years and 1 in 6 will become addicted if use occurs under the age of 18 years.[6] Long term and frequent use have been associated with increased risk for psychosis and schizophrenia.



As legalization of marijuana has spread across the USA, the perception of safety in pregnancy has also increased.[7,8,9] Approximately 1 in 25 pregnant women are estimated to use marijuana during pregnancy.[10] In a research letter using data from

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the National Surveys of Drug Use and Health from 2005 to 2012 reported that the percentage of women who reported "no risk" of harm rose from 25.8 % in 2005 to 65.4 % in 2012.[11] This paper will review the pharmacology and the potential effects of marijuana use in pregnancy and lactation.

Pharmacology

Marijuana is composed of the leaves and flowers of the Indian hemp plant. The potency varies based on location of origin, method of cultivation, and method of storage. The active ingredient tetrahydrocannabinol (THC) is present in all parts of the plant. However, the most concentrated and strongest marijuana comes from the resin in the flowering tops of the female plants. The plant contains greater than 400 other chemicals including approximately 60 compounds chemically related to THC known as cannabinoids. Additionally, there are over 2000 compounds produced by thermal decomposition during smoking.[12]

The psychoactive metabolite of cannabis is delta-9-tetrahydrocannabinol (THC) that acts on cannabinoid receptors within the central nervous system (CNS) and peripheral tissues.[13] THC acts on cannabinoid receptors – CB1 found in CNS and CB2 found in peripheral tissues.[14] THC is similar in chemical structure to the human brain chemical anandamide. Anandamide is an endogenous cannabinoid which functions as a neurotransmitter within the endocannabinoid system.[13,15] This system plays a critical role in the normal functioning of the nervous system and homeostasis. The endocannabinoid system is involved in a wide variety of processes including pain, memory, mood, appetite, stress, sleep, metabolism, immune function, and reproductive function. Therefore, interfering with this system can have profound effects. For example, THC can alter functioning of the hippocampus affecting memory and focus. THC also can disrupt functioning of the cerebellum and basal ganglia resulting in loss of balance, coordination, and a decrease in reaction time.[16] This similarity in structure between THC and anandamide allows the brain to recognize THC in a manner like anandamide.

Psychological effects include euphoria as THC can increase the release of dopamine. This effect may lead to psychological habituation noted below. Effects of THC can vary amongst individuals. Some will experience visual disturbance, laughter, increase in appetite, and distortion in judgment, time, and space. Visual hallucinations, anxiety, depression, psychosis, mood disturbance can also occur. If marijuana is used as an edible or beverage, the effects can be delayed by approximately 30 minutes to an hour due to tablets and within the digestive tract. Eating or drinking marijuana results in significantly less THC in the bloodstream when compared to smoking an equivalent amount. Because of these delayed effects, increased consumption of THC can lead to toxicity.[17]

The physical effects of cannabis use include but are not limited to red eyes, dryness of the mouth, increase in heart rate, chest tightness when smoked, drowsiness, and unsteadiness with decreased muscle coordination.

Chronic use does not appear to lead to physical dependence. Therefore, withdrawal is not a known effect of cannabis use when discontinued. However, this drug can be psychologically habituating. THC remains in the body for approximately 48 hours after smoking. Therefore, the residual effects on cognitive function including memory can last up to 48 hours.[18]

THC is metabolized within the liver, brain, lung, and intestine to hydroxylated and carboxylated metabolites. These metabolites are stored within the peripheral tissues and eventually excreted in the urine or feces dependent upon mode of use, inhalation or edible, respectively. Within a 5 day window, approximately 80 to 90 percent of THC is eliminated.[19]

Indirect exposure can occur during passive smoking of cannabis. Fifty percent of THC survives pyrolysis during smoking with 6 to 53 % released in the air. Therefore, passive inhalation can occur if the individual is within proximity of the smoker. A positive drug screen is possible following passive exposure.[20]

Marijuana Exposure in Pregnancy

The incidence of marijuana use in pregnancy has increased. According to Centers for Disease Control (CDC) estimates, approximately 1 in 20 women self-reports the use of marijuana in pregnancy.[21, 22] As with most self-reporting, this likely underestimates the number of women utilizing marijuana in pregnancy. A recent study found that this number has increased to approximately 18% or approximately 1 in 6 women. These numbers are likely to further increase as more states legalize recreational use of marijuana, resulting

in the perception that marijuana use is safe. A research letter using data from the National Surveys of Drug Use and Health from 2005 to 2012 reported that the number of women who recently used marijuana and believed the drug to be safe in pregnancy increased over this time frame from 25.8 % to 65.4 %.[7] Women prior to pregnancy and during pregnancy utilize cannabis by many different routes including but not limited to smoking, edibles, vaping, lotions and other.[23]

Maternal Effects

The maternal risks of marijuana use are related to method of ingestion, associated risk behaviors, polysubstance abuse, and associated mental health complications. Cannabis use disorder is defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th edition by impaired control, social difficulties, risky use, tolerance, and withdrawal.[24]

Multiple studies have shown an association with depression, anxiety and other psychiatric conditions.[25, 26] Such associated mental health conditions can lead to addiction as the marijuana is used to treat the underlying psychiatric illness. Screening for and referral for management of co-existent psychiatric conditions is imperative to decrease the use of marijuana in pregnancy.

Also important for the obstetrical care provider is awareness of cannabinoid hyperemesis syndrome. [27, 28] Cannabinoid hyperemesis syndrome (CHS) can be challenging to differentiate from hyperemesis gravidarum. CHS should be considered in patients presenting with hyperemesis gravidarum with a history of chronic marijuana use, atypical presentation, and failure to improve with the usual course of management. CHS is characterized by a history of chronic marijuana use; acute-onset nausea, vomiting, and abdominal pain; symptoms alleviated by hot showers; and episodes lasting 24 to 48 hours.[28, 29, 30] Resolution requires discontinuation of marijuana use.[28, 30]

Although robust studies are lacking in regard to maternal complications of marijuana use in pregnancy, the data available to date suggests that pregnant women need to be educated to the potential adverse effects on their health and encouraged to discontinue marijuana use in pregnancy.

Fetal and Long-Term Childhood Effects

Studies regarding the use of marijuana in pregnancy have provided conflicting results.[31-43] This is likely due to the challenges in controlling for confounding factors including but not limited to other associated drug use, challenges in quantifying the amount of drug used, difficulties in evaluating childhood development due to other familial/ socioeconomic economic factors. Thus, definitive guidelines regarding marijuana use in pregnancy are challenging.

The American College of Obstetrics and Gynecology (ACOG) published a committee opinion in 2017.[44] In this opinion, the ACOG recommends that women attempting pregnancy, currently pregnant, or breastfeeding avoid marijuana use. The American Academy of Pediatrics also recommends against marijuana use in women who are breastfeeding.[45]

The literature regarding marijuana use in pregnancy is varied and many of the studies have limitations as would be expected in studying a drug in pregnancy. There are recall biases for self-reporting amount and timing of use, confounding variables difficult to control, and metanalyses with variability in study design. Taking the aforementioned in consideration, the following findings are applicable at this time pending further study.

The inherent physiologic endocannabinoid system is known to be important in human pregnancy. This system has been shown to be important for implantation and pregnancy maintenance.[46] The role of THC use in implantation and pregnancy maintenance is unclear at this time.

There has not been consistent data to date to suggest an increase in fetal anatomic abnormalities. Likewise, there is no consistent data to show an association with preterm delivery and other adverse pregnancy outcomes in patients reporting only marijuana use.[31, 32, 33] Preterm labor and delivery can be increased in women using other substances such as tobacco.[34] Earlier data suggested that perinatal morbidity/intrauterine fetal demise does not appear



to be increased in patients using marijuana alone in pregnancy. Like preterm delivery, use of other substances such as tobacco may slightly increase the risk of stillbirth in this patient population. A recent retrospective cohort analysis controlling for many of the confounders that affected other studies showed newborns exposed to marijuana had increased rates of lower birth weight - 218 g less; low birth weight, deliver preterm; admitted to the neonatal intensive care unit, and have lower Apgar scores than matched newborns not exposed to marijuana.[35] This adds to the literature for concern regarding marijuana exposure in pregnancy.

Regarding neurobehavior development, THC crosses the placenta and enters the fetus at a level of approximately 10% maternal levels.[47] This level is likely increased with heavy and repetitive use as the half-life of THC can vary based on amount and repetition of use. Fetal brain development can therefore be impacted as the fetal brain contains cannabinoid receptors type 1 as early as 14 weeks' gestation necessary for normal brain development. The THC can preferentially bind to these cannabinoid receptors potentially resulting in abnormalities in brain development and response to endogenous neurotransmitters.[47, 48] Newborns with in utero exposure to THC can undergo a neonatal abstinence like syndrome characterized by tremors, increased startle reflex and reduced habituation to light.[49]

Children exposed *in utero* to have been found to have lower scores on tests of visual problem solving, visual–motor coordination, and visual analysis, decreased attention span, behavioral challenges than children who were not exposed to marijuana in utero.[50, 51, 52] There have been no consistent findings regarding cognition and school performance. This is likely due to the multiple confounding variables in studies involving education and school performance. However, studies have shown these children have challenges throughout the educational milestones.

Most recently, a large retrospective analysis of live births in Ontario, Canada has shown an association between cannabis use in pregnancy and the incidence of autism spectrum disorder in their offspring. Women who reported cannabis use without associated tobacco, alcohol or opioid use had an adjusted hazard ratio of 1.51 (confidence interval of 1.17 to 1.96) for a child with a diagnosis of autism.[53] This study also found an increase incidence of intellectual and learning disabilities in the children of women who used cannabis in pregnancy. These results support previous studies reporting similar findings as referenced above.

Lactation

To date, most of the literature assessing the effects of marijuana exposure to the neonate through breastfeeding have studied the pharmacokinetics of THC and breast milk.[54, 55, 56] As cannabinoids are lipophilic, cross the blood brain barrier, affects to the developing fetal brains raise significant concerns. Studies have shown that the concentration of THC in breast milk is variable based on the amount and frequency of maternal ingestion. Unlike many other drugs and medications that are excreted into breast milk but are not concentrated in breast milk, THC is excreted and concentrated in the breast milk. Breast milk can have up to eight times the concentration of maternal plasma and can be detectable for up to 6 days.[56]

Additionally, THC can be found in breast milk approximately 1 hour following ingestion.[56] Therefore, pumping and dumping between feeds is not likely to significantly decrease the exposure to the neonate.

As individuals with passive inhalation of secondhand marijuana smoke have been shown to have THC present in bodily fluids, one must assume that secondhand exposure can also effect the breast milk and therefore the neonate. Passive or secondhand exposure to marijuana while breastfeeding should be avoided given the potential for harm.[57]

Medical Marijuana

A review of the literature regarding the effectiveness of medical marijuana in decreasing pain and in management of chronic pain syndromes is outside the scope of this paper.

Medical marijuana is not regulated by the Food and Drug Administration. Given that maternal, fetal, and neonatal effects are present as noted above, women managed with medical marijuana should be encouraged to discontinue the medical marijuana and adopt more traditional strategies for management of their underlying medical condition(s) in pregnancy.

Cannabidiol

Cannabidiol (CBD) is a chemical obtained from the Cannabis sativa plant primarily from the hemp

type.[58, 59, 60] Hemp and marijuana are both in the Cannabis family, but hemp contains very little (less than 0.3 percent) of the psychoactive compound delta-9-tetrahydrocannabinol (THC). CBD, unlike marijuana, does not produce a psychoactive response. The FDA has approved only one CBD product as a prescription drug indicated for the management of rare forms of seizure disorder in children.[59]

The Farm Bill passed in 2018 made the sale of hemp and hemp products legal in the United States. It remains illegal to tout medicinal properties of CBD. Despite lack of scientific evidence for efficacy, CBD has gained in popularity in products such as cosmetics, creams and ointments for pain relief, dietary supplements, treatments for anxiety, management of some neurologic disorders as seizures and Parkinson's, and in edibles. The science and pharmacology of CBD is unknown. Effects on the brain is a proposed mechanism of action. There are no approved dosing regimens. The amount of CBD in these products is variable and the safety of CBD is unclear. Reported side effects include but are not limited to: dry mouth, low blood pressure, light headedness, and drowsiness. Liver injury has been reported. Possible interactions with prescription medications, alcohol, or other illicit drugs remains unknown potentially causing serious side effects.[59]

The Food and Drug Administration (FDA) citing lack of data and concern from animal studies strongly advises against the use of cannabidiol (CBD) in any form during pregnancy or while breastfeeding.[59] High doses of CBD given to pregnant test animals suggest abnormalities in the reproductive system of developing male fetuses including decreased testicular size, low testosterone, and abnormalities of spermatogenesis. [61] There is an extrapolation from information available to suggest that some amount of CBD will be transferred to babies through breast milk.

There are the additional concerns for CBD products to be contaminated with other potentially harmful substances to the developing fetus or neonate including but not limited to: THC, pesticides, heavy metals, bacteria, and fungus.

In summary, the use of CBD in any form should be discouraged during pregnancy and during lactation.[59]

Conclusion

As states continue to legalize medical and recreational marijuana, more women planning pregnancy, pregnant, or breastfeeding will present with exposure to marijuana. In summary, the literature available for review suggests that no amount of marijuana use in pregnancy and lactation is safe. Marijuana use has the potential for adverse maternal, fetal, and long-term childhood development. Women contemplating pregnancy or pregnant should discontinue marijuana use. Consultation with an addiction specialist and/or mental health provided may be indicated. Passive or secondhand exposure to marijuana also may have potential effects and should also be avoided. Given the concerns regarding the potential for adverse pregnancy outcome, prenatal care should be adjusted to screen for the potential adverse outcomes.

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Medicinal Marijuana, Stress, Anxiety, and Depression: *Primum non nocere*

by Mark Gold, MD

Medications are viewed as dangerous until proven safe and effective by science and approved by the FDA. Drugs of abuse are taken for many other purposes but often considered safe until proven unsafe.

Higher levels of stress are associated with an increased risk of substance use disorders (SUDs) and other mental health conditions like depression. Stress may exacerbate underlying medical and psychiatric conditions and weaken individual response systems that process events and build resilience. Stress can also make licit and illicit substance use more appealing as a quick self-treatment for anxiety. Stress may also cause SUD slips and relapse in patients who are in treatment for opioid and other substance use disorders. Deaths of despair,[1] including overdoses, have increased during the pandemic.[2]

The use of cannabis, vaping, or other tetrahydrocannabinol (THC) products may carry unique risks for those "self-medicating" and make depression worse when used as an ersatz antidepressant.[3] So-called 'medical marijuana' shouldn't be so lightheartedly rendered or prescribed as a relaxation tool. Short and long term changes in mood, depression, and suicidality can begin during adolescence and exacerbate by teen marijuana use according to a recent study.[4] This longitudinal cohort study of over 30 years found that cannabis use during adolescence is not a medicine, but is associated with both depression and suicidality in adult life. Early use is the riskiest. The younger the user of regular cannabis, the higher the risk of depression in adulthood. Recent use of marijuana for pain has also had unintended consequences, not replacing opioids but adding cannabis and even *de novo* cannabis use disorders to opioid risks.

Adults and youth with pain have heard and read claims about cannabis smoking or THC vaping for non-opioid pain relief. However, they are vulnerable to adverse cannabis outcomes, including continued opioid use and the development of additional substance use disorders.[5] Public "medicinal" opinions on hydroxychloroquine and actual FDA- quality studies of safety and efficacy in SARS COVID 19[6] or voting marijuana a medicine is quite different than proving in a prospective, random assignment, placebo-controlled double-blind studies. FDA standards protect us from unsafe and ineffective drugs and require that studies are specific to a particular disease at a precise dose and by a particular route and also superior to existing FDA treatments for that disease. While hopes for cannabis-derived medicines are rational, medicinal claims are premature.[7]

While not approved by the FDA for pain relief, it might have seemed logical to think and hope that medicinal marijuana would reduce opioid use. On the contrary, when studied, medical marijuana users are significantly more, rather than less, likely to use and misuse prescription drugs.[8] Drugs of abuse are unique in that they stimulate their taking but also because they all cause euphoria, loss of self-control, and self-administration through virtually the same net effect on the brain's dopamine systems. So even drugs initially supported by evidence of effectiveness may later prove to be more harmful than beneficial. Recommending marijuana as if it was an FDA approved and tested medication is currently a topic of great concern, debate, and consternation. *Primum non-nocere*, i.e., first do no



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harm. Medications are viewed as dangerous until proven safe and effective by science and approved by the FDA. Drugs of abuse are taken for many other purposes but often considered safe until proven unsafe. The reversal in the burden of proof means that drugs of abuse are field-tested en masse and consequences discovered over time. Vaping is a recent disastrous example.

Smoking and Vaping Marijuana and THC

The University of Michigan's Monitoring the Future reported that in 2019 (www.monitoringthefuture.org), there was a significant increase in daily cannabis use in the younger grades. Medicinal re-branding of marijuana smoking has accelerated trends in teens' perceptions of the risks of marijuana use; teens' view of risks has steadily declined over the past decade. In 2019, 11.8% of 8th graders reported marijuana use in the past year, and 6.6% were considered current users. Among 10th graders, 28.8% had used marijuana in the past year, and 18.4% were current users. Marijuana use among 12th graders is surprising since 35.7% had used marijuana during the year before the survey, and 22.3% used in the past month. An especially alarming, 6.4% of current high school seniors use marijuana daily or near-daily. Marijuana use is now at a 35-year high for college students. Daily or near-daily use of marijuana was 5.8% in 2018 for college students. It has been between 4% and 6% in the past five years. Among same-age non-college youth, it was 11.1%, nearly double the level for college youth. NIDA's Director Volkow[9] has discussed these findings, concerns of cannabis use disorders, and likely health, memory, and performance problems caused by regular marijuana use. With the growing popularity[10] of vaping, teens have increased vaping THC, with nearly 4% of 12th graders saying they vape THC daily. The use of tobacco, nicotine, and THC products is widespread among teens. Marijuana use has many adverse consequences, especially for children and teens, whose use is considered dangerous.[11]

Rates of cannabis smoking and vaping are similar to those reported for cigarettes, and cigarette smoking is related to marijuana use. Cannabis and tobacco use and misuse frequently co-occur,[12] and in some cases, cannabis smoking precedes tobacco smoking, and in others, tobacco smoking precedes marijuana smoking. THC use is also rising in many states that have legalized the substance, and among the young, for whom the effects of THC are different and likely more dangerous than they are for older individuals. The NIH's 2019 Monitoring the Future survey also found a spike in rates of youth vaping marijuana, concerning because of the substance and the risky delivery route. Learning to inhale drug vapors may be the gateway event worth additional study.[13] Most of the public health attention has been focused on vaping THC and death or severe toxic effects on lung and pulmonary function. The field testing of THC vaping and e-cigarettes have led to the CDC recommending no use of all e-cigarette or vaping, THC, and nicotine products.[14] Many more current and potential consequences of cannabis smoking and vaping THC are coming to light. Marijuana use has increased in teens following the reduction in perceived danger, ballot initiatives, and largely unproven medical marijuana claims.[15]

Whether it's logical to use alcohol or THC products for stress relief, instead of exercising or meditating or taking a walk or doing yoga or talking to a friend or therapist, is a different question from why some individuals do it. People often report anxiety as a primary motivation for using THC

Adolescent cannabis exposure results in impaired cognition, sleep, and driving ability.



products, and it isn't hard to find someone who will swear by the substance as a tranquil godsend without which life would be far less exciting and considerably more fraught. Researchers have focused more recent cannabinoid stress and anxiety efforts on inhibition of monoacylglycerol lipase (MAGL) to enhance signaling of the most abundant and efficacious endocannabinoid ligand, 2-arachidonoylglycerol (2-AG). Preclinical evidence supports a role for this system in the regulation of anxiety-related outcomes and stress and anxiety in the brain (doi:10.1016/j.biopsych.2020.01.015). Many research groups are hopeful that this work will provide us with answers to the question of why some individuals turn to marijuana for acute stress relief only to find that their stress and anxiety may make smoking cannabis or vaping THC more reinforcing.

Marcus et al. found[16] that a molecule, called 2-AG, helps create and move stress-related chemicals in the brain. These chemicals move along a brain path that connects the amygdala, which handles emotion, to the prefrontal cortex, which helps us make decisions. When individuals experience more stress, this path between the amygdala and prefrontal cortex becomes more active. The molecule works to manage stress and anxiety by limiting the chemicals that pass through the connecting path. 2-AG is part of the brain's anxiety-managing endocannabinoid system, in which the effects of marijuana are also felt. The brain's anxiety-limiting molecule and marijuana operate through the same receptors. In this study, researchers made mice stressed through exposure to foot shocks and bad odors. Then they observed the mice's brains and behavior to measure the effects of 2-AG and the path connecting the amygdala and prefrontal cortex. They found that making the mice stressed inhibited the effects of the molecule's ability to limit anxiety and led to more activity in the connecting path as the mice behaved more anxiously. These new findings indicate that more substantial levels of stress interfere with 2-AG's effects on blocking anxiety, overwhelming the endocannabinoid system and allowing anxiety-related chemicals to speed through the brain.[17]

Why Is This New 2-AG Study So Important?

Cannabis use proponents claim it is a medicine and treatment for anxiety, stress, pain, and also the opioid crisis. It is easier to make claims of safety and efficacy than to prove them. A formal study may determine safety and effectiveness, but in the meantime, cannabis has many advocates who argue that it is as good as any medication or therapy for anxiety and stress. But, no one has provided the kind of evidence that would be presented to the FDA as part of a new drug application. These claims have not been studied in random assignment, double-blind or comparable efficacy scientific trials. In the interim, it is safer to conclude that this also is not true.

This new study[17] finds specific pathways in the brain that lead to anxiety—especially the impairment of 2-AG—and suggests that new medications could be designed to work on this system to be more effective anti-anxiety medication. The authors of this study hope to do more research on how the cannabinoid system becomes impaired after stress exposure, how it repairs its anxiety-limiting function after impairment, and which molecules are involved in these processes. Well-functioning cannabinoid systems have a critical role in stopping or limiting anxiety. Genes and specific efforts to support this system like exercise,[18] diet, meditation, may explain why some individuals exposed to extreme stress or trauma don't develop severe mental health conditions. This research refers to stressed-out mice, not humans. Again, only further study can prove any of this.

Risks and Concerns

Advancements in the understanding of the endogenous cannabinoid system, neuroscience, and pharmacology of cannabis have led to numerous proposed uses. Medical cannabis is now legal in a majority of states, and THC and cannabidiol (CBD), the prominent cannabinoids found in cannabis, have both been utilized in the development of FDA-approved drugs. Medicinal claims and cannabis legalization have been influential and related to the emergence, and frequency of cannabis use disorders.[19] Cannabinoid exposure in rat adolescence reprograms the initial behavioral, molecular, and epigenetic response to cocaine.[20] Smoking marijuana for problems with pain management may result in a new substance use disorder without any change in the underlying disease or relief. As cannabis marketing, legal status and clinical studies of cannabis-related 'medications' continue, physicians are often lost without FDA guidance and will need to balance the real potential of these compounds with their limitations and adverse effects.[21]

Early exposure to cannabinoids in adolescent rodents decreases the reactivity of brain dopamine reward centers later in adulthood. To the extent that



In a recent survey, marijuana use among 12th graders is disturbing and concerning: 35.7% had used marijuana during the year before the survey, and 22.3% used in the past month.

these findings generalize to humans, this could help explain the increased vulnerability for addiction to other substances of misuse later in life that most epidemiological studies have reported for people who begin marijuana use early in life. It is also consistent with animal experiments showing THC's ability to "prime" the brain for enhanced responses to other drugs. For example, rats previously administered THC show heightened behavioral response not only when further exposed to THC but also when exposed to other drugs such as morphine—a phenomenon called cross-sensitization. Adolescent cannabis exposure results in impaired cognition, sleep, and driving ability. Cannabis Use Disorders are increasing, especially in teens and young adults, as a result of escalating use and consequences. Supportive and traditional behavioral therapies are currently the mainstay of treating cannabis misuse, with no pharmacotherapies presently approved by the FDA for cannabis use disorder in youth.[22]

Medicinal Cannabis and CBDs

There are no FDA-approved cannabinoid medications approved for psychiatric disease or even for the treatment of psychiatric symptoms. But, we have learned a great deal and have more to learn about marijuana as a medicine and CBD. The FDA has recently approved Epidiolex or CBD oral solution for the treatment of seizures associated with tuberous sclerosis and previously approved for the treatment of seizures associated with two other rare and severe forms of epilepsy, Lennox-Gastaut syndrome (LGS) and Dravet syndrome (DS). Epidolex is the only FDA-approved drug that contains a purified drug substance derived from cannabis. That means the FDA has concluded that this particular drug product is safe and effective for its intended use. The FDA has also approved Marinol and Syndros, medications which include a synthetic delta-9-tetrahydrocannabinol (dronabinol, THC) for the treatment of anorexia associated with weight loss in AIDS patients. Some valid researchers are optimistic that pharmaceutical-grade cannabinoids may be found through additional controlled study to be a useful medication for other diseases. CBD has also been shown to have promise as a treatment for specific distressing symptoms, especially in patients with precipitated craving and anxiety.[23] This does not mean that it is safe and effective for stress management, anxiety, depression, and other problems that can and are safely treated by psychiatrists and other health providers with approved and well-studied evidence-based approaches. Developing better tools to manage stress and anxiety makes the most sense. Developing better coping mechanisms is likely to be especially beneficial for individuals using risky

substances. Research continues to suggest that smoked or vaped marijuana or THC is one of these hazardous substances. As Harvard's Kevin Hill, MD,[24] has said recently, "Medical cannabis may ultimately prove to be effective in treating many other medical conditions, including posttraumatic stress disorder and Tourette syndrome, but as yet, there is little evidence to show that this is the case."

The risks of marijuana smoking and THC vaping are mostly unknown, but no news is not necessarily good news. Many substances, like marijuana, without overdose death risks, are considered safe because we can not imagine all of the ways that they can be dangerous. Of course, edibles have gained in popularity because it is evident that smoking exposes everyone to second hand (SHS) and third-hand smoke risks. SHS or "second hand" designation a sanitized way to say exposure to carcinogen-polluted air or intoxication without permission (doi:10.1371/journal.pone.0153327) and second-hand tobacco smoke is a significant cause of death each year. Inhaling someone's smoke vapors is a major second-hand problem, but there are other concerns like impaired drugged driving. Traffic accidents are increasing in cities and states where cannabis is legal and widely used. A recent study found that individuals using cannabis are worse drivers.[25] Impaired driving ability in tested simulations included crossing the centerline, speeding, hitting pedestrians, and missing stop signs. Study participants who started using cannabis before the age of sixteen fared even worse.

Cannabis use is presented in the media as a stress-relieving substance, a mostly harmless escape from life's ups and downs. It's also portrayed as an option to alcohol for those seeking an alternative to relaxation, meditation, or exercise to unwind chemically. Scientists rarely evaluate these urban myths, and once one is evaluated, a new claim is made for a new problem of modern living in real-time. A person may initiate cannabis smoking or vaping THC, believing that they may be self-medicating stress and anxiety. But, not only has this not been proven to work, but, if anything, research suggests that it is not a treatment but a significant risk.

Many more cannabinoids are likely to be approved as medicines, but it is not clear at this time as to which cannabinoid, in what dose, by which route, and in what disease. The role of cannabis in medicine is expanding, often with claims preceding testing. Use is not without other risks. One risk identified in new studies that cannabis and several cannabinoid-based medications may make other drugs of abuse more reinforcing.[26] Marijuana use is also linked to other substance use disorders, including alcohol and nicotine addiction.[27] Many findings are consistent with the idea of marijuana as a "gateway drug." The majority of people who use marijuana do not go on to use other "harder" substances. It may be becoming clear that current marijuana use makes cocaine and other drug use more reinforcing. New studies have suggested that parental use may cause such sensitization in their children to opioids.[28] Cross-sensitization is not unique to marijuana. Alcohol and nicotine also prime the brain for a heightened response to other drugs and are, like marijuana, also typically used before a person progresses to other, more harmful substances.[29]

Conclusion

It may be useful to recall that alcohol and tobacco[30, 31, 32] are not medicines, but medicinal uses were proposed for them. The U.S. Treasury Department, during prohibition, authorized physicians to write prescriptions for medicinal alcohol for cancer, GI distress, and depression. Of course, alcohol is not a safe and effective medicine for these problems and may cause them. The same may be true for cannabis claims and effects. Medicinal applications that are advertised or made for cannabis typically would require a pharmaceutical company to prove the treatment works for a specific illness. Physicians might wonder or ask if alcohol, tobacco, or cannabis can ever be called medicines without FDA approval? This cannabis- as-medicine process and outcome have made it easier to argue with the FDA over the definition of a medicine. Should we decide if hydroxychloroquine or cannabis is a medicine for COVID-19 by utilizing the FDA or by asking elected officials? A prescription should be tested rigorously in dose-safety – efficacy studies, successfully navigate the entirety of the FDA's new drug approval process and utilize modern science to separate therapeutic molecules from the smoke. Sure we might think about eating or smoking foxglove but is quite toxic. Digoxin was isolated from the foxglove plant, and Digitalis has become a great addition to the treatment of heart diseases recognized by the World Health Organization on its shortlist of safe, effective, and "Essential Medicines." Decriminalizing or legalizing adult recreational cannabis, like Budweiser or alcohol,[33] is one thing, but physicians and the public in short-circuiting the FDA protections are another. Short-



circuiting science from the new medicine decision-making process is a slippery slope. The 18th Amendment or National Prohibition Act enforced the ban on alcohol with a few specified exceptions. It allowed physicians to prescribe alcohol for most any ailment, farmers to produce wine for their consumption, and Clergy to provide alcohol during ceremonies. In his book on alcohol prohibition,[34] the author writes: "Presumably, doctors were doing examinations and diagnoses, but it was mostly bogus." Much remains to be settled about the claims, safety, and efficacy of cannabis. The FDA has just approved CBD again, this time for the treatment of seizures associated with tuberous sclerosis. Many more clinical trials are in progress. It is logical to expect pharmaceutical companies to successfully translate cannabinoid science to make new treatments and classes of medicines. In the meantime, Physicians should insist on science and data first, FDA controlled studies, and "First do no harm."

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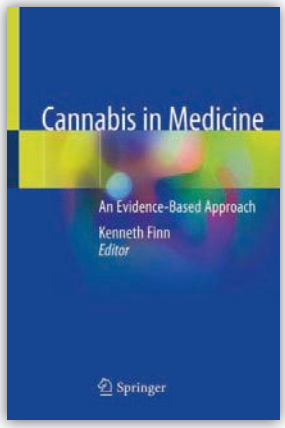
BOOK REVIEW

Cannabis in Medicine: An Evidence-Based Approach

Springer Publishing
ISBN: 978-3-030-45968-0

Edited by Kenneth Finn, MD

Reviewed by J. Michael Bostwick, MD, Professor of Psychiatry, Mayo Clinic, Rochester, MN



The title of "Cannabis in Medicine: An Evidence-Based Approach" contains an irony. In chapter after chapter in this multi-authored book written predominately by providers associated with mainstream medical facilities in Colorado, the authors point out the inadequacy of the evidence we have and the absence of the evidence we need to determine how – or even if – cannabis has medical legitimacy. The foreword's title, "Losing Ground: The Rise of Cannabis Culture," sets the tone. David Murray, a senior fellow at the Hudson Institute, argues convincingly that "the current experiment with cannabis, underway nationwide [is] leading us towards a future of unanticipated consequences, a future already established in the patterns of use 'seeded' in the population but as yet unmanifested." In other words, the cannabis horse has not only fled the barn but has been breeding prolifically to the point that we couldn't get rid of it and its progeny if we wanted to!

The 20 chapters following the foreword are divided into basic science (three chapters) and clinical evidence (17 chapters) sections. Over and over in the clinical evidence chapters, individual authors remind the reader of the lack of quality control in production, the dearth of strong evidence from adequately designed research trials, and the intensifying potency of cannabis with attendant dangers, particularly for youth. The organization of this section lacks consistency in that some chapters focus on specialty (e.g. pulmonary medicine), others on patient groups (e.g. the pediatric and adolescent population), others on physiological implications (e.g. clinical cardiovascular effects; neuropsychiatric effects), others on specific diseases (e.g. gastrointestinal disorders; ocular conditions), and still others on public health topics (e.g. cannabis-impaired driving). While all are relevant, a specialty or organ system focus, with a separate public health section might lend the book more coherence. It would also be worth exploring how "cannabis culture" has become in essence a parallel medical system, with many of cannabis's most ardent proponents as dropouts from establishment medicine after its nostrums for diagnoses like chronic pain, anxiety, and depression have failed to bring them relief.

I would have liked a chapter specifically grappling with the porous boundary between federal and state jurisdictions over cannabis as medicine and marijuana as recreational substance. Lawyer David G. Evans' admirable chapter on "The Legal Aspects of Marijuana as Medicine" moves in that direction when he writes that, "'medical marijuana' is not a 'states' rights' issue." To wit, for no other drug than cannabis has the federal government ceded regulatory responsibility to states that are variably (but mostly not) equipped to handle it. The truth, complex in its contradictions and inconsistencies, is that in the United States, marijuana remains a Schedule I drug without recognized medical value; the Federal Drug Administration overseeing American pharmaceuticals throws roadblocks in the way of studying it, thereby interfering with the development of a robust evidence base; the federal government has looked the other way and even colluded with the states as one after another has legalized cannabis medically, recreationally, or both; and physicians risk their federal licenses to prescribe if they do more than recommend this drug. In a nutshell, any effort to impose logic is doomed because the American scene vis-à-vis cannabis is seemingly irretrievably illogical.

The editor of this volume, Kenneth Finn, MD, a PMR and pain management specialist in Colorado Springs, Colorado, is to be commended for encouraging individual chapter authors to develop encyclopedic bibliographies. The book can thus serve as a resource for practitioners wishing to delve into a vast and growing literature that continues to offer little that is conclusive. The book can also serve as a primer on what is known about cannabis as medicine, keeping in mind a slant throughout – not necessarily unjustified, at least from an allopathic or osteopathic perspective – that cannabis is neither legitimate as medicine nor safe, even for recreational use.

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No Legal Recreational Marijuana in Missouri: We Have Enough Problems with Addiction!

by John C. Hagan III, MD

Do your part to oppose any petition or referendum aimed at making high THC marijuana legal for recreational use. Only the COVID pandemic prevented legal recreational cannabis from being on the November 2020 ballot. Commercial and street level THC or CBD are not valid medications.

Big Weed (commercial interests profiting from harmful cannabis use), not satisfied with their 2018 victory passing sham medical marijuana into Missouri constitutional law, is geared up to enrich themselves further at the expense of their habituated customers. Only the intervention of the COVID pandemic prevented recreational cannabis from being on the 2020 November General Election ballot. Millions of dollars and scores of paid, mostly marijuana-using, workers were hitting Show-Me sidewalks to get legal-recreational cannabis on the November 2020 general election ballot as a referendum. You could find and smell them collecting signatures while loitering around vaping and CBD stores that are (appropriately) sprouting faster than weeds and grass.

When COVID is over, Big Weed will be back in 2021, 2022, 2023…you get the idea. With enough time, money, paid workers, and fake news about the benign effects of regularly stoning out on 95% THC cannabis products, they only need win once as with 2018 sham medical marijuana.



Sham medical marijuana is a social and medical disaster in Missouri as in other states before us. (Figure 1). This issue of *Missouri Medicine* and many previous articles clearly demonstrate that commercial and street level THC or CBD are not valid medications. Pharmaceutically pure, FDA tested and approved CBD drugs (Epidiolex, Marinol, Syndros, Cesamet) being the sole exception for a limited number of indications.

The Missouri recreational marijuana referendum is financed by a despicable conglomerate of entities ranging from George Soros, to the Mexican drug cartels, to mainline businesses such as the alcohol industry which considers 95% THC (the high/euphoria producing chemical of cannabis products) the next 'logical' adult beverage to accompany beer, wine, and liquor. [1,2,3] Collectively, I refer to this unsavory and unwholesome alliance as "Big Weed." As physicians, parents, grandparents, responsible Missourians, we can't let them succeed!

Do not be confused. This is not sham medical marijuana. After a decade of effort, tens of millions of dollars of advertising, promotion, and half-hearted, ineffectual opposition by the healthcare professions, no opposition by the Missouri Hospital Association and support by the *Kansas City Star* and *St. Louis Post-Dispatch* newspapers, sham medical pot was passed into constitutional law in 2018.[1]

John C. Hagan, III, MD, FACS, FAAO, MSMA member since 1975, is a Kansas City, Missouri, ophthalmologist and *Missouri Medicine* Editor since 2000. He is a multi-year Diamond Contributor to MMPAC.



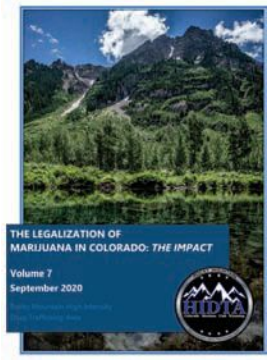
Figure 1. Both the passage of so-called 'medical marijuana' and legal recreational marijuana in Colorado raised domestic violence and increased homelessness and theft.
Source: Denver.Post.com

That ship has sailed and, for better or for worse (my bet the latter), we will have to live with the consequences. At least until there is enough overwhelming scientific evidence of the harms of sham medical marijuana to roll back the tsunami of state pot laws. That has happened before. Heroin was an over the counter 'medicine' until 1914 when all use became illegal.[1] Eventually, the public understood that nicotine has catastrophic healthcare consequences. Cannabis is now used more than nicotine, some users believing Big Weed's narrative about its medicinal properties, just like Big Tobacco, convinced the public and many physicians with their phony nicotine research about its medicinal properties.

The implications of living with medical marijuana as law is very comprehensively discussed in a recent FP: Missouri Family Physician article.[4] Recreational marijuana is not decriminalization of marijuana. That arrow is already in the air. Missouri's law enforcement and judicial systems are no longer prosecuting small amounts of pot for personal use; those incarcerated for same are being released and their criminal records expunged. Many states and municipalities have already decriminalized small amounts of personal use weed. Throwing their arms around the personal use pot clemency issue is deliberate obfuscation on the part of slimy and dishonest Big Weed. Widespread, easy access, high THC marijuana disproportionately works against the young, the poor, minorities, and the ill.

The Missouri State Medical Association has declared our organization against making high THC cannabis products legal in Missouri for recreational use. MSMA joins other influential Missouri physician organizations including Missouri Association of Osteopathic Physicians

Figure 2. The Legalization of Marijuana in Colorado: The Impact



The Legalization of Marijuana in Colorado: The Impact

Volume 7, September 2020

by the Rocky Mountain High Intensity Drug Trafficking Area program

Medical and recreational marijuana are destroying the health and social fabric of Colorado the Centennial State. Efforts are already underway to introduce recreational marijuana into law in Missouri via public referendum.

Executive Summary

The Rocky Mountain High Intensity Drug Trafficking Area (RMHIDTA) program has published annual reports every year since 2013 tracking the impact of legalizing recreational marijuana in Colorado. The purpose is to provide data and information so that policy makers and citizens can make informed decisions on the issue of marijuana legalization.[1]

Section I: Traffic Fatalities & Impaired Driving

• Since recreational marijuana was legalized, traffic deaths in which drivers tested positive for marijuana **increased 135%** while all Colorado traffic deaths **increased 24%**.

• Since recreational marijuana was legalized, traffic deaths involving drivers who tested positive for marijuana **more than doubled** from 55 in 2013 to 129 people killed in 2019.

  • This equates to one person killed every 3.5 days in 2019 compared to one person killed every 6.5 days in 2013.

• Since recreational marijuana was legalized, the percentage of all Colorado traffic deaths that were marijuana-related **increased from 15%** in 2013 to **25%** in 2019.

Section II: Marijuana Use

Since recreational marijuana was legalized in 2013:

• Past month marijuana use (ages 12 and older) **increased 30%** and is **76%** higher than the national average, currently ranked **3rd** in the nation.

• Adult marijuana use (ages 18 and older) **increased 19%** and is **73% higher** than the national average, currently ranked **3rd** in the nation.

• Past month college age marijuana use (ages 18-25) **increased 6%** and is **50% higher** than the national average, currently ranked **3rd** in the nation.

• Past month youth marijuana use (ages 12-17) **decreased 25%** and is **43% higher** than the national average, currently ranked **7th** in the nation.

Section III: Public Health

• Marijuana *only* exposures more than **quadrupled** in the seven-year average (2013-2019) since recreational marijuana was legalized compared to the seven-year average (2006-2012) prior to legalization.

• Treatment for marijuana use for all ages **decreased 21%** from 2009 to 2019.

• The percent of suicide incidents in which toxicology results were positive for marijuana has **increased** from **14%** in 2013 to **23%** in 2018.

Section IV: Black Market

• RMHIDTA Colorado Drug Task Forces (10) conducted **278 investigations** of black market marijuana in Colorado resulting in:

  • 237 felony arrests
  • 7.49 tons of marijuana seized
  • 68,600 marijuana plants seized
  • 29 different states the marijuana was destined

• Seizures of marijuana reported to the El Paso Intelligence Center in Colorado **increased 17%** from an average of 242 parcels (2009-2012) to an average of 283 parcels (2013-2019) during the time recreational marijuana has been commercialized.

Section V: Societal Impact

• Marijuana tax revenue represent approximately **0.85%** of Colorado's FY 2019 budget.

• **67%** of local jurisdictions in Colorado have banned medical and recreational marijuana businesses.

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https://rmhidta.org/files/D2DF/RMHIDTA%20

& Surgeons, Kansas City Medical Association, Greene County (Springfield) Medical Society, Missouri Society of Eye Physicians & Surgeons, and Missouri Academy of Family Physicians. Additional medical organizations are in the process of officially opposing recreational marijuana. Make no mistake, we cannot do this alone. We desperately need the support of other healthcare professionals, nurses, dentists, and most especially the Missouri Hospital Association. Anecdotal reports from Missouri suburban hospitals and emergency rooms published in *Missouri Medicine* already indicate easy access medical marijuana is resulting in increased cannabis related ER visits and hospitalizations.[5]

Missouri Medicine has published more scientific and perspective articles on the unscientific nature of the studies of medical marijuana and the deleterious effects of moving from legal sham medical marijuana to legal recreational marijuana than any other state medical journal. The most important are open access, referenced and linked.[6] We need a big tent and a huge coalition. We must reach out to school system administrations, teachers, PTAs. We must ask for the help of clergy, religious denominations, law enforcement, the business community, civic organizations, state, county, and local government. We need to ask questions such as: Why is Mothers Against Drug Drivers (MADD) committed to stopping death and disability due to alcohol but not cannabis DUI? Every state passing medical and recreational marijuana has had an increase in traffic accidents, deaths and disability.[1,2] Why shouldn't we encourage more lawyers and organizations (e.g. https://www.civel.org/) opposing widespread cannabis to go after Big Weed via litigation as they did against Big Tobacco?

The best insights about legalizing marijuana come from studies in states like Colorado that have legalized medical marijuana then doubled down with recreational marijuana. Once among the healthiest of states, Colorado public health indices are in free fall.[7,8,9] (Figure 1.) Colorado state leaders are so alarmed about the adverse effects of legalized marijuana that they have appointed a commission to study and report on it annually. Named The Rocky Mountain High Intensity Drug Trafficking Area Program, the most recent, disturbing 2020 executive report is shown in Figure 2. Note that the anticipated revenues from recreational marijuana are a pitiful 0.85% of Colorado's annual budget and are dwarfed by the law enforcement, educational, medical and social costs of easy access, high potency recreational marijuana. Missouri does not need to repeat this disastrously sad social experiment.

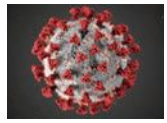
Educate yourself. Educate your patients. Educate the medical, religious, social, educational circles you move in. Physicians once advocated and contributed to the medical problems of tobacco and shilled for Big Tobacco. Physicians once contributed to the problems of over prescribing opioids. Let's not make the same mistake with slimy Big Weed. Let's get out ahead of the problem. Do your part to oppose any petition or referendum aimed at making high THC marijuana legal for recreational use. While you are at it keep a look out for evolving problems with the sham medical marijuana law. Let's not let Missouri go to pot!

Disclosure

None. Dr. Hagan did refuse a generous financial offer from Big Weed to be a paid medical cannabis consultant (2019).

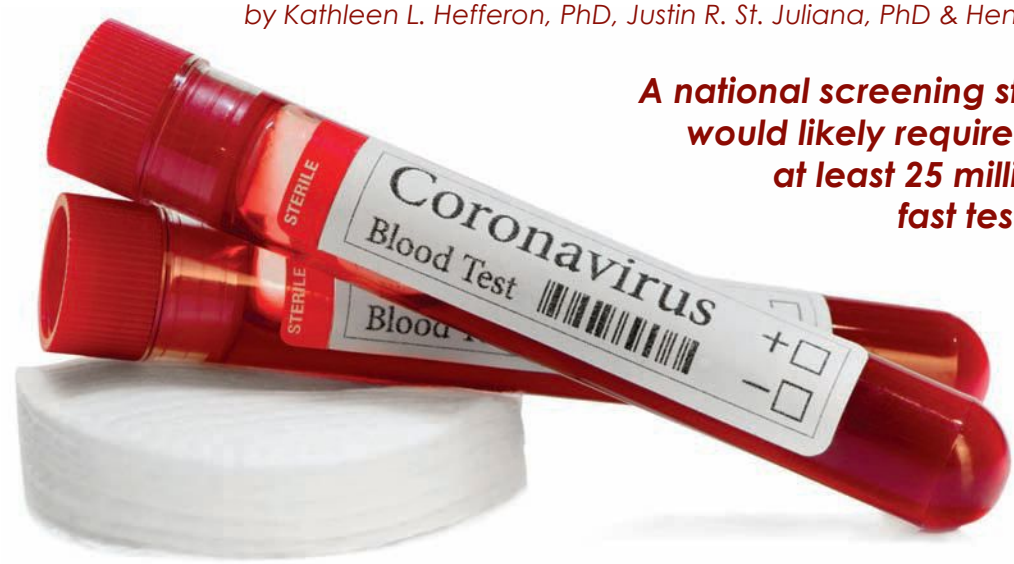
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COVID-19 Testing Tests Our Mettle

by Kathleen L. Hefferon, PhD, Justin R. St. Juliana, PhD & Henry I. Miller, MD



A national screening strategy would likely require at least 25 million fast tests per week.

Public health experts are unanimous that testing— along with contact tracing, wearing masks, social distancing, and avoiding crowds—is one of the pillars of gaining control over the COVID-19 pandemic. Testing can answer critical questions, such as how many people of various demographic groups in the population are or have been infected. Those data can, in turn, answer critical questions about important characteristics of COVID-19 that are essential to formulating policies to predict and control its spread. They include: How readily is the virus transmitted from person to person? How many people will an infected person subsequently infect? What is the length of the incubation period and the usual course of the disease? What percentage of people tested have positive tests? How long does post-infection immunity to infection persist?



Henry I. Miller, MD, (left), a physician and molecular biologist, is a Senior Fellow at the Pacific Research Institute in San Francisco, California. He was the founding director of the FDA's Office of Biotechnology. Kathleen L. Hefferon, PhD, is in the Department of Microbiology and Justin R. St. Juliana, PhD, is in the Department of Ecology and Evolutionary Biology; both at Cornell University, Ithaca, New York.

But "testing" is complicated and has many facets, both conceptual and practical. The results, and how they are used to inform decisions, can vary greatly depending on what type of test is used to generate the data. Moreover, the testing landscape is evolving, with public health officials and epidemiologists calling for a shift in testing strategy away from diagnosing people who have symptoms or were exposed to the virus and toward screening large populations using faster, cheaper, sometimes less accurate tests. Identifying and isolating infected individuals more quickly should slow the virus' spread and expedite the safe reopening of schools and workplaces.

There are three fundamentally distinct kinds of tests relevant to the SARS-CoV-2 virus and to COVID-19, the illness it causes; they measure different things. The first involves taking a nasal swab (or, less commonly but increasingly, a saliva sample) and testing for the presence of virus genetic material, RNA (a molecule similar to DNA), or fragments thereof.[1] This test uses nucleic acid amplification technology (NAAT), of which polymerase chain reaction, or PCR, is by far the most widely available. A swab contains only a very small amount of virus RNA, so the PCR test multiplies the amount of RNA in the sample repeatedly, to obtain an amount of RNA in the sample large enough to detect. This is what is currently often referred to as "COVID-19

testing." Many of us have already had this kind of testing done; most often, a health care worker takes a swab from one nostril using an extra-long Q-tip and sends the sample to a testing facility. There, the RNA is isolated from the sample and amplified by PCR, using short sets of highly specific oligonucleotide "primers" that seek out and bind to the SARS-CoV-2 virus's genetic material. Within a few days' time, the samples that contained viral RNA, either intact or fragmented, will produce a positive result.

Although most of the tests currently used have good analytic sensitivity (the ability to detect viral RNA if it is present, leading to only a very small number of false negative results), and specificity (the ability to give a positive result only for RNA from SARS-CoV-2 RNA but not for related coronaviruses), the length of time needed to receive a result—currently, days—is a significant weakness. Your test could be negative, but you could become infected while awaiting the result (with a subsequent test showing positive). Or while awaiting the results of the (positive) test, you could infect other people during your day-to-day activities, making contact-tracing difficult, if not impossible. The good news is that as more and more attention is being paid to COVID-19, our test kits are rapidly improving.

The United States is currently carrying out about a million tests a day, more than when the pandemic began but still short of the three million or more per day that experts say is the minimum required.[2] A new development in PCR testing for viral RNA recently approved by regulators is "sample pooling," which is important because it allows for more people to be tested quickly using fewer testing resources.[3] It allows the pooling of samples from multiple people—four are currently permitted by regulators—to be tested in a pool or batch using a single test, rather than running each individual sample on its own. If the test is negative, it is assumed that all four individual samples are negative, but if the pool is positive, it means that one or more of the individuals tested in that pool is infected, and each of the samples in that pool is tested again individually. This testing strategy is most efficient in areas with low prevalence, in which case most results are expected to be negative.

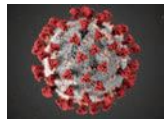
A second type of testing is known as antigen testing. Antigens are substances that can elicit a response from elements of the immune system. In the case of a virus, antigens could be proteins or other molecules in the virion, often present on the surface. Antigen tests specifically detect the presence of SARS-CoV-2 proteins, and so, like testing for RNA, they measure components of the virus; and if positive, indicate active or clearing infection. They don't use nucleic acid amplification and can be completed much more quickly, in some kits even at home. A drawback is that their accuracy is generally lower than NAAT tests, making them most appropriate as a screening, rather than a true diagnostic test when disease prevalence is high.[4] Newer versions are being developed that have greater accuracy and wait times that deliver results in minutes.

The third type of test measures antibodies in the blood or saliva. When infected with a pathogen, a person's immune system—specifically, white blood cells called B cells—produces specific antibodies of several types to neutralize the organism causing that particular infection. The SARS-CoV-2 spike (S) protein plays the most important role in viral attachment, fusion and entry, and, therefore, is a promising target for the development of antibodies, entry inhibitors and vaccines. Antibodies to the receptor-binding domain (RBD) of the spike protein are considered to be the best surrogate for "neutralizing antibodies" that will not only bind to, but actually prevent the spike protein from promoting infection.

Antibody tests, which are performed on a blood sample instead of a nasal swab or saliva, measure whether antibodies that can bind to the COVID-19 spike protein are present. The presence of these antibodies is, therefore, a sign of previous infection. After the infection is cleared (and the PCR-based tests become negative), the immune system will continue to produce these same antibodies to help resist reinfection.

There are several key differences between the nasal swab test for virus RNA and the blood test for antibodies to the virus. A positive test for antibody production does not mean that the subject is currently infected with COVID-19 and contagious, but indicates that the individual has been exposed to the virus and become infected (symptomatic or asymptomatic) at some point in time. (It takes roughly 10-14 days from the time of exposure for antibodies to appear.)

Antibody testing can provide important information about how, where, and when the virus



has spread through the general population and, possibly, about a person's resistance to future infection. The appropriate use of both tests will help to turn the tide for the current pandemic and plan future strategies to address it.

The distinction between RNA and antibody (seroprevalence) tests becomes most evident from recent data collected by the CDC. This interactive dashboard shows patterns of antibodies to COVID-19 from blood samples tested in various geographic areas and over time.[4] The specimens were taken from people who had entered medical centers or hospitals for reasons other than COVID-19 infection. The data reflect that the number of people infected with the coronavirus throughout different parts of the United States varied greatly, as much as two to 13 times higher than the reported rates for those regions using the nasal swab testing. The discrepancy is startling, but not terribly surprising.

There is a significant difference in the sub-populations who have had nasal swabs (RNA/PCR tests) versus blood tests (presence of antibodies). People who test positive for SARS-CoV-2 RNA are more likely than randomly selected subjects in the population to have had COVID-19 symptoms or to have been exposed to someone believed to be infected; in other words, there was self-selection because of concerns about infection. On the other hand, people who tested positive for antibodies from a blood sample collected from a hospital or a routine medical clinic visit, were more likely to be tested for reasons that had little to do with exposure to or symptoms of COVID-19, and are more likely to have been asymptomatic. Neither group is representative of random population samples, and there is an urgent need for more systematic data collection so that existing knowledge gaps can be filled.

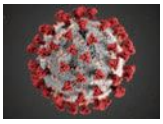
Although testing for levels of antibodies is important, blood samples can provide other clues to immunity to COVID-19. Immune cells other than B cells, called T cells, have been shown to mount a robust response to the virus long after the COVID-19 infection itself is over.[6] Collecting data through testing will help to tease apart these details. However, the presence of antibodies is not, per se, synonymous with immunity to infection, although as noted above, neutralizing antibodies to the receptor-binding domain (RBD) of the spike protein are considered to be the best surrogate for antibodies that will actually neutralize, or prevent, the spike protein from functioning and promoting infection.

A few reports have suggested the possibility that some patients who previously contracted COVID-19, then cleared the virus and had a negative test, subsequently tested positive again with a fresh onset of symptoms. It is currently unclear whether reinfection is a real phenomenon or an artifact of false positives/false negatives in the testing.[7] Again, more data are needed, much of which can be gleaned from careful study of a combination of RNA and antibody testing. Any differences between natural immunity and vaccine-induced immunity are also unclear and will have to be explored in detail once successful vaccine candidates are in hand. This information will be immensely helpful for addressing future outbreaks of COVID-19 and guiding public policy.

Done correctly, testing can provide essential information of several kinds, but the data we have currently, from antigen screening, the presence of virus RNA, and antibody tests are far from an accurate representation of the general population. So far, partially due to the lack of available test kits, systematic data from a large and genuinely random pool of participants are not available. Thus, for most of the country, we don't know how many people are COVID-19 positive but asymptomatic spreaders. Similarly, the blood test data taken from hospitals represent people who were seen for non-COVID-19 illnesses at the time; again, not a random sample of the local population. For the purposes of modelling the spread of virus or measuring the penetration of COVID-19 in the population at large, these biases in the populations tested limit the usefulness of the data.

By identifying new cases of COVID-19 and making it possible to quarantine them and isolate their contacts, testing for RNA or viral antigens will have an essential role in curbing the pandemic going forward. That could prevent the return of restrictions such as sheltering in place and the closing of non-essential businesses. The challenge will be to make tests reliable, plentiful, and available, and to have results accessible soon after samples are taken.

An emerging issue is the need for a transformation of our testing capacity and implementation.[7] We must make the transition from testing smaller sub-populations of people with little in common with each other to larger, more appropriately selected populations that are more representative of the true state of infection. This can now be accomplished in a rapid, less



expensive manner with screening using the antigen tests described above. However, because they are currently significantly less accurate than PCR tests at detecting viral material, their primary value is in screening, rather than diagnosis. Positive results should be considered "presumptively positive" and should be confirmed by subsequent RNA/PCR tests, but until the results of the latter are in, persons who test positive should be isolated, and their contacts traced and tested.

This transformation won't be easy. Among the hurdles facing widespread, repeat screening is the scarcity of tests that yield rapid results; biweekly testing of everyone at schools and certain workplaces with such tests, especially on pooled samples, could detect COVID-19 infections early on and keep the number of new cases to a manageable level, or even cause them to disappear in some locations. A national screening strategy would likely require at least 25 million fast tests per week, according to Jonathan Quick, who heads pandemic response for the Rockefeller Foundation.[8] On July 16, 2020, the Foundation released a national COVID-19 testing plan that called on the federal government to spend $75 billion to provide 30 million screening and diagnostic tests per week.

There isn't a moment to lose.

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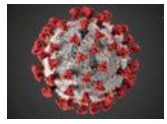
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Mental Health on the Frontlines: Before, During, and After COVID-19

by Simone A. Bernstein, MD & Jessica A. Gold, MD



COVID-19 has impacted the psychological wellbeing of healthcare providers, worsening an already heightened baseline, and is likely to continue long into the future.

The essential nature of healthcare workers during the SARS-CoV-2 (COVID-19) pandemic has placed them at significantly heightened risk. Most simply, they are more vulnerable to a COVID-19 infection than the general population and many, with estimates greater than 900 in the United States (U.S.) according to *The Guardian*, have died as a result.[1] However, this increased risk of infection does not just affect their physical health, but affects them mentally as well. This strain is only worsened by other stressors unique to the pandemic work environment like the shortage of personal protective equipment, limited treatment options for patients, or working extended hours. It is not surprising, then, that there are studies outlining how employers can implement steps to reduce this significant burden on clinicians.[2]

Yet, mental health concerns, including burnout, substance use, depression, and suicide among physicians are not new and were issues long before COVID-19.[3-7] These stressors are only compounding an already increased baseline. And, as we look towards the future, with rising cases across the country, and consider the ramifications of previous pandemics on mental health lasted up to three years, we also know that the outcomes are far from over when the pandemic itself is controlled.[8] Therefore, we must consider the



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continuum for mental health in healthcare workers: before, during, and after the pandemic, as a way to better target interventions that can have long-lasting impacts on physicians in need.

Before COVID-19

Wellness has been a "buzzword" and topic of conversation in graduate medical education for many years. Prior to COVID-19, research has shown that depression was prominent in medical students (27.2%), residents (28.8%), and licensed physicians (13% in men and 20% in women).[9-11] Substance use was also prevalent and at some point in their career, 10-15% of medical professionals misused substances, with alcohol the most commonly misused. Prescription drug use was also much higher than the general population.[12] For example, 13-23% of female physicians used prescription opioids as compared to 1%-3% of the general population.[12] That number was 14-23% (vs 1-4%) in men.[12]

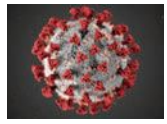
Given these numbers, one could make the argument that more strict and encompassing policies in medical schools and residency programs could help prevent some of the substance use issues in the medical field, similar to random drug and alcohol screens for pilots or ship captains whose impairment also impacts public safety.[13-14] While this may be controversial for physicians and many programs simply test at the beginning of employment, random testing could detect and deter drug use and misuse over time. Massachusetts General Hospital randomly tested anesthesiology residents over 13 years, and there was no detected substance abuse among 628 residents, while there were four incidents the 10 years before initiation of their random urine drug screening. [15] While this decreased used is based on a single-center comprehensive program, it suggests a larger study would be useful to determine if random drug screening reduces substance use disorders in medicine. However, these policies are unpopular even with the public and in 2014, California voters rejected a proposal that would have required physicians to submit to random drug testing.[16]

Burnout is also high in the medical profession. Though the definitions vary between studies, it is often defined as "emotional exhaustion," feeling "used up" at the end of the workday, and a sense of reduced personal accomplishment.[17] Physician burnout has many implications, including financial, and costs exceed $213.1 million.[18] Burnout is particularly relevant as it can lead to people leaving the profession, which, as the data from the Severe Acute Respiratory Syndrome (SARS) pandemic in Toronto suggests is only worsened during a pandemic.[19]

Given these high numbers, some policy changes were previously put into effect in medical education and training, like duty hours restrictions in 2003.[20] In 2017, additional changes were made by the Accreditation Council for Graduate Medical Education (ACGME) including the creation of policies and programs that support faculty members and residents to attend appointments for personal care, even during work hours. Additionally, the policies mention availability and access to confidential, affordable mental health counseling and treatment.[21]

One unique way to increase utilization of mental health services is an opt-out approach to a universal well-being assessment. In an opt-out study at a medicine residency program in the U.S., residents were scheduled for appointments when they were relieved from clinical responsibilities and it resulted in 93% of trainees attending their appointments.[22] Residents who participated also described satisfaction with these appointments and said they were likely to return for visits if they had mental health concerns.[22] While this is one study, it does suggest that opt-out programs could be one way to decrease barriers to care.

However, even if pathways are created to allow for care seeking, help seeking remains low in medicine due to a culture of stigma and fear. In fact, one study found that not a single female physician who died by suicide disclosed suicidal intent to a doctor prior to her death.[23] While there are many reasons why physicians do not disclose information about their mental health, one study found that 60% were concerned it could affect their medical licenses.[24] This causes some to get



Post-COVID Care

While the response to the impact of COVID-19 on mental health and wellbeing has significantly varied between institutions, all programs can find ways to improve discussions to create long-term solutions. This is critical...as we know from past pandemics that this will have mental health repercussions long into the future.

care outside of the system—receiving prescriptions from friends who are not formally treating them—and can lead others to delay treatment until a crisis occurs, if treatment is sought at all.[24] As we know that approximately 300-400 physicians die by suicide in the United States, this is not just an urgent issue, it is a critical one.[25]

During COVID-19

On top of an already strained emotional baseline, healthcare workers faced the sudden onslaught of a pandemic. Their day-to-day schedules changed, work environments looked different, patients were sicker, and their own risk much higher. All levels of medical training were affected in different ways. Medical school students on clerkships were removed from classrooms and rotations in the hospital, and those on research had their projects put on hold. Resident physicians were assigned to different rotations than ones originally scheduled, often to protect them from exposure. Yet, in some programs, trainees were sent to work in COVID-19 units, in specialties that were not their own, or graduated early to perform needed tasks. Faculty completed many outpatient appointments on virtual modalities, so patients were able to get care, but other procedures and "non-essential" work was put on hold. Not only did the life of a physician change inside the hospital, but home life shifted as well, and it became difficult to maintain a balanced life. Some also worried about infecting their families and chose to isolate in separate housing to keep them safe.

These changes had real mental health outcomes. In a study conducted in 34 hospitals in China, healthcare workers who engaged in direct diagnosis, treatment, and care of COVID-19 patients endorsed more severe degrees of depression, anxiety, insomnia, and distress.[26] Among healthcare workers in New York, positive screens for psychological stress were common, including 57% for acute stress, 48% for depressive symptoms, and 33% for symptoms of anxiety. Interestingly, 61% of participants also expressed an increased sense of meaning and purpose since the outbreak, which is worth more analysis.[27] At Washington University in St. Louis, a study was completed that compared trainees exposed to COVID-19 vs those that were non-exposed.[28] Compared to the non-exposed group, the exposed group had a higher prevalence of stress (29.4% vs 18.9%) and burnout (46.3% vs 22.7%).[28] Meaning and purpose can be further explored in Victor Frankl's book, *Man's Search for Meaning*, a memoir of surviving a concentration camp. [29] This book reflects that for a meaningful life, you must pursue meaningful work.[29] One study of academic physicians showcased that value-aligned work protected from burnout.[30] Therefore, including and thinking about these concepts might be protective factors in mental health of healthcare workers or at least important foundations for treatment.

Mental health risk will only continue to worsen as cases increase across the country and possibilities of additional waves and repeated resource strains occur. It is also emotionally exhausting for physicians to continue to express their lived experiences and attempt to contradict the narratives about testing and protective equipment daily through public advocacy.

To help combat the emotional needs of healthcare workers during the pandemic, the World

Health Organization provided recommendations to give psychological support including information about community-based health care, clinical management guidelines, strengthening health systems, and mental health.[31] While comprehensive, this can be challenging if an organized structure of support was not in existence before COVID-19, as was the case in many hospitals.

As such, some hospitals have quickly created wellness initiatives including a hotline, virtual support groups and mindfulness sessions, and made mental health appointments more readily available via telehealth. Nationally, pro bono therapy programs have sprung up like Project Parachute, and a hotline run by psychiatrists was founded to address the needs for the nation's providers, especially those in institutions that can't help or those who feel more comfortable seeking help outside their institution.[32-33] While these initiatives are needed and important, they remain underutilized and culture change is still necessary. It is also key for healthcare systems to plan for the longer term to design sustainable models of care for providers.

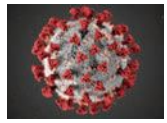
After COVID-19

While the response to the impact of COVID-19 on mental health and wellbeing has significantly varied between institutions, all programs can find ways to improve discussions to create long-term solutions. This is critical...as we know from past pandemics that this will have mental health repercussions long into the future.[34] For example, following the SARS pandemic in Toronto, for up to two years, health care workers had significantly higher than normal levels of burnout.[19] This pandemic and the effects are different and could have longer term impacts or more widely distributed ones.

To better take care of healthcare providers into the future, we need to first identify, screen, and follow at risk groups.[35] We know this includes providers who have directly taken care of COVID-19 patients, or who have been exposed to it themselves. This also includes quarantined providers, those with a history of mental illness, and trainees. While crisis intervention is good, we need to refer these groups to long-term care in an accessible and affordable way. It also needs to be valued and not stigmatized at the highest level of leadership and through changes to licensing and credentialing. Yet, in 2017, two thirds of state medical applications still asked questions that stigmatized mental health.[36] As the way physicians are asked about mental health diagnoses and treatment affects their care seeking, and nearly 40% of physicians reported that they would be reluctant to seek treatment, these questions need to be changed urgently.[36] The Federation of State Medical Board recommends focusing the phrasing to address current impairment, or not asking the question at all.[37]

Focusing on physician mental health and wellness will not only help physicians and keep people in medicine, but it will improve patient care.[38-39] Burnout affects empathy and the number of patient errors. For example, the number of major medical errors have been correlated to burnout in surgeons and a decreased sense of altruism amongst medical students.[38-39] One way an institution can focus on mental health is through increased training and discussions with healthcare providers to identity signs and symptoms in themselves and their patients. While healthcare providers monitor the psychosocial factors of their patient population and ask questions related to mental health, they will get comfortable with a mental health focused culture. This culture shift is needed as a culture that self-stigmatizes mental health will also not screen or refer patients to treatment or feel like a safe place for mental health conversations. Normalizing starts at the top.

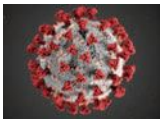
COVID-19 has impacted the psychological wellbeing of healthcare providers, worsening an already heightened baseline, and is likely to continue long into the future. Using evidence from the impact of outbreaks like SARS and data from studies of healthcare providers worldwide working with COVID-19, healthcare institutions can continue to put into place solutions to address both the short and long term needs of frontline providers in their hospital systems. If COVID-19 has taught us anything, it has finally cemented that a wellness lecture or a tiny policy change is not enough to address the mental health needs in physicians. We need large and sustainable change, to culture, policy, and infrastructure, and we need it now.



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MM



COVID-19 REPORT

Break the Silence: Physician Suicide in the Time of COVID-19

by Amanda M. Kingston, MD

Abstract

The rates of physician burnout, depression, and suicide have been on the rise over the past 50 years. Despite increased attention to these topics over the past decade these numbers have remained steady. In the age of SARS-Cov-2 and COVID-19 these numbers are predicted to show a steep increase due to the increased work demands, social isolation, decreased self-care, and increased exposure to emotionally traumatic events at work and home. The potential solutions to these issues generally remain the same; however, we are now in an environment with even more barriers to those solutions.

Introduction

The increased rate of suicide among physicians has been known since 1858;[1] however, physician suicide has remained a silent epidemic for the past 150 years. Over the past few years there has been growing attention on this topic in the age of increased rates of physician burnout[2] and mental health diagnoses among physician populations. In recent years, the American Medical Association[3] and the Association of American Medical Colleges[4] have launched campaigns to identify, educate, and guide physicians on burnout. Now, amidst the COVID-19 pandemic, there has been increased media attention to burnout, mental health diagnoses, and suicides attributed to the stress and workload of being a physician during this unprecedented time in medicine. With the spotlight being directed toward this once silent issue, there has been an increased focus on the stresses of working in healthcare. This highlights the longstanding issue of physicians struggling with mental health issues including depression, anxiety, and substance abuse. These issues once kept in the dark, are now front and center of the national discussion regarding COVID-19 and the healthcare workers treating these patients.



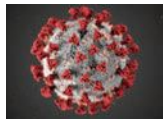
Amanda M. Kingston, MD, MSMA member since 2019, is Assistant Professor, Forensic Psychiatry Fellowship Training Director, Department of Psychiatry, University of Missouri, MU Health Care. This paper is based on her presentation at the MSMA Annual Convention April 2019.

Characteristics of Physician Suicide

Factors that have been identified which lead to increased risk of depression and suicide in physicians includes female gender, personal history of mental illness, family history of mental illness, lack of social support, and substance use or abuse. Similar to the general population, the biggest predictor of future suicidal thoughts or attempts is a personal history of a suicide attempt.[5]

There are several factors that contribute to the higher rates of suicide seen among physicians. Physicians have extensive knowledge of pharmacology including the lethal doses of medications which makes suicides by overdose more frequently lethal than in the general population. Physicians also have increased access to potentially lethal medications within hospital and clinic settings. Physicians tend to use suicide methods of higher lethality including firearms and hanging.[5] This increased knowledge and use of highly lethal means equates to a higher percentage of suicide attempts by physicians being lethal.

Survey-based studies show that the rates of mental illnesses, primarily depression and anxiety disorders, are higher among physicians; however, physicians seek care for mental health diagnosis much less frequently than the general population.[6] There is significant societal stigma related to mental illnesses and this extends and is amplified among physicians. Many physicians fear repercussions from state medical boards or employers if their mental health diagnoses are learned. This culture of stigma leads many physicians to attempt to treat their own mental health issues with





As we move forward as a country and profession from this pandemic and all that it has changed in our daily lives, it will be vital to track the rates of burnout, depression, anxiety, suicide, and substance abuse and intervene early.

prescription medications or self-help style therapies. This idea of "physician, heal thyself" has proven to be grossly inadequate.

Physician suicide has a double peak with the highest incidence occurring in late-middle age and the second peak during the training years of residency and fellowship.[7] The peak during training is often attributed to the intense and stressful time of training with working long hours, risk of medical errors, and balancing work and family obligations. The higher peak later in life has been attributed to physicians' loss of identity either by retirement or deterioration of their own physical health.

Mental Health Diagnoses

The most common mental health diagnoses of physicians mirrors that of the general population; however, the rates of these diagnoses are much higher and as noted above, physician engagement in treatment is much lower. The most common mental health issues include depressive disorders, anxiety disorders, and substance use and abuse. Rates of depression among physicians have been estimated at 19%[8] and 28.8% among resident physicians[9] compared to 7.1% in the general population.[10] The incidence depression increases rapidly in medical training, increasing four--fold in the first four months of the internship year.[11] This increased rate is often attributed to the high stress culture of medicine, long work hours, relative neglect of self-care, less time with family and friends, financial stresses of medical education, and perceptions of inadequacy.[8]

Anxiety disorders also have higher incidence among physicians. The field of medicine likely selects for individuals at high risk for anxiety disorder due to the coveting of perfectionistic traits. Anxiety and depressive disorder are highly comorbid and intertwined which increases risk for physician burnout and suicidal thoughts. With physicians seeking care from their own primary care physicians or mental health professionals much less frequently, they may also turn to other ways to self-medicate either by self-prescribing or the use or abuse of alcohol or illicit drugs.

Substance Abuse

Substance abuse is independently a risk factor for suicide with more than 50% of all suicides involving alcohol or drugs.[12] Substance abuse is particularly prevalent among physicians with the highest rates effecting anesthesiology, psychiatry, and emergency medicine.[13] Prescription drug abuse is significantly higher in physician populations likely due to the increased access to addictive medications. However, female physicians also have increased rates of alcohol

abuse and dependence compared to females in the general population. These increased rates of substance abuse combined with increased access and knowledge of pharmacology and underlying psychiatric illness can be a very dangerous recipe and likely contributes to the increased rates of suicide completion within the physician population.

Physician Burnout

Burnout is a long-term stress reaction marked by emotional exhaustion, depersonalization, and a lack of sense of personal accomplishment.[2] Approximately 50% of physicians in the United States will report symptoms consistent with burnout at some point in their career.[14] Rates of burnout are climbing which is attributed to increased bureaucratic oversight, loss of physician autonomy, increased documentation requirements, increased administrative burden, and decreased time spent with patients. Many hospital systems and professional organizations have created and instituted educational curriculum and self-care programs which have shown some improvement in some areas of burnout but have generally not reversed the trend of increasing physician burnout.

Potential Solutions

Particularly in the past 10 years, there have been increased efforts to treat these alarming trends of burnout, depression, and suicide among physicians. These solutions have included initiatives such as physician wellness programs, state physician health programs such as the Missouri Physician Health Program, increased education during training years, increased screening measures, and increased access to treatment resources including therapy and psychiatry referrals for physicians who are struggling.[15] Data showing the efficacy of these initiatives is not robust but generally has not demonstrated significant improvement in outcomes.[16] In this time of COVID-19 we are in uncharted territory and although these same solutions may prove to be effective, the new realities of fighting this pandemic present new barriers. These barriers include decreased time away from work for physicians to seek care, reduction of onsite staff and personal to perform screenings and treatment, deferral of all non-emergent medical and psychiatric care, and increased stigma for physicians taking time off from work to address personal care and medical appointments.

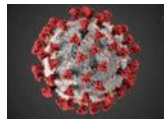
Impact of COVID-19

With the coming of SARS-Cov-2 in 2020 the rates of physician burnout have climbed due to increased emotional demands including increased patient deaths, lack of feelings of control, personal blame for inability to do more for patients, increased work hours, and increased emotional stress within their support system.[17] Increased rates of burnout, symptoms of depression and anxiety, and increased social isolation suicide rates are also predicted to climb both in the general population and within the population of U.S. physicians.

At this point, large data sets regarding the impact of COVID-19 on physician mental health and suicide are not available. However, the stories published in the press regarding suicide by health professionals paints a grim picture. The story of Dr. Laura Breen, and ER physician who contracted COVID-19 and then later died by suicide[18] illustrates not only the physical toll of this pandemic, but the intense emotional toll to those who are working on the frontlines. There are also stories of paramedics, nurses, techs, and other workers in the medical field who have died by suicide during this incredibly difficult time. These few stories which reach the press are likely only a small fraction of the true loss of life during this time as much of the airtime is devoted to those dying from the infection itself rather than the emotional and mental consequences of fighting it.

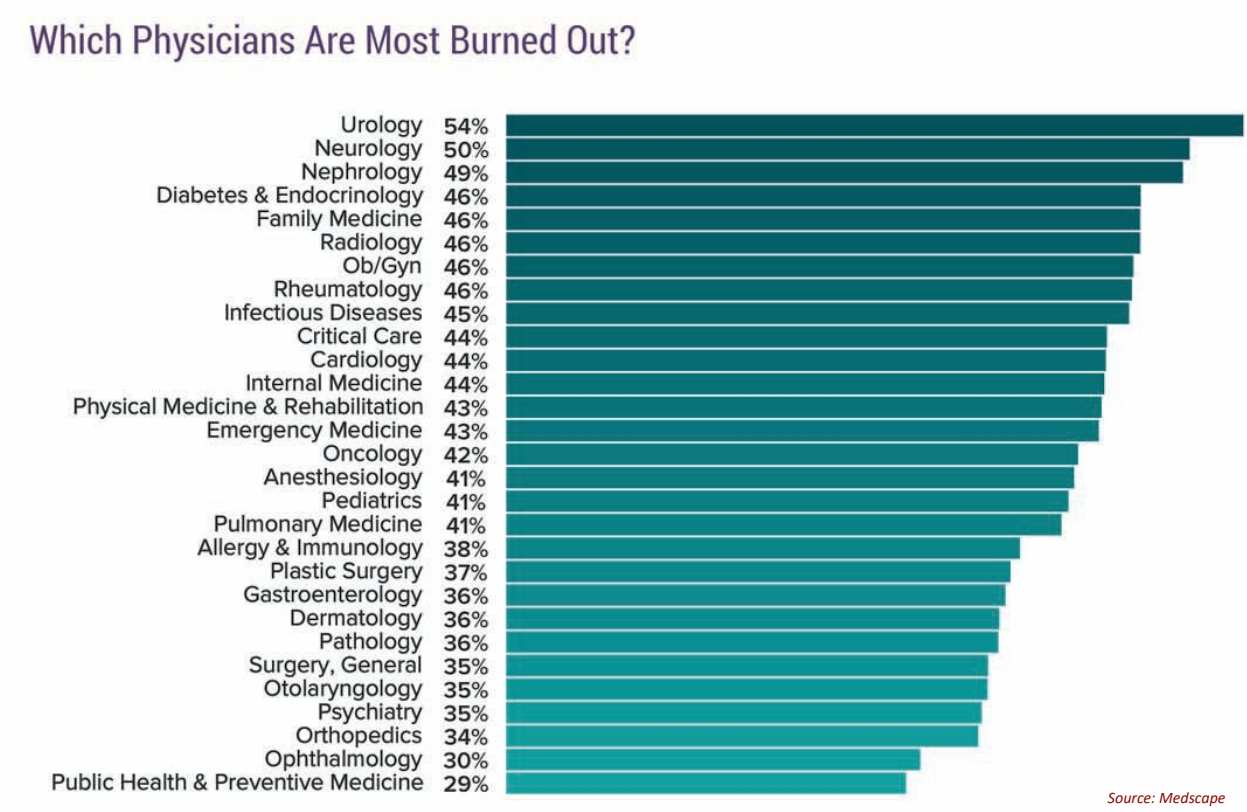
Future Directions

As we move forward as a country and profession from this pandemic and all that it has changed in our daily lives, it will be vital to track the rates of burnout, depression, anxiety, suicide, and substance abuse and intervene early. All of us are working long hours, picking up extra shifts, and putting our own self-care last during this pandemic which will have dire consequences if gone unchecked. We know from previous research that physicians are a vulnerable group for depression and suicide and hesitant to seek care in the best of circumstances. With these new demands and shifts in work responsibilities we must not lose sight of these underlying facts. This is a marathon, not a sprint; we must continue to take care of our physicians so that they can continue to care for those who need them most.



1 PICTURE = 1,000 WORDS

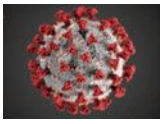
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MM



SEND IN THE ARMY!

MILITARY ROLES IN THE PANDEMIC

by Charles W. Van Way, III, MD

I remember my introduction to the Army Medical Corps. I'd just finished surgical residency, and was (I thought) on my way to Vietnam. They rushed me to San Antonio and the Officers' Basic Course. I learned to march and salute (very badly), fire a rifle (better), and was introduced to military medicine.

Now, my initial view of military medicine was pretty much based on the movie, MASH. All trauma, not much else. Boy, was I wrong. I learned that the main problem of armies throughout history wasn't the enemy. It was disease.

Up until the 20th Century, soldiers died more than twice as often from epidemic diseases than from battlefield injuries. Typhus, dysentery, and pneumonia have, throughout history, killed far more soldiers than had the collective enemy. Sure, caring for trauma is important. But it's only a part of the big picture. A central object of military medicine is keeping the troops from getting sick and treating them when they do.

As my career progressed, I also learned about biological warfare. Armies throughout history have used diseases as weapons. We don't use biowarfare. Honest, we really don't. But we have to figure out what to do if someone uses it on us. That means we have military research laboratories which study how to counter biowarfare.



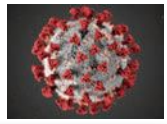
Charles W. Van Way, III, MD, FACS, FCCP, FCCM, MSMA member since 1989, is Colonel, US Army Reserve, Medical Corps, Retired; Missouri/AMA Delegate, *Missouri Medicine* Contributing Editor; and Emeritus Professor of Surgery, University of Missouri - Kansas City.

The Army Institute of Infectious Diseases (USAMRIID), studies such things as malaria, to be sure. But it also studies bacteria like anthrax, *Escherichia coli,* smallpox, and plague all of which are possible bioweapons. Other studies are carried out by Army, Navy, and Air Force laboratories, the Public Health Service. And there are studies in civilian institutions funded by grant programs under the Department of Defense.

Epidemics are epidemics. Even after one has run its course, it may not be possible to tell whether it was caused by enemy action or by natural causes. It follows that military physicians and institutions know a lot about epidemics, how to prevent them, and what to do if they strike. This includes public health measures, treatment options, vaccination, and all the rest.

Examples? The Panama Canal couldn't be built until malaria and yellow fever had been brought under control. Who did that? William Gorgas, an Army physician. In Cuba, after the Spanish-American War, yellow fever was brought under control by another Army doc, Walter Reed, building on work by Dr. Gorgas and Dr Carlos Finley, a Cuban physician.

So, now we come to the COVID19 pandemic. What have the various branches of the military done to respond? Well, we've seen some things in the news. The hospital ship *Mercy* was deployed to New York City. It didn't treat a whole lot of patients, but it did serve as a backup. There was a naval field hospital set up in New York; again, it served largely as a backup. Other field hospitals have been set up around the country. Military medical centers in places like San Diego have treated civilians, and military medical teams have been fielded where needed. But in general, military medical assets have been used to take care of the millions of servicemen and women, and their civilian dependents.



The medical services have done very well in taking care of their own. There have been few outbreaks of disease in the military. Considering the number of soldiers, sailors, and airmen packed into crowded ships, barracks on bases, and working in close proximity, that's a major accomplishment. There have been failures. The aircraft carrier USS Theodore Roosevelt had an outbreak of disease while at sea, on a "show the flag" cruise to Vietnam. The Navy took immediate action, by firing the Captain when he tried to get higher command to take infected sailors off the ship. As many as 1100 sailors were eventually infected, and one died. There was an outbreak on Okinawa, among Marines and Air Force personnel. At least 140 people were infected, with no deaths. The outbreak was contained locally, by isolation and quarantine measures. Outside of sporadic cases elsewhere, that's about the extent of serious outbreaks.

A lot of soldiers have been seen around the country, so that pictures of soldiers in camo uniforms wearing masks has been a staple of news coverage (Figures 1, 2, 3). Who are they? Mostly National Guard. Over 31,000 airmen and soldiers from Army and Air Force National Guard have been called out, mostly distributing supplies and otherwise providing support to hospitals, public health agencies, and emergency response organizations. One of the things the Army is very good at is supply and logistics. To date, 43 states and the District of Columbia have received federal funds to activate National Guard units.



Figure 1. Air National Guard Deployment



Figure 2. Army National Guard Deployment



Figure 3. National Guard Troops in Protective Gear

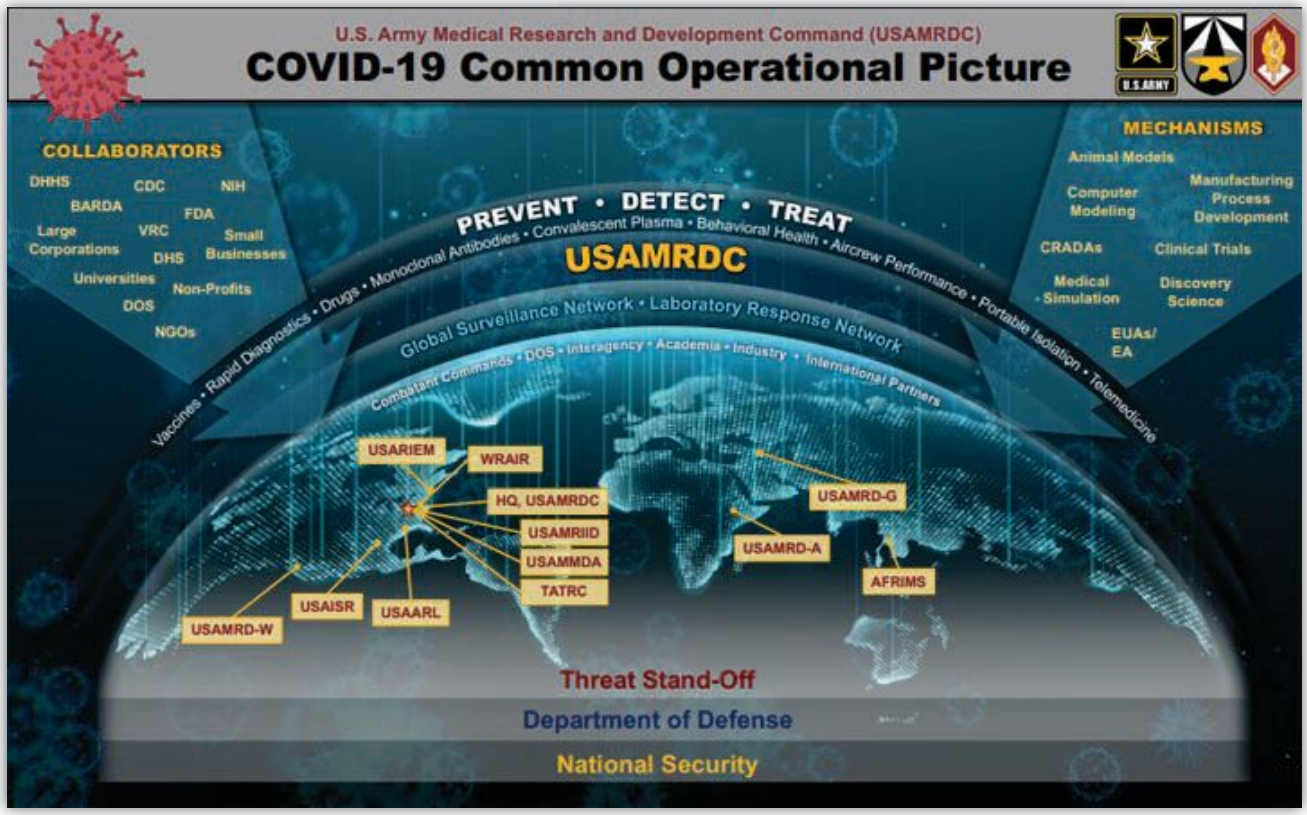


Figure 4. Army Medical Department Responses Worldwide

The Army, and the Dept of Defense (DoD) in general, are heavily involved in the overall Federal response. Operation Warp Speed is a major Federal program. It has been organized and heavily funded ($10 billion and counting) to develop and produce vaccines and treatment. One goal is to have 300 million doses of vaccine by early 2021. It is overseen jointly by Health and Human Services and the Department of Defense. The chief operating officer is Gustave Perna, an Army four-star general. His day job is head of the US Army Materiel Command (AMC). Gen. Perna is going to be in charge of distributing those 300 million doses of vaccine. If we get them. When we get them.

What about military medical research? Has it had much of a role? In the Army, the US Army Medical Research and Development Command (USAMRDC) has been involved in developing vaccine, monoclonal antibodies, diagnostic material, treatment, and protective equipment. Walter Reed Army Institute of Research (WRAIR) has developed a detailed view of the spike protein receptor binding domain, which binds the virus to the lung. WRAIR has developed a vaccine candidate which is currently in Phase I trials. The accompanying graphic indicates the scope of the efforts across Army Medical Research. Other efforts are being made by Navy and Air Force research institutes (Figure 4).

While we usually think of the National Institutes of Health as a civilian institution, the US Public Health Service is in fact a uniformed service. Officers of the USPHS are involved at all levels of the "civilian" response of the Department of Health and Human Services, the NIH, and the Biomedical Advanced Research and Development Authority (BARDA). BARDA is specifically charged with developing countermeasures to epidemics and/or biowarfare, and is a major player in Operation Warp Speed.

In short, all of our military medical resources are being mobilized to fight the coronavirus. And that's as it should be. COVID-19 is as much a threat to the United States as any armed enemy. Nearly three times as many people have died from COVID in a few months as were killed in seven years of the Vietnam War. Soldiers, sailors, airmen, Army docs, Navy nurses, and all the rest are working hard to help defend us against this new and deadly enemy. For once, the phrase "your tax dollars at work" really means something that benefits all of us. **MM**

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- Telemedicine
- Trauma Surgery
- Urgent Care
- Urology
- Vascular Surgery

Correspondence

Sports Medicine COVID-19 Task Force Update

With schools starting back in multiple forms this fall within the state of Missouri, the St. Louis Sports Medicine COVID-19 Task Force wanted to update Missouri Medicine on our continued work towards a safe return to sports in our region. Again, this is a collaboration between medical experts at BJC HealthCare, Mercy Health Systems, and SSM Health. We have been working with the Missouri State High School Activities Association (MSHSAA) as well in their planning.

Please see the latest update on our recommendations: https://www.mercy.net/newsroom/2020/05/19/st--louis-health-care-systems-collaborate-to-offer-guidance-for-/

Also, this is a link to our video for screening and contact tracing: https://www.youtube.com/watch?v=LV-C4bJFGXQ

We were happy to see MSHSAA move forward with fall sports, even if a school is starting virtually. We believe, if done correctly, we can continue to have Missouri youth stay active and benefit from everything that sports offers. The number of Covid-19 cases directly from youth sports has been shown to be very low. However, we need to continue to work hard on the peripheral activities of the participants, coaches, and parents.

Each area of the state may be able to return at different participation phases. As we move forward, it is vital that we adjust each phase according to the local Covid-19 case numbers. Our task force will continue to offer guidance as we move through fall sports in the St. Louis region and the State of Missouri.

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Save Daylight Savings Time

In the March/April 2020 M*issouri Medicine*, Charles W. Van Way, MD, wrote "The Curse of Time", wherein he decried the existence of Daylight Savings Time.[1] I present an alternative view. Daylight Savings Time (DST) is useful and should be retained. It prolongs the duration of daylight after a typical work or school day and helps encourage citizens to get out of their homes and enjoy the fresh air and exercise.

I will not quibble with Dr Van Way's recounting of the history of DST, as noted in "Origins of the Curse". I do take issue with his examples, citing that English and Norwegian people may not like DST, because English and Norwegian opinions are not relevant to our nation.

The reason for this is that England and Norway exist much closer to the poles than does St. Louis or Kansas City. The photoperiod in England and Norway is longer in summer than is ours. St. Louis is 38o 37 min north of the equator and our longest day has a photoperiod of about 15 hours. London, England, sits 51o 30min north of the equator and its longest photoperiod (June 21) is nearly 17 hours long. Oslo, Norway, sits 59o 55 min north of the equator and its longest photoperiod is about 19 hours.

Thus, even without DST, London and Oslo residents would have plenty of time after the end of a June workday to be outside enjoying fresh air and exercising. However, if a Missourian reached home after work at 6:00 p.m. during June, they would have only about 90 minutes between arriving home and sundown. In March and April, and September and October, they would have even less time, because the longest day photoperiod occurs near June 21.

To maximize the duration of daylight after the end of a workday has special value to Missouri, because Missouri is highly burdened by obesity. In our state, 35% of adults and 31% of children are either overweight or obese.[2]

Simply stated, from a societal perspective, DST provides more time after the end of school or work duties to go outdoors and exercise. From my perspective as a racing cyclist, DST gives me and my fellow cyclists and triathletes more time to ride outdoors between the end of an office day and sundown during the summer. I can typically work in a bike ride of 20-30 miles and a four-mile walk with my wife while the sun is still in the sky during the summer months.

Missouri physicians should advocate for the retention of DST, as an adjunct to encourage exercise and improved health. To rescind DST would be to consequently further favor the development of obesity in our citizens. Retention of DST is especially valuable in March and April, and in September and October, because it enables post-work day daylight to enable heathy and safe outdoor post-workday activity choices. If not for DST, workers would arrive home in the dark during the spring and the fall.

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Response to "Saving Daylight Savings Time"

My old friend Gary Gaddis makes some fair points on Daylight Savings Time. DST may indeed give people another hour of daylight in the evening, during which they may be able to do more exercise. Personally, I do my exercise regimen in the morning. We can certainly acknowledge that dedicated bicyclists are a group which may benefit from DST. However, as I noted, there is a body of evidence in the literature that DST is generally harmful, or at best not beneficial. Most of it has to do with ill effects of the twice-a-year transitions. There may be offsetting benefit from increased exercise during the summer months, but it hasn't been shown in the literature. Nor have there been studies on any correlation between Standard Time and increased obesity.

In the U.S., obesity rates have been rising since around 1960, and began accelerating around 1980, with further acceleration after 1995. Only in the last decade or so has the rate of obesity begun to level off, but at a high level.[1] As noted in my article, DST became universal in the U.S. in 1966, and after some fluctuation settled at seven months per year after 1986. Now, this positive correlation of DST with obesity certainly does not indicate causation. But it does make one think.

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Sarah Younger, MD - Neonatal-Perinatal Medicine – Columbia



Letters to the Editor

Submissions reflect readers' opinions and may be edited for length. Use in subject line: "For Publication"

Email
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Missouri Medicine in the News

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



Stephen Keithan, MD, has been named the *Missouri Medicine* Editorial Board member for Internal Medicine/Pediatrics. Dr. Keithan, MSMA member since 1998, is a board certified physician in Internal Medicine and Pediatrics. He currently is Clinical Associate Professor, Departments of Internal Medicine and Child Health at University of Missouri School of Medicine ,and Medical Director, Woodrail General Internal Medicine and Pediatrics Clinic in Columbia, Missouri.



April Tyus-Myles, MD, is the new *Missouri Medicine* Editorial Board Member for Pediatrics. An MSMA member since 2020, she is board certified in pediatrics and practices for SSM Health Medical Group Pediatrics in St. Louis. She replaces Nancy Bunge, MD, whom the Journal thanks for her service on the Board since 2011. Dr. Bunge has been honored with the *Missouri Medicine* Distinguished Service Award.



MSMA is honored to have Nathaniel Barbe, DO, as MSMA District 9 Vice Councilor and for his service leading up to this position through the MSMA Resident and Fellow Section. We salute him on his return to Mountain Grove for his first year of practice at Mercy. Pictured here is Dr. Barbe, with his father David Barbe, MD, MSMA and AMA Past President.



MSMA is proud to call Ethan Crider, MD, a young physician member of MSMA for the past three years. We wish to recognize and congratulate him on his achievements and on joining Mercy Clinic in Washington. MSMA salutes the success of our young physician members!



Congratulations to Humeyra Karacal, MD, an MSMA member since 2013, on joining Premiere Eye Associates in Festus. Dr. Karacal practices general ophthalmology and performs eye surgery.



MSMA wishes to express our sincere admiration for Amy Patel, MD, recently elected Chair of the American College of Radiology Young and Early Career Professional Section. Dr. Patel is the first chair from Missouri to this position. She's been a valued member of MSMA for the past 15 years.



A round of applause for Robert Shaw, Jr., MD, FAAFP, of Willow Springs for being presented with the MAFP Physician of the Year Award at the Annual Show Me Family Medicine Conference of the Missouri Academy of Family Physicians. The Conference was held virtually in mid-August. In January 2020, Dr. Shaw celebrated 40 years of membership in MSMA.



Randy Tobler, MD, FACOG, CPE, of Scotland County Hospital, has earned the prestigious Certified Physician Executive credential through the American Association for Physician Leadership. Way to go, Dr. Tobler! Thank you for being a long-standing supporter of organized medicine since 1981.



Gerald Wilmes, MD, HMDC, MSMA member since 2008, is a family physician in Maryville. MSMA is proud to share the news of his recertification through the Hospice Medical Director Certification Board.

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MSMA Members Up For Election on November 3

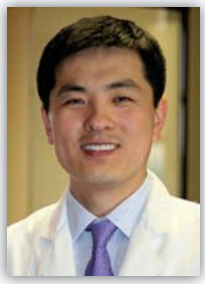
MSMA is proud to have three members running in this election cycle: Jon Patterson, MD, Lisa Thomas, MD, and Sam Page, MD.

Dr. Patterson is a general surgeon running for his second term to represent the Lee's Summit area in the House of Representatives.

Dr. Thomas is a psychiatrist running to represent Camden and Miller Counties in the House.

Dr. Page is an anesthesiologist seeking re-election to the office of St. Louis County Executive.

Best of luck to Drs. Patterson, Thomas, and Page in the November general election!



Dr. Patterson



Dr. Thomas



Dr. Page

As we move ever closer to the November elections, get to know your candidates' positions on healthcare-related issues. We always love to hear from our members about the candidates in the areas where you live and practice. To support their campaigns and the campaigns of other candidates who are friends of medicine, contact the Missouri Medical Political Action Committee (MMPAC) at 800-869-6762.

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ATSU | A.T. Still University
FIRST IN WHOLE PERSON HEALTHCARE

Transitioning Medical Education and Healthcare Delivery

by Margaret Wilson, DO

As physicians and healthcare leaders, keeping our communities safe and healthy is our top priority. At the home of osteopathic medicine, A.T. Still University-Kirksville College of Osteopathic Medicine (ATSU-KCOM) in Kirksville, Missouri, faculty, staff, and students have rallied together and taken the necessary actions to protect themselves and community members against the COVID-19 pandemic. The College has continued to operate as safely as possible while monitoring the situation closely. As more knowledge becomes available, it is becoming increasingly likely this virus will have long-term implications for medical education and the healthcare delivery system.

Every educational institution is dealing with its own set of circumstances and challenges during this uncertain time. ATSU-KCOM has learned one thing is certain: The College community has shown its compassion and resiliency even in the most deleterious situations. Students have taken disruptions to their daily routines in stride and quickly adapted to an online learning environment. Faculty and staff have made necessary accommodations to keep classes and daily operations running smoothly, with essential personnel keeping the campus safe and accessible.



Margaret A. Wilson, DO, MSMA member since 2012, is Dean, Kirksville College of Osteopathic Medicine, and Professor, Department of Family Medicine, Preventive Medicine, and Community Health, A.T. Still University, Kirksville College of Osteopathic Medicine, Kirksville, Missouri.

Because ATSU-KCOM anticipated the need to be nimble and responsive to the ever-changing pandemic environment, a contingency plan was put into place quickly. First- and second-year students transitioned to an online didactic curriculum with the ability to complete courses and assessments online. Providing opportunities for hands-on learning, such as physical exam skills and osteopathic manipulative treatment (OMT) technique development, proved to be more challenging. The College relied on videos created by content experts who broke down each skill and technique into components and demonstrated those components on a model. In some cases, students practiced on another person with whom they were isolated and then uploaded a video of themselves performing this maneuver for critique by faculty.

Continuing to hone student communication skills with patients was another challenge. Communication skills encompass aspects of time management, humanistic behavior, professionalism, and information gathering, so ATSU-KCOM implemented a series of phone consults between students and standardized patients with varied respiratory-type complaints. Students were instructed to triage patients, deciding whether they need to be seen face-to-face in the clinic, and if not, what type of follow-up was necessary. The intent was to challenge the students to use best practices in communication without the visual cues they typically have from patients.

Educational delivery for third- and fourth-year students was ATSU-KCOM's most difficult transition. All osteopathic medical colleges in the U.S. were instructed to pause student participation in clinical education activities. ATSU-KCOM



ATSU Gutensohn Clinic, located in Kirksville, Missouri, is home to A.T. Still University's Kirksville Family Medicine and Osteopathic Manipulative Medicine clinics.

administration was actively involved at the national level in decision-making with the Association of American Colleges of Osteopathic Medicine and the Coalition for Physician Accountability, and all students were removed from clinical rotations for the last several weeks of the academic year. ATSU-KCOM uses a unique, disseminated clinical training model where students are placed in 30 regional sites across the country. To ensure students were able to continue their academic progression, they were enrolled in credited online courses. Additionally, the College's faculty put together curricular courses for students to take as electives during this time. However, regional differences in the incidence of COVID-19 caused additional considerations for planning re-entry of these students to the clinical environment.

The primary academic priority for fourth-year students was to make sure they were able to earn the credits they needed to finish their graduation requirements. ATSU-KCOM has a very proud and long tradition of providing the healthcare workforce for the nation. This spring, match results of the National Resident Matching Program yielded record highs for osteopathic medical students. ATSU-KCOM is happy to report its four-year rolling match rate, which includes the class of 2020, is 98.93%, with the majority of graduates being matched to primary care.

As one class graduates, another class matriculates, and these incoming students have experienced ATSU-KCOM like no other previous class. Through student interviews, welcome days, orientation, and the start of the academic year, the College has continued to adapt its curriculum and events for these new students based on public health needs. Using a hybrid curriculum of online and small-group learning, hands-on activities will continue to be delivered using safe social distancing practices.

On campus, the ATSU Gutensohn Clinic has been a constant presence in the Kirksville community. It has remained in operation since the stay-at-home orders were announced and



Lisa Archer, Director of Simulation & Performance Assessment, reviews camera footage within the Drabing Human Patient Simulation Center with osteopathic medical students.

continues to lead community action against the spread of COVID-19.

When cases began appearing in the U.S., the clinic immediately began adhering to best practices and guidance from the Centers for Disease Control and Prevention to start screening patients and visitors regarding coronavirus risks and symptoms. Then, the clinic implemented a physician-resident platoon system, where teams of physicians and residents work in different areas to avoid cross-contamination. The three teams rotate once a week through the clinic, hospital, and home, allowing all healthcare providers to be fresh and healthy, if needed. By the end of March, the clinic started a complete foyer screening and roster system for everyone entering the building.

One positive outcome from the COVID-19 situation was the opportunity to develop and enhance the clinic's telehealth application. In a matter of weeks, the clinic went from zero telehealth utilization to 15-20 patients per day on average.

When news stories across the nation began focusing on shortages of personal protective equipment (PPE), ATSU-KCOM administration started discussing possibilities of creating PPE with staff members from A.T. Still Memorial Library, which houses a 3D print shop. The library's public services and 3D print shop manager collaborated with the ATSU Gutensohn Clinic's executive director of clinical operations to identify shortages of PPE and approve prototypes of needed items. With help from community members with access to additional 3D printers, they have been printing face shields designed to be worn over the N95 masks, giving healthcare providers an additional layer of protection. Additionally, the library staff was able to come up with a prototype to print Montana masks, which are reusable masks with replaceable filters. These 3D-printed items have been distributed through the ATSU Gutensohn Clinic to community partners, including the local hospital, area nursing homes, all physicians and healthcare clinics, the Adair County Ambulance District, and city police and fire departments. In a small, rural community with limited resources, this unique, creative collaboration resulted not only in much-needed PPE but also in community support for fellow frontline workers.

As the new academic year began in July, the institution moved forward with the hybrid model of



A.T. Still University-Kirksville College of Osteopathic Medicine hosted its annual Peds Lab for osteopathic medical students Sharyl Alendry, OMS II, and Dallas Garrison, OMS II, to hone their interactions and communication skills with pediatric patients.

education with didactic lectures continuing to be delivered virtually. Hands-on activities, such as gross anatomy dissection, physical exam skills, and OMT skills, are being delivered in person in small, static groups using appropriate PPE and social distancing.

Everyone at ATSU-KCOM has been doing their part during these trying times, and it is amazing what can be done when everyone works together. However, COVID-19 has been a harsh reminder for the need to better prepare future generations of physicians for public health needs and emergency response.

Healthcare and medical education has been forced to adapt quickly to rapidly changing situations. Moving forward, physicians and healthcare leaders must rethink healthcare and education delivery and how this delivery can be improved with the increased use of advanced technology. It is imperative for healthcare organizations and educational institutions to use the research and lessons learned from this pandemic to maintain safe and healthy communities.

Disclosure

This Dean's Report was updated in August 2020. At the time of publication, COVID-19 related circumstances may have altered ATSU-KCOM's curriculum delivery, clinical processes, and campus events and activities. **MM**



A.T. Still Memorial Library, ATSU Academic Technologies, and Kirksville Vocational Technical Schools collaborated to print Montana masks to aid local healthcare professionals as they provide patient care during the COVID-19 pandemic.

Impact of the Single Accreditation System on Missouri Osteopathic Graduate Medical Education

by Richard J. LaBaere, II, DO & Kerrie J. Jordan, MS

ATSU A.T. Still University
FIRST IN WHOLE PERSON HEALTHCARE

The transition to the Single Accreditation System has eliminated costly duplication of institutional accreditation processes and ensured all medical student applicants are eligible to enter accredited programs after graduation.



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Abstract

The single accreditation system (SAS) through the Accreditation Council for Graduate Medical Education was introduced in 2014. Its goals included increasing consistency in training and providing a dedicated place for delivery of osteopathic educational competencies. From 2015 to 2020, most osteopathic primary care and specialty residencies in Missouri successfully achieved accreditation. Nearly all osteopathic surgical specialty residencies and traditional internships did not make the transition. The current article examines the challenges and opportunities of SAS.

Background

In early 2014, the Accreditation Council for Graduate Medical Education (ACGME), the American Osteopathic Association (AOA), and the American Association of Colleges of Osteopathic Medicine (AACOM) entered into a memorandum of understanding to transition all graduate medical education (GME) in the United States to a unified single accreditation system (SAS) by July 2020.[1] This agreement arose from preliminary discussions among the three groups in 2012. The official launch of SAS was July 1, 2015, at which point AOA-accredited programs could apply for ACGME accreditation. The SAS created access to GME for all allopathic (MD) and osteopathic (DO) medical school graduates and generated unique opportunities for growth in both professions nationwide. In Missouri, the birthplace of osteopathic medicine in the United States, we have seen this transition evolve and have identified its effects on medical education. In the current article, the perspective of two Missouri osteopathic medical education institutions was explored to convey the present landscape and share the challenges and opportunities that impact the future of the healthcare workforce in Missouri.

Transition to the Single Accreditation System

The conditions for change to a SAS began in 2009.[2] At that time, the ACGME shifted its accreditation structure to include educational outcomes that focused on six core competencies. Likewise, the AOA identified seven related osteopathic competencies, which included a specific competency for osteopathic practice. In 2011, the ACGME announced changes in their common program requirements that limited the

eligibility of DO graduates from moving into fellowship programs. Early in 2012, representatives from the ACGME, AOA, and AACOM met to address concerns of exclusion and consider strategies that would serve all invested stakeholders. After almost two years of meetings that included negotiations, planning, and an initial proposal that was not accepted, a memorandum of understanding was signed to create a unified SAS. Afterwards, the appropriate governing bodies approved the agreement developed by these three principal organizations.[3]

To encourage stakeholder onboarding, several benefits of the SAS were outlined. For instance, the SAS preserved the access of DO graduates to accredited GME training during a time when the number of DO graduates was expanding beyond the capacity of AOA-accredited programs to provide training.[1] Further, the unified SAS provided consistency of quality in relation to the curriculum and training requirements of both professions.[1] Another benefit was the inclusion of osteopathic elements into the framework of GME so both MDs and DOs were exposed and developed those competencies.[1] A benefit for the osteopathic profession meant they had a unified voice for GME access and funding issues, strengthening the profession's advocacy. Finally, the SAS hardwired distinctive characteristics of the osteopathic profession into GME.[1]

After approval of the SAS, many changes in GME followed that benefited the osteopathic profession, such as the appointment of AOA and AACOM representatives to the ACGME Board of Directors, the appointment of DOs to review committees, the modification of requirements so DOs could fully participate as faculty and program directors, the creation of an osteopathic principles committee, the formation of an osteopathic neuromuscular medicine review committee, and most notably the creation of a new ACGME designation called Osteopathic Recognition.[4]

Transition Process and Timeline

As part of the transition to a unified SAS, the memorandum of understanding indicated that AOA institutions and programs would "have until June 30, 2020, to apply for ACGME accreditation."[5] Failure to apply had severe negative consequences because the AOA would no longer accredit academic sponsors or GME programs after that date.[5] Once an AOA program applied for ACGME accreditation, however, they had to achieve "initial" ACGME accreditation no later than June 30, 2020.[5]

To protect residents from being misplaced during the transition to ACGME, the AOA set deadlines for AOA programs.[6] Specifically, the programs had to apply for ACGME accreditation or stop accepting new residents by the deadline. One-year and two-year programs had until January 1, 2019, to apply for ACGME accreditation. Three-year programs had until January 1, 2018, to apply, and four-year and five-year programs had until January 1, 2017, to apply. Any program that had not achieved initial or continuing accreditation from the ACGME by June 30, 2020, was allowed to finish teaching out any residents remaining under the AOA accreditation system but only if the program had an approved plan from the AOA to ensure the quality of residency training. After remaining residents were finished, the program was required to close.[6]

Osteopathic Recognition

During the transition to SAS, the ACGME designation of Osteopathic Recognition was created so that the distinctive characteristics of osteopathic medicine continued in GME training. For instance, the ACGME created a new chapter for osteopathic medicine and established the Osteopathic Principles Committee. The purpose of the committee was to designate, through an application process, which ACGME programs incorporated Osteopathic Principles and Practice into the GME curriculum. Therefore, programs with Osteopathic Recognition have different educational program and resident experiences. According to the AOA, programs that achieve Osteopathic Recognition "help ensure the unique principles and practice of osteopathic medicine" continue to provide benefits and advantages to students who receive this specialized training.[7]

Another consequence of Osteopathic Recognition is that graduates of allopathic can obtain osteopathic training during residency if they match in a program that is accredited for Osteopathic Recognition by the ACGME. Further, Osteopathic Recognition has been proven to reduce costs and improve patient care because it emphasizes patient communication and alternatives to medication.[6] As such, Osteopathic Recognition programs anticipate attracting more qualified applicants who want to complete an

Osteopathic Recognition focused training program and advance their osteopathic manual skills and practice.

Status of American Osteopathic Association Accredited Programs in 2015

Before SAS, the AOA accreditation of GME programs required that each program be part of an accredited Osteopathic Postdoctoral Training Institution (OPTI). An OPTI is an AOA-accredited educational consortium that consists of a program in a college of osteopathic medicine that serves as an academic sponsor of programs. In that role, OPTIs provided oversight of accreditation and support for curricular development and assessment, faculty development, and research. In Missouri, there are two OPTIs: Kansas City University Graduate Medical Education (KCU-GME) Consortium and Still OPTI, which is affiliated with A.T. Still University's Kirksville College of Osteopathic Medicine (ATSU-KCOM) and School of Osteopathic Medicine in Arizona (ATSU-SOMA). Together, these OPTIs provided academic support for 21 programs in Missouri and 21 additional programs in other states, including Arizona, Arkansas, Colorado, Florida, Illinois, Indiana, Ohio, and Wisconsin.

After the Single Accreditation System

Starting July 1, 2015, applications were accepted under SAS for sponsoring institution accreditation. Both Missouri-based OPTIs—KCU-GME Consortium and Still OPTI at ATSU-KCOM—applied for and achieved initial accreditation. Further, these sponsoring institutions currently have ACGME continuing accreditation.

During the transition to the SAS, the majority of primary care, internal medicine, and family medicine residencies successfully achieved continuing accreditation. Five of six programs achieved this status (Table 1). One program, a community-based internal medicine program, chose to not pursue ACGME accreditation. It was believed at the time that the necessary resources relative to adequate faculty were not available to sustain the program. Specialty-type residencies, such as emergency medicine, dermatology, and osteopathic neuromuscular medicine, all had a successful transition into continuing accreditation.

Surgical and surgery-related programs were less successful. Two of three otolaryngology, both general surgery, and both anesthesia programs in Missouri failed to progress. One of two orthopedic surgery programs achieved initial accreditation. One anesthesia program achieved initial accreditation but received a warning after initial review. In that instance, the sponsoring institution withdrew from accreditation and completed the training of their residents through the AOA pathway because they were concerned remaining residents would be displaced if accreditation was withheld by the ACGME beyond 2020. Although the anesthesia review committee recognized progress (the program was getting guidance, being creative, and striving to address shortcomings), numerous citations for faculty and program director scholarship, faculty qualifications in specialty areas, and inadequate resident complement (5 vs 9 minimum) were insurmountable barriers to compliance.

The three traditional osteopathic internships were not pursued for conversion to transitional year programs by sponsoring institutions. Commonly, these traditional intern positions were not filled. However, it seems somewhat ironic that what was once the foundation of osteopathic GME has now disappeared from the landscape in Missouri. Despite this loss, the two AOA-accredited OPTIs have both achieved ACGME accreditation.

Discussion

Challenges

Initially, the unified SAS left many GME programs with unanswered questions. In addition, it was challenging for administrators and educators to learn new accreditation requirements. However, through involvement in dedicated ACGME and AOA educational offerings, 58% of all programs and 83% of primary care, internal medicine, and family medicine programs are now ACGME accredited. Another challenge experienced and overcome was related to condensing two different residency matches into a single match. Historically, AOA programs participated in a match called the National Matching Service. Programs that were accredited by the AOA and ACGME could participate in the National Matching Service and the National Resident Matching Program. After the transition, in spring 2020, only the National Resident Matching Program was used to enroll eligible candidates into residency programs. As a result of program directors, faculty, and staff successfully learning the new system, all positions but one were filled in the 2020 match season.

Table 1. Collated Data on the Number of Accredited Missouri Graduate Medical Education Programs and Sponsoring Institutions from 2014 to 2020[8,9]

Specialty	Total ACGME Programs/SI 2020-2021	Former AOA Currently ACGME Accredited	AOA Accredited Programs in 2014	Net Change	Osteopathically Recognized 2020
Anesthesia	4	0	2	-2	0
Dermatology	3	1	1	0	1
Emergency Medicine	4	1	1	0	0
Family medicine	9	3	3	0	3
Internal medicine	9	2	3	-1	0
ONMM	1	1	1	0	0
Orthopedics	5	1	2	-1	0
Otolaryngology	4	1	3	-2	0
Surgery	5	1`	3	-2	0
Transitional year/traditional intern	1	0	2	-2	0
SI	14	2	NA	+2	NA

Abbreviations: ACGME, Accreditation Council for Graduate Medical Education; AOA, American Osteopathic Association; ONMM, osteopathic neuromuscular medicine; SI, sponsoring institutions.

Another challenge of the SAS is that ACGME-accreditation requirements for institutions and programs have specific language that drives up residency costs; such requirements were not stipulated by the AOA. One example of this expense-generating difference is related to the requirement of an associate program director in family medicine. The ACGME requirements mandate that an associate program director be designated and that their effort must be at least 40% dedicated to the administration of the program.[10] The AOA has no equivalent requirement.[11] Also, all ACGME-accredited programs must have a dedicated program coordinator who contributes a minimum of 50% of their time to the program.[12] The AOA program requirements do not indicate any required coordinator full-time equivalent.[11]

The ACGME requirements also define new, additional activities for faculty that require dedicated time.[12] For example, ACGME programs must have an appointed clinical competency committee consisting of at least three faculty members who are required to meet semiannually to review resident evaluations and milestone progress. These review sessions can take a full day to complete. Further, each ACGME program must have an appointed program evaluation committee that meets annually to review the training program that monitors faculty development, graduate performance, program quality, and areas for program improvement. The ACGME also expects faculty to maintain a

scholarly environment by funding resident and faculty scholarly activity.[13] However, programs can define how they will assist the scholarly activity of faculty, such as by providing faculty development opportunities.[14]

Programs that are currently part of the SAS need to focus on outcomes, scholarly activity support for research, and quality improvement projects. Creating protected time for these activities has increased staffing costs for programs. These process challenges—protected program director and faculty time for research, curricular issues, mandated transplant rotation and required specialty faculty, required companion programs, and dedicated coordinator staff—were contributing factors to why programs in Missouri did not fully transition to ACGME accreditation.[15] In addition, another challenge has been that some programs lack sufficiently trained faculty who can provide Osteopathic Recognition training, so those programs are unable to offer that training.

Opportunities

All medical schools and colleges of osteopathic medicine in Missouri are either a sponsoring institution or part of a consortium-type sponsoring institution. Each of these organizations have expertise in program accreditation and teaching resources across nearly all disciplines. External collaborations with these institutions, like Missouri's Health Care Workforce coalition, may be able to assist struggling or new GME programs by coordinating support through sharing clinical resource rotations and providing partners for community-based scholarship. Through advocacy and collective and innovative action plans, training positions in Missouri may be preserved in the communities served, and clinical care and population-based research advanced.

Another opportunity for GME-training programs involves taking advantage of rural and community-based faculty in programs that are sunsetting their AOA-accredited programs. These faculty are committed and have expertise in providing meaningful clinical learning experiences related to the development of required skill sets in programs like general surgery and anesthesia. Since research suggests recruitment of graduates from programs that provide a rural track result in successful rural-based community practices,[16] there is benefit in taking advantage of the experience of current anesthesiology and general surgery faculty who have the skills and passion for teaching these specialties in relation to the needs of rural Missouri. In addition, creating rural training track or other elective experiences in conjunction with other Missouri-based GME could meet the healthcare workforce demands of the state.

Outside rural areas, rural training track programs are generally allowed to receive additional or alternative funding for urban teaching hospitals that may have a Medicare GME reimbursement cap. Further, urban hospitals may receive a new rural track full-time equivalent limit that allows additional Medicare GME funding, which may make these programs more appealing. However, rural training track programs require residents to spend at least 50% of their time training in rural areas. This approach may also boost and maintain more osteopathic graduates who want to train in rural areas. In addition, osteopathic training programs faced with closure may be able to leverage rural training track programs to entice DO and MD candidates who want to be in rural areas and gain additional Medicare GME funding.

Another opportunity of SAS arises from collaboration with the ACGME so that options for programs and training capacity that are rurally based can be more fully explored. Recently, the ACGME hired a director of medically underserved areas/populations and graduate medical education (Paul Johnson, email communication, April 22, 2020). This person will lead a new programmatic unit of the ACGME that will coordinate efforts to address health and healthcare in medically underserved areas and populations and that will participate in the development of relevant educational programming and outreach activities. In conjunction with a better understanding of the needs of these patients and of what programs are able to offer for training, this unit can establish innovative ways to deliver training and produce the types of physicians needed for those vulnerable populations. Perhaps the requirements themselves may evolve and provide some additional flexibility to meet training and population needs.[17]

A final opportunity provided by SAS in Missouri includes harnessing the potential of osteopathic training and Osteopathic Recognition support available through both of our state's osteopathic medical schools. The Kansas City University College of Osteopathic Medicine and ATSU-KCOM offer guidance and support for developing curricula,

assessment tools, face-to-face workshops, faculty development, and opportunities to participate in related scholarship activities. There are now over 215 osteopathically recognized programs in the United States, and osteopathic medical students have expressed a desire to pursue osteopathic training beyond their DO degree.[14] Therefore, providing an Osteopathic Recognition track or other types of osteopathic training experiences in a residency program will help distinguish that program from others. Broadening the exposure for all residents creates a diversity of perspective that enables residents to better understand patients who seek care from osteopathic physicians and the approach provided by those physicians in the delivery of their care.

Conclusion

The unified SAS introduced by the ACGME in 2014 was intended to benefit the entire GME community. Further, the SAS established and maintained consistent evaluation and accountability for the competency of resident physicians across all accredited residency and fellowship programs. It also provided a mechanism for the ongoing development of osteopathic clinical skills that was accessible to both DOs and MDs. Further, the transition to SAS has eliminated costly duplication of institutional accreditation processes and ensured all medical student applicants are eligible to enter accredited programs after graduation. The SAS was fully implemented in the 2020 match season and allows graduates of osteopathic and allopathic medical schools to complete their residency or fellowship training in ACGME-accredited programs while demonstrating achievement of typical milestones and competencies. In addition, the SAS creates diverse opportunities for everyone by opening up more programs that maintain osteopathic identity through the ACGME Osteopathic Recognition designation, which in turn amplifies the value of DO and MD residents training side-by-side. The five-year transition to SAS has served our medical institutions and the healthcare of the public by enriching the education of the next generation of physicians. Although SAS created challenges that resulted in some programs not transitioning to ACGME, most osteopathic primary care and specialty residencies in Missouri successfully achieved accreditation. A lasting benefit of SAS is that it has highlighted the needs of rural training in Missouri, opportunities for growth, and the dedicated resources available through our osteopathic medical schools that will advance the medical training and the healthcare workforce of Missouri.

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Disclosure

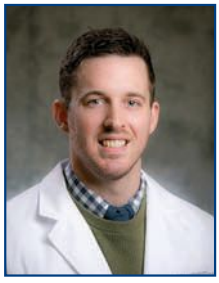
None reported. **MM**

Interprofessional Approach to Learning Vascular Access with Ultrasonography by Medical Students and Nurses

by Spencer Batten, MS, OMS IV, Vanessa Pazdernik, MS, Robert Schneider, DO & Tatyana Kondrashova, MD, PhD

ATSU | A.T. Still University
FIRST IN WHOLE PERSON HEALTHCARE

Interprofessional education (IPE) can be defined as "two or more professions learning with, from, and about each other to improve collaboration and the quality of care.



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Abstract

The current study evaluated an interprofessional approach involving medical students and nurses for learning vascular access with ultrasonography. Vascular access laboratories included needle-guidance training and provided an efficient way to master technically difficult venipuncture cases. Most agreed ultrasound technology was useful for these venipuncture cases. Participants felt prepared to perform venipuncture using ultrasonography in a clinical setting after training. Such laboratories should be considered for interprofessional learning of difficult procedures in the medical school curriculum.

Introduction

Active learning and communication within a team require shared learning and dialog, often leading to the acquisition of additional knowledge through interprofessional collaboration.[1] Thus, interprofessional collaboration is an approach in which healthcare professionals work together to deliver the best patient care.[2]

A recent statement from the National Health System recommended improved teamwork between healthcare professionals,[3] and previous studies have investigated what working together can accomplish and where it can fail.[4, 5] Those studies concluded that participants have to welcome the challenge, need to be confident enough to face the unfamiliar, and have to be respectful and trusting enough to listen openly to others.[4,5] In the critical care environment, interprofessional collaboration is especially challenging because of increased stress. For instance, several studies reported an association between weak collaboration in intensive care units and poor patient outcomes.[6, 7] In the emergency room environment, difficulty in obtaining intravenous access can result in adverse outcomes, such as delays in diagnostics and treatments.[8] With improved cross-training and communication among the team members these delays can be avoided.

Interprofessional education (IPE) can be defined as "two or more professions learning with, from, and about each other to improve collaboration and the quality of care."[9] When IPE includes medical and nursing students, it has been shown to

increase fellowship and enhance knowledge and perceptions of the expertise of the other profession.[10]

Modern healthcare has an increasing overlap in the knowledge and skills required by various healthcare professionals. Recent changes in the delivery of healthcare have blurred the boundaries that once defined the roles and responsibilities that established the identities of different healthcare professionals.[10-12] Since IPE provides opportunities for sharing knowledge and inculcating respect for one another, its early introduction in the medical education and nursing curricula may reduce the tendency to stereotype professional groups.[13, 14] For example, IPE implemented during intermediate life support courses increased teamwork, collaboration, and personal identity between medical and nursing students.[9] Medical and nursing students also showed improved perceptions of interprofessional collaboration and changes in stereotypical views of each profession after a short series of interprofessional simulation-based educational exercises.[15] In another study, IPE increased medical and pharmacy students' confidence in various aspects of the transition of care process.[16] When IPE is included in undergraduate medical education, it is believed to better prepare students for the evolving team-based environment they will encounter during practice and to enhance collaboration among various medical disciplines, especially in areas of medicine that deal with a high acuity of care.[12]

The use of ultrasonography by trained emergency room nurses has been shown to decrease the perceived difficulty and increase successful access rates in procedures that are considered "difficult sticks."[8] Using ultrasonography to visualize anatomy could be valuable in IPE experiences involving medical and nursing students because it would enable students to learn about the other discipline while also learning from each other. Numerous studies have explored IPE approaches in healthcare training, but to our best knowledge, there is no data on using an interprofessional approach to teach venipuncture with ultrasonography to medical students and nurses.

Therefore, the purpose of the current study was to evaluate an interprofessional approach involving medical students and nurses for learning vascular access with ultrasonography. After participating in a vascular access laboratory, improvements in knowledge of ultrasonography, anatomy, and nursing techniques related to venipuncture were assessed. We hypothesized that medical students would show most improvement in learning about nursing techniques and nurses would show most improvement in learning ultrasound techniques related to venipuncture.

Methods

Second-year medical students (n=11) and nurses (n=6) participated in the current study. Participants signed informed consent before participating in the laboratory, and the local institutional review board granted exempt status for all educational procedures used in the study.

Student participants received ultrasonography training through four semesters of clinical ultrasound coursework. The clinical ultrasound course was taught during the first two years of the medical curriculum by a physician licensed in diagnostic medical sonography. During semester 1, students learn how to use the ultrasound machine and perform upper and lower limb musculoskeletal ultrasound and neck vascular and ocular ultrasound examinations. Semester 2 includes abdominal, echocardiography, upper and lower extremity vascular, and pelvic ultrasound examinations. Second-year ultrasound courses are more clinically oriented, so semester 3 focuses on lung, endocrine, obstetrics, gynecology, and breast ultrasound examinations. During semester 4, students master nerve imaging, needle-guided procedures, and focused assessment with sonography for trauma (FAST). [17] Nurses who participated in the current study had completed their nursing training and had at least five years of clinical experience but did not have any prior ultrasound training.

Interprofessional vascular access laboratories focused on identifying structures of interest using ultrasonography and on performing venipuncture under ultrasound guidance. Individual interprofessional laboratory groups included two medical students and one nurse. Laboratory content included the following: (1) introduction

Table 1. Summary statistics of pretest and posttest scores of medical students (n=11) and nurses (n=6) participating in an interprofessional vascular access laboratory

Question Type	Group	Mean (SD) [Min, Max] or No. (%)				*P* Value
		Pretest Score, %	Posttest Score, %	No. Participants Improved	Change, % (Post-Pre)	
All (18 questions)	Medical Student	74 (11) [50, 83]	96 (5) [83, 100]	10 (91)	22 (14) [0, 50]	0.002
	Nurse	42 (6) [33, 50]	87 (9) [72, 100]	6 (100)	45 (12) [22, 56]	
Ultrasonography	Medical Student	82 (12) [50, 88]	98 (8) [75, 100]	10 (91)	16 (15) [-13, 50]	0.007
(8 questions)	Nurse	48 (9) [38, 63]	96 (6) [88, 100]	6 (100)	48 (9) [38, 63]	
Anatomy (5 questions)	Medical Student	93 (13) [6, 100]	96 (8) [80, 100]	2 (18)	4 (15) [-20, 40]	0.01
	Nurse	47 (10) [40, 60]	87 (24) [40, 100]	5 (83)	40 (25) [0, 60]	
Nursing (5 questions)	Medical Student	44 (22) [0, 60]	93 (10) [80, 100]	11 (100)	49 (27) [20, 100]	0.88
	Nurse	27 (16) [20, 60]	73 (24) [40, 100]	6 (100)	47 (27) [20, 80]	

The *p* values indicate comparisons for changes in test scores between medical students and nurses.

to ultrasound, (2) vascular anatomy of the upper extremity with ultrasound, (3) ultrasound needle-guidance training using vascular models, and (4) venipuncture with ultrasound needle-guidance training on the partner. Laboratories were preceded by a PowerPoint (Microsoft Corp.) presentation that explained the objectives and clinical relevance of the ultrasound exercise followed by a live demonstration of the ultrasound scanning and venipuncture technique. To enhance participant success, ultrasound-compatible vascular access training models (Blue Phantom's Branched 2 Vessel Ultrasound Training Block Model, CAE Healthcare, Inc.) were used for ultrasound needle-guidance training. This vein access training model contains a blood vessel that branches into two vessels, allowing the user to guide needles into the targeted vessel using ultrasound imaging. Participants performed upper extremity vascular ultrasound examination using a Mindray-5 ultrasound machine with a 10L4s linear ultrasound transducer with a frequency bandwidth of 8.0/10.0/12.0 MHz (Shenzhen Mindray Bio-Medical Electronics Co., Ltd.). After identifying upper limb vascular structures of interest using ultrasonography, participants performed a supervised venipuncture under ultrasound guidance on the partner. Additional instruction on identifying venous structures with ultrasonography and venipuncture technique was provided during the venipuncture training time. All procedures were supervised by a licensed medical sonographer and registered nurses.

Before the vascular access laboratories, medical students and nurses completed an 18-question pretest consisting of three types of questions related to ultrasonography, anatomy, and nursing (specific to venipuncture) (Appendix). After completing the vascular access laboratories, the participants took an identical 18-question posttest and a voluntary, anonymous paper survey created specifically for the current study. The 10-item survey included seven Likert-scale questions and three open-ended questions. The survey was designed to assess participant perception of ultrasound technology and its use for venipuncture as well as their perception of the interprofessional vascular access laboratories. The Likert-scale questions included the following: (1) I feel capable of operating an ultrasound machine, (2) I feel capable of performing an upper extremity vascular ultrasound exam in a clinical setting, (3) I find it challenging to interpret a 2D ultrasound image, (4) I find it challenging to interpret an ultrasound image with color Doppler, (5) The use of vascular training block models during the interprofessional ultrasound laboratories was beneficial for the development of my clinical skills, (6) I believe that the ultrasound needle-guidance vascular training block model is a useful tool to learn and practice skills associated with venipuncture, and (7) Ultrasound technology is useful for technically difficult venipuncture cases. A standard Likert scale (strongly disagree, disagree, neither agree nor disagree, agree, and strongly

agree) was used to evaluate agreement or disagreement with the questions. The last three survey items were open-ended questions: (8) What is one thing that you found most useful about the interprofessional vascular access laboratories? (9) What is one thing you would like to see as part of the interprofessional vascular access laboratories that we did not include? and (10) Please leave comments about the use of ultrasound technology in medical/nursing education.

All data analyses were completed using SAS software version 9.4 (SAS Institute, Inc.). Frequency and percentage were reported for survey responses. The Wilcoxon rank sum test was used to test for differences between medical students and nurses for survey responses or change in test scores. The Wilcoxon signed rank test was used to test for differences from "neither agree nor disagree" in the median survey responses or for changes in test scores. A $p<0.05$ was considered statistically significant.

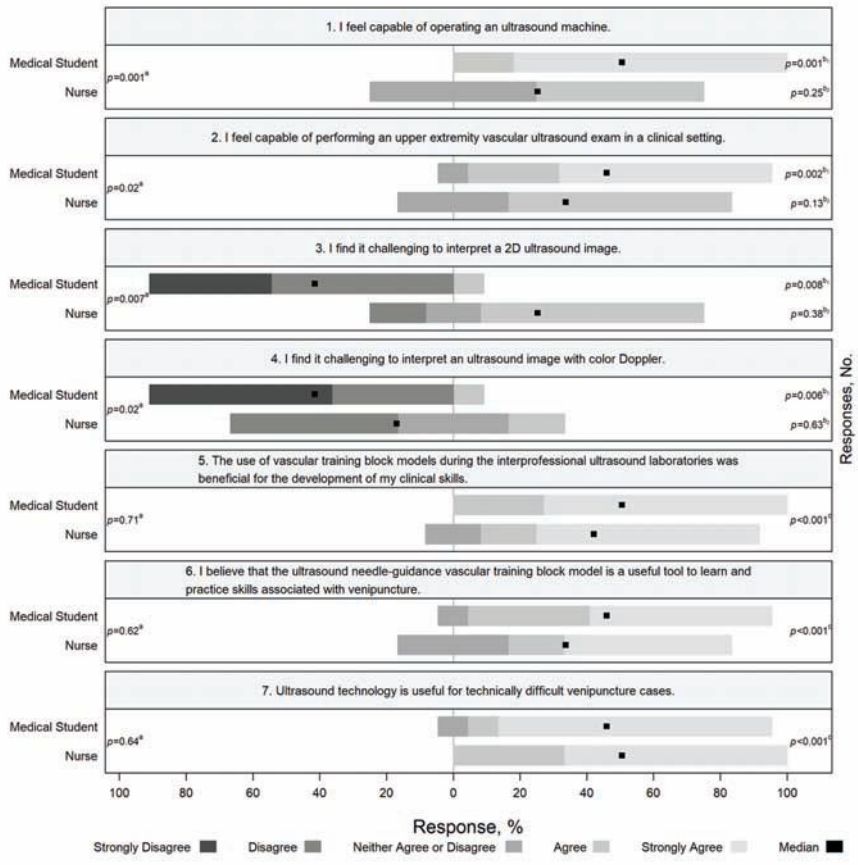


Figure 1. Performance of medical students (n=11) and nurses (n=6) on the pretest and posttest by total score and by score for question type. Error bars represent the minimum and maximum scores.

Results

Pretest and Posttest Scores

Pooling test results for both medical students and nurses, improvements were found in performance on posttest questions in total and for each of the three question types (ultrasonography, anatomy, and nursing specific to venipuncture) when compared with the pretest (all $p\leq0.03$) (Table and Figure 1). By question, all participants answered questions 1 and 2 correctly both times, so there was no change. For all other questions, more medical students and more nurses answered correctly on the posttest than pretest, with the exception of question 9 (anatomy question) where one less nurse answered correctly at posttest.

Among those with a score change, we found a greater likelihood to be correct on the posttest for questions 3 and 4 (ultrasonography questions) and questions 14 through 18 (nursing questions, all $p\leq0.03$). When considered by group, results were consistent for medical students for questions 3, 16, and 18 (all $p\leq0.03$). For nurses, no question had enough evidence to support a greater likelihood to be correct at posttest (all $p>0.06$).

Differences in improvement were found between medical students and nurses overall and for the three types of questions: overall (22% points and 45% points mean improvement for medical student and nurses, respectively), ultrasound questions (16% points and 48% points mean improvement for medical students and nurses, respectively), and anatomy questions (4% points and 40% points mean improvement

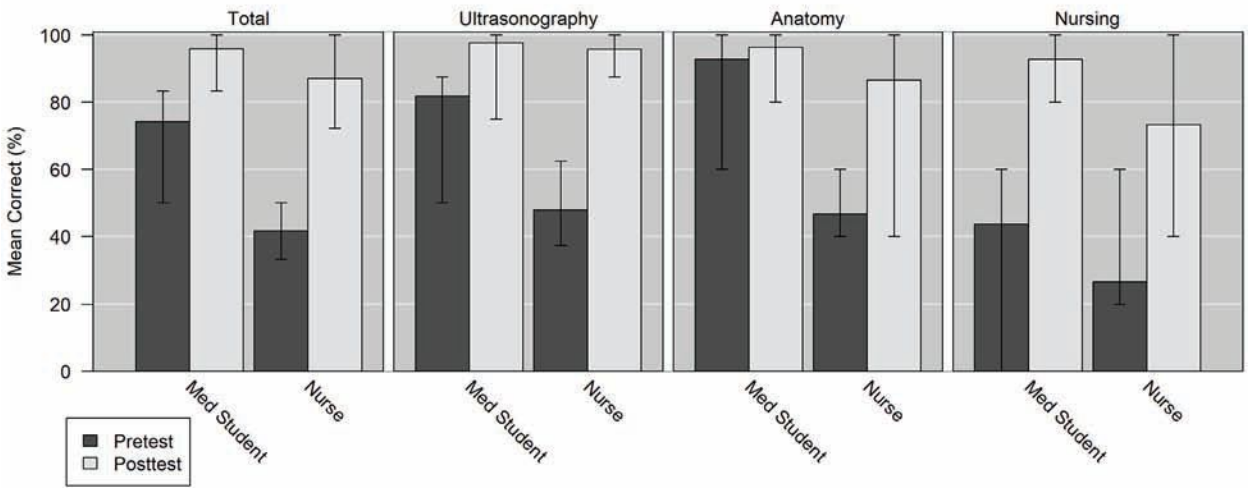


Figure 2. Levels of agreement between medical students (n=11) and nurses (n=6) for all Likert-scale survey questions
a. Wilcoxon rank sum test for difference between medical students and nurses.
b. Wilcoxon signed rank test for median difference from "neither agree or disagree" by group, where 1=medical student and 2=nurse.
c. Wilcoxon signed rank test for median difference from "neither agree or disagree" after pooling groups.

for medical student and nurses, respectively; all $p<0.01$) (Table 1). No differences were found for the nursing questions (49% points and 47% points mean improvement for medical student and nurses, respectively; $p=0.88$).

Survey Results

Medical students' and nurses' responses to the survey Likert-scale questions are shown in Figure 2. Differences were found between medical students and nurses for survey questions 1 through 4 (all $p\leq0.02$), but not for questions 5 through 7 (all $p\geq0.62$). After pooling all participants for questions 5 through 7, those with an opinion were more likely to agree than disagree (all $p\leq0.008$). Medical students tended to agree more with questions 1 and 2 and disagree more with questions 3 and 4 than nurses (all $p\leq0.04$). When agree and strongly agree responses were combined, 100% of medical students and 50% of nurses reported feeling capable of operating an ultrasound machine, 91% of medical students and 67% of nurses felt capable of performing an upper extremity vascular ultrasound exam in a clinical setting, 9% of medical students and 67% of nurses found it challenging to interpret a 2D ultrasound image, and 9% of medical students and 17% of nurses found it challenging to interpret an ultrasound image with color Doppler. All medical students (100%) and the majority of nurses (83%) noted that the use of vascular training block models during the interprofessional ultrasound laboratories was beneficial for the development of their clinical skills, 91% of medical students and 67% of nurses believed that the ultrasound needle-guidance vascular training block model was a useful tool to learn and practice skills associated with venipuncture, and 91% of medical students and 100% of nurses noted that ultrasound technology was useful for technically difficult venipuncture cases. In written comments, the majority of participants indicated the interprofessional vascular access laboratory was useful for learning vascular access.

Discussion

The current study evaluated an interprofessional approach involving medical students and nurses for learning vascular access with ultrasonography after participating in a vascular access laboratory. A survey was used to determine their level of comfort with performing venipuncture under ultrasound guidance and to evaluate their perceptions of venipuncture laboratories delivered in an interprofessional environment. The majority of participants believed the interprofessional vascular access laboratory was beneficial to their learning. We found significant

differences between medical students and nurses on questions about capability of operating an ultrasound machine, performing an upper vascular ultrasound exam, and interpreting the ultrasound image. Medical students had completed two years of ultrasound coursework before the vascular access laboratory, which likely explains their higher level of comfort with the ultrasound equipment and imaging. However, their experience seemed to be beneficial during this team-based collaboration. Because the students were more knowledgeable in ultrasonography, they could enhance the education of the participating nurses by helping them to master this imaging modality. This benefit was reflected in the nurses' written comments, which emphasized that the use of ultrasound technology was very important. For the open-ended question about how the laboratory could be improved, the only suggestion from the nurses was to provide more time to use the ultrasound machine.

We also found significant improvements in performance for medical students and nurses on posttest questions for total scores and for the three question types when compared with the pretest. Both groups benefited from the exercise. Students showed most improvement in nursing questions, and nurses improved significantly in all three areas (knowledge of ultrasound, anatomy, and nursing aspects of venipuncture). Our hypothesis that students would show most improvement on the nursing questions was supported by the results of the study. However, the improvement of the nurses in all three areas was not expected. These results indicate that practicing nurses who have been away from the classroom and didactic exercises might benefit from exposure to basic information related to ultrasonography, anatomy, and even nursing techniques.

The interprofessional approach of this training exercise, where two medical students were paired with an experienced nurse, allowed participants to learn from each other to interpret ultrasound images, identify the vein for venipuncture, and perform the invasive procedure. All students successfully completed the venipuncture procedure, performing it under the guidance of the experienced nurses; and all nurses successfully interpreted the ultrasound images and visualized the veins with help from the medical students. The success of the laboratory objectives suggested that participants were competent in obtaining and interpreting ultrasound imaging and performing ultrasound-guided venipuncture.

Acquiring intravenous access in the emergency department and intensive care unit is a common task. Several studies have evaluated the use of ultrasound guidance for central venous access by physicians in the emergency department.[18, 19] Some patients, such as those who are obese or hypovolemic, use drugs intravenously, or have vascular pathology, are known as "difficult sticks" for peripheral intravenous placement. Therefore, an ultrasound-guidance technique was recently adopted for better peripheral venous access.[20,21] Several studies have noted the positive effect of ultrasound guidance on the perceived difficulty experienced by emergency nurses when obtaining peripheral intravenous access.[8, 21] Written comments from the medical students and nurses in the current study indicated they were receptive to IPE of an invasive procedure using ultrasound technology in both their education and future practice. The majority of participants also agreed that ultrasound technology was useful for technically difficult venipuncture cases. Students also commented that they felt more prepared for clinical rotations, while the nurses emphasized that ultrasound technology added to their confidence when performing "difficult sticks." The qualitative analysis of our open-ended survey items revealed that participants were overwhelmingly positive about the IPE exercise. The most common comments from students reflected the fact that they learned a lot from the nurses about the venipuncture technique. For instance, students commented that "I learned a lot from her advice," "Got some knowledge/tricks from a nurse," "They were able to provide insight in vascular access," and "Learning how to obtain venous access from nurses helped me learn some of the differences between performing the procedure with and without ultrasound and the indications for using ultrasound." Students

also commented that this training should be included in the medical school curriculum.

One limitation of the current study was that participants did not have access to a difficult patient when performing the venipuncture. As one participant commented, "we were all young and had nice veins." In addition, students commonly indicated that they would have liked to practice ultrasound-guided venipuncture more often. Another limitation was the small group size: the current study was the first time the IPE approach was used for venipuncture with ultrasound guidance learning and was meant to serve as a pilot for future studies.

In the current study, medical students and nurses showed marked improvement in their understanding of the aspects of ultrasonography, anatomy, and nursing techniques associated with venipuncture. Results suggested that the interprofessional vascular access laboratory was beneficial for all participants. For medical students, it helped them improve their understanding of the venipuncture procedure and build technical skills. For nurses, it boosted their confidence in performing "difficult sticks" and introduced them to the use of ultrasound technology for peripheral venous access. Thus, the interprofessional approach provided realistic exposure to venipuncture for medical students and a review of related anatomy and imaging for practicing nurses. As such, the interprofessional vascular access laboratory of the current study was beneficial for the future physicians and practicing nurses who participated, and it should be considered as a model for IPE of procedures that otherwise are difficult to address in a medical school curriculum.

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MM

Use of the Contralateral Knee as a Control in the Destabilization of Medial Meniscus Osteoarthritis Rat Model

by Michelle Hintz, MS, OMS IV, Taylor L. Ernest, MS, OMS IV & Peter Kondrashov, PhD

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FIRST IN WHOLE PERSON HEALTHCARE

Because of the disability caused by osteoarthritis in a large portion of the aging US population, it is important to have well-defined animal models to study the disease and possible treatments.



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Abstract

Destabilization of the medial meniscus (DMM) induces osteoarthritis (OA) in a rat model, but using the contralateral limb as control is unknown. We examined DMM and obesity in an OA rat model using contralateral limbs as control. Femoral condyles and tibial plateaus were evaluated. No differences were found between knees across diet groups (P=.61) or between surgery scores in diet groups (both P>.49). Thus, contralateral limbs may be a control for short-term (≤4 weeks) studies.

Introduction

Osteoarthritis (OA) is the most common degenerative joint disease affecting the aging US population.[1,2] It is characterized by the slow degeneration of articular cartilage of synovial joints, osteophyte formation, remodeling of subchondral bone, and synovial inflammation. The joints most commonly affected include the knees, hips, and hands. Risk factors include older age, sex, obesity, previous injury, previous inflammation, chondrocalcinosis, occupational knee bending, and physical labor.[3-5] At this time, there are no disease-modifying treatments for this condition.[6] Because of the disability caused by OA in a large portion of the aging US population, it is important to have well-defined animal models to study the disease and possible treatments.

Destabilization of the medial meniscus (DMM) is a surgical procedure for inducing OA in animal models.[7] The procedure causes a slowly progressing development of moderate OA that resembles OA in humans more closely than other surgical models.[8] During surgery, the knee joint capsule is opened, and the medial meniscotibial ligament, which anchors the medial meniscus to the tibial plateau, is transected. Over the following weeks, OA develops in the surgical knee and can be studied using a variety of methods. Although this surgery is a well-established procedure in the rodent model, there is a lack of information on the use of the contralateral knee as the control. Therefore, the purpose of our study was to determine the utility and validity of the contralateral knee as a control in a rat model of DMM-induced OA. Being able to use the contralateral knee as a control has positive implications for reducing costs and the number of animals required.

Methods

Forty female Lewis rats were obtained from Hilltop Lab Animals (Scottsdale, PA, USA). From a power analysis, we determined that a sample size of 40 rats was adequate for a power of 0.77. Rats were housed in an animal care facility that operates at 23°C and has a 12:12 hour light-dark cycle.

Table 1. Mean (SE) Osteoarthritis Research International (OARSI) Scores of Knee Articular Cartilage in the Contralateral (Non-surgical) Limbs of Study Rats by Diet and Surgery Groups

Diet Group	DMM Surgery	Sham Surgery	*P* Value[a]
High-fat diet	0.91 (0.27)	0.91 (0.24)	.63
Regular diet	0.66 (0.20)	0.89 (0.27)	.41
P value[b]	.72	.99	

[a]Comparison of DDM vs sham surgery groups.
[b]Comparison of high-fat vs regular diet groups.
Abbreviation: DMM, destabilization of the medial meniscus.

Rats were kept in R20 polypropylene cages (Ancare, Bellmore, NY, USA) with bedding of Nepco Lab aspen shavings (El-Mel, St. Charles, MO, USA) in groups of no more than three rats. The cages were 27 cm × 48 cm × 20 cm in dimension and had stainless steel wire bar lids that were 27 cm × 48 cm in dimension. The rats were allowed free access to food and water and were allowed to acclimatize to the animal care facility for 10 days before the start of the experiment. All researchers who participated in the study and cared for the animals were trained in animal care, and the experimental protocol was approved by the local Institutional Animal Care and Use Committee.

Rats were randomly assigned to four groups: (1) sham surgery and regular diet (control group), (2) DMM surgery and regular diet, (3) sham surgery and high-fat diet, or (4) DMM surgery and high-fat diet.[9] The regular diet consisted of Purina 5001 lab rodent lab diet pellets (El-Mel, St. Charles, MO, USA), and 13% of calories were from fat. The high-fat diet consisted of pellets that contained casein, L-cystine, corn starch, sucrose, maltodextrin 10, soybean oil, lard, cellulose, dicalcium phosphate, calcium carbonate, potassium citrate, vitamin mix V10001, choline bitartrate, and Brilliant Blue food coloring dye (D12492, Research Diets, Inc., New Brunswick, NJ, USA). These pellets had 60% of calories from fat, 20% of calories from carbohydrates, and 20% of calories from protein. The diets were maintained for eight weeks. Rats were weighed three times per week. We defined obesity as an increase in body weight of at least 20%.

After four weeks on their respective diets, the rats underwent the DMM or sham surgery under sterile conditions on a random knee. Rats were anesthetized with 5% isoflurane (Fluriso, VetOne, Boise, ID, USA) via inhalation with 90% O_2 and 5% CO_2. Rats were placed on a sterile surgical dressing with a heat pad underneath to maintain temperature. In the experimental knees, an incision was made medial to the knee joint. The capsule was identified and incised over the anterior aspect. The medial meniscotibial ligament was identified and transected to free the medial meniscus from the tibial plateau. The capsule was sutured and the incision closed using staple clips. Triple antibiotic ointment was applied over the joint capsule after suturing and over the skin after stapling. In the sham knees, only the joint capsule was opened and sutured. Rats were given a subcutaneous injection of 0.01 mg/kg buprenorphine (Buprenorphine Hydrochloride, Par Pharmaceutical, Chestnut Ridge, NY, USA) in saline to limit the pain endured by the animal.

Rats were monitored immediately after surgery, 8-12 hours after the surgery, and every 8-12 hours after that as necessary. If any animals showed signs of pain and distress,[10] a veterinarian was consulted; and if its condition did not improve, the rat was taken out of the study.

Four weeks after surgery, the rats were sacrificed using a fatal dose of pentobarbital. At this point, the study knees and contralateral knees were harvested. The contralateral knees were stored in 10% buffered formaldehyde solution. The study knees were decalcified in a rapid decalcifying agent, processed, embedded in paraffin blocks, and sliced at 10-µm thickness. Slides were stained with safranin O stain with fast green as a counterstain. The knees were histologically evaluated for degenerative changes by a blinded scorer using the Osteoarthritis Research International (OARSI) scoring system.[11] Four articular surfaces of each knee were scored: medial and lateral condyles of the femur and medial and lateral tibial plateaus.

The mean and standard error (SE) of the OARSI scores were calculated for all rat knee groups (Table 1). A generalized linear mixed model was used to analyze differences between the rat knee groups. Analyses were conducted using SAS version 9.4 software (SAS Institute, Inc). A $P<.05$ was considered statistically significant.

Results

In a previous study, we examined the effects of DMM and obesity on the development of OA in a rat model, and DMM surgery resulted in significantly greater OARSI

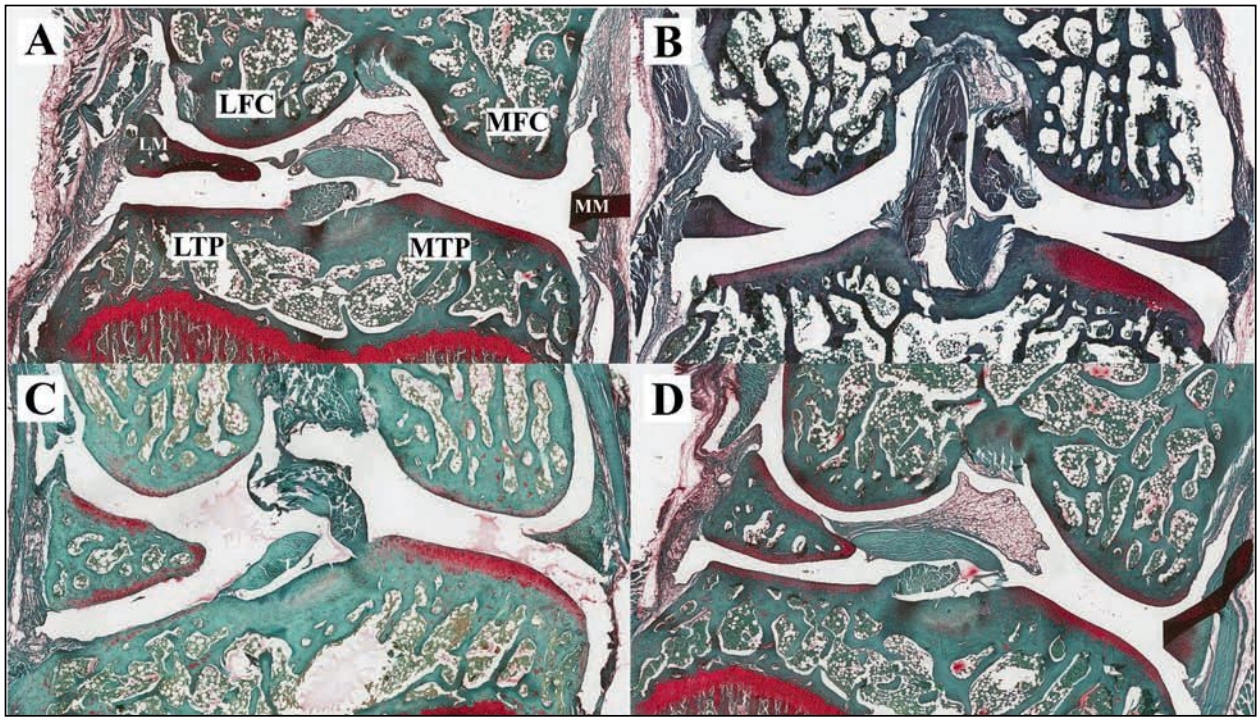


Figure 1. Coronal sections of rat knees (contralateral to the surgical limb) stained with safranin O. A, right knee, sham surgery group, regular diet; B, right knee, sham surgery group, high-fat diet; C, right knee, DMM surgery group, regular diet; D, right knee, DMM surgery group, high-fat diet.
Abbreviations: LFC, lateral femoral condyle; LM, lateral meniscus; LTP, lateral tibial plateau; MFC, medial femoral condyle; MM, medial meniscus; MTP, medial tibial plateau.

scores on the operated knee than the sham surgery in both the high-fat and regular diet groups (P<.004).[9] In the current study, the articular cartilage of the contralateral knees showed no signs of damage (Figure 1). There was no difference in OARSI scores for the contralateral knees between the DMM (score=0.77) and sham surgery (score=0.90) groups (P=.61). When comparing within each of the diet groups, no differences in OARSI scores were found in the contralateral knees between the DMM and sham groups in the high-fat (P>.99) or regular (P=.49) diet groups (Table 1). The comparison of the four major surfaces showed that the medial tibial plateau had slightly lower scores than the other three surfaces (P<.001).

Discussion

The purpose of the current study was to determine whether the contralateral limb could be used as the control in a rat model of DMM-induced OA. The use of the contralateral knee as a control has implications for efficiency and for reducing costs and the number of animals required. Currently, there is insufficient literature on this topic. Guinea pigs have been shown to develop spontaneous OA in the knee joint, and the contralateral limb of guinea pigs has been used to compare spontaneous OA to traumatically induced OA.[12-14] In the rat knee, however, spontaneous OA has not been found to develop.[12-15] According to the Recommendations for Histological Assessments of Osteoarthritis in the Rat published in the OARSI Histopathology Initiative in 2010,[16] no model of spontaneous rat OA exists because only minor medial degenerative changes may occur, which is also true for genetically modified strains. Data from the current study and the previous study by Ernest and Kondrashov[9] support these findings since our control group (regular diet, sham surgery) did not have increased OARSI scores, suggesting that spontaneous OA did not develop within the time frame of the study.

With regard to the concern that postsurgical compensations in joint loading negate the viability of the contralateral limb as a control,[17] our data suggest that in short-term studies this is not a problem. The current literature on this topic is somewhat contradictory, though. Previous studies of traumatic OA development have shown

that animals (especially rodents) do not compensate by decreasing use of the affected limb.[11] Specifically, gait analyses in postsurgical rats revealed little if any change in load-bearing of the operated knee.[12] However, results of studies focused specifically on range of motion and gait compensation analyses after surgical OA induction have shown that rats do, in fact, compensate for injury-induced OA by favoring the operated knee shortly after treatment.[18-20] Our results suggest that, in the short term, DMM does not cause significantly higher OARSI scores in the contralateral knee because we found no significant score differences within or across surgery and diet groups. Therefore, our findings strengthen the utility of the contralateral limb as a control in short-term DMM rat models.

In the current study, we also found that even though all surfaces of the knee had healthy cartilage the medial tibial plateau had slightly higher OARSI scores than the other three articular surfaces studied. This finding suggests that rats may naturally load the lateral compartment of the knee. However, weight distribution was not specifically evaluated in this study. In previous studies, researchers investigated the effects of altered joint loading in the development of OA in the rat knee.[21-23] Results showed that application of a varus loading device that increased loading on the medial knee compartment and decreased loading on the lateral knee compartment led to degenerative changes resembling OA in the medial compartment.[21-23] However, the literature on the topic of normal joint loading in the rat knee is insufficient at this time and serves as an important study question for future experiments.

A limitation of the current study was the short time frame (4 weeks) over which the experiment was performed. There is a possibility that extending the study beyond four weeks would yield higher OA scores across the experimental groups. In the future, the integrity of articular cartilage in the contralateral knee in the DMM model should be evaluated in a long-term study because the longer study duration would result in greater damage to the surgical limb.

Conclusions

We believe that the contralateral limb can be used as a control in short-term (4 weeks or less) OA studies using DMM in a rat model. This approach will save time and resources because an adequate sample size can be achieved with fewer animals.

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Disclosure

None reported. **MM**

Development of Competency in Needle-Guided Procedures Through the Use of Soft-Embalmed Cadavers

by Tatyana Kondrashova, MD, PhD, Ryan Canaan, BS, OMS III, Brady Gunn, BS, OMS III, Vanessa Pazdernik, MS & Jeremy J. Houser, PhD

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These results suggest a Thiel-embalmed cadaver can be used as a clinical training tool for learning needle-guided procedures.



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Abstract

This study evaluated soft-embalmed human cadavers for ultrasound needle-guidance training. Second-year medical students used peripherally inserted central catheter (PICC) line and central line models and a Thiel-embalmed cadaver for training and provided feedback. Most (85%) agreed the cadaver was useful. There were positive correlations between performing the PICC line (r=0.44, P=.11) and central line (r=0.63, P=.03) procedures on a cadaver and in a clinical setting. Thiel-embalmed cadavers may provide important hands-on training.

Introduction

Ultrasound needle-guided procedures are commonly used across a variety of medical specialties,[1-3] so medical students and residents are taught to master these procedures throughout their medical training.[4, 5] However, since it is unacceptable for students to practice clinical skills on patients,[6] medical educators are constantly searching for new methods to teach procedural skills.[7, 8]

Since training for technical procedures is often disorganized and unstructured, there is an ongoing effort to find the best methods to learn invasive procedures with ultrasonography using simulators.[5, 9, 10] Simulators for learning needle-guided procedures include engineered models (phantoms), cadavers, animal models, computer-based methods, and virtual reality models.[11] However, there is a lack of evidence regarding the applicability, rationality, and reliability of most of these tools for learning needle-guided procedures. Phantoms have low background echogenicity, which enhances the needle visibility but can lead to false confidence with regard to clinical ability.[11] On the other hand, meat phantoms have excellent feasibility, are cheap, can be constructed with minimal preparation, and can be disposed of easily.[12, 13] Animal models can also be useful simulators, but they lack the physical reality of an actual human patient and have a limited lifespan (1-2 days).[13] Computer-based training imparts knowledge, but it is insufficient to improve procedural skills.[14] The quality of modern synthetic models is very high and they provide a realistic experience with needle penetration, but these models are expensive and require additional training by the faculty.[4]

Cadavers can be used for learning ultrasound anatomy and practicing skills, such as hand-eye coordination, probe handling on an irregular surface (e.g., the supraclavicular region), and needle-probe alignment.[15] For medical education purposes, cadavers are traditionally embalmed with formalin for long-term preservation.[16] However, formalin causes the cadaver's tissues to have a rigid feel[17] and can negatively affect the color. Moreover, the formaldehyde in formalin is linked to several health hazards,[18] such as headache, skin irritation, and mucous membrane irritation.[19] Formaldehyde is also classified as a carcinogenic substance and can cause long-term health consequences for students and faculty.[20] Reducing the hazards associated with formalin-embalmed cadavers involves improving laboratory air flow, decreasing formaldehyde content, or using alternative embalming solutions.[21] Embalming solutions with low formaldehyde content are low cost and preserve the lifelike quality of tissue. However, this type of embalming only lasts for several weeks.[22] Because of the time constraint, this type of embalming is not suitable for most medical schools where anatomy courses run for several months. Neutralizing formaldehyde is another cost-effective way to reduce formaldehyde content while providing long-term preservation of cadavers.[21] Adding monoethanolamine after the embalming process is one way to reduce formaldehyde, but it extends the required time for embalmment[23] and leaves a white film on the cadaver's tissues.

Soft-embalmed human cadavers are increasingly being used as a model to train surgeons and anesthesiologists because they look and feel like real patients. A recent soft-embalming solution was developed by Walter Thiel in 1992.[24] This method uses a mixture of 4-chloro-3-methylphenol and various salts for fixation, boric acid for disinfection, and ethylene glycol for preservation of tissue pliability.[25] Thiel embalming solutions are less carcinogenic (8.9% formaldehyde) than formalin embalming (37%-40% formaldehyde), but Thiel cadavers are much more expensive.[26] A Thiel cadaver can cost 10-20 times more than a formalin cadaver.[27] Despite the high cost, Thiel-embalmed cadavers are described as exceptionally lifelike with representation of structures almost corresponding to a real patient.[28] They also produce more realistic ultrasonography images and fascial "pop" sensations than fresh (recently deceased) cadavers.[28, 29] A Thiel-embalmed cadaver has well-preserved organs and tissues with natural color, consistency, and flexibility.[25] Moreover, vessel diameters are well preserved.[30] The retained structure and consistency of tissues leads to clearer ultrasound images than those obtained from formalin cadavers.[31] Because they are exceptionally lifelike, Thiel-embalmed cadavers have been reported to have a positive impact on dissection and skills training.[32] Because Thiel embalming is a relatively new method, research investigating learning and skills training with these cadavers is limited.[27]

Although many medical schools and residency programs include ultrasound in their curricula,[33-36] there is limited evidence on the comparative efficiency of different training modalities for teaching and learning invasive procedures with ultrasonography in medical education. Therefore, the purpose of the current study was to evaluate student perception and potential benefits of using soft-embalmed human cadavers for ultrasound needle-guidance training.

Materials and Methods

In the current study, we recruited second-year medical students (N=13) to voluntarily participate in ultrasound needle-guidance training sessions that used a peripherally inserted central catheter (PICC) model (Figure 1A), a central line model (Figure 1B), and a Thiel-embalmed cadaver (Figure 1C). Student participants used PICC line and central line models for mastering procedures with ultrasound needle-guidance before they practiced the same procedure on the Thiel-embalmed cadaver. The local institutional review board granted exempt status for the current study.

The PICC line training used the PICCLineMan Model (Simulab Corporation), which contains the basilic, brachial, and cephalic veins; median nerve; brachial artery; and the humerus (Figure 1A and 1D). Palpable landmarks included the antecubital fossa, clavicle, sternum, 1st-4th intercostal spaces, acromion, ribs 1-7, and the humeral head.

The Gen II Ultrasound Central Line Training Model (CAE Healthcare), which contains the internal jugular vein and common carotid artery, was used for the central line training (Figure 1B and 1E).

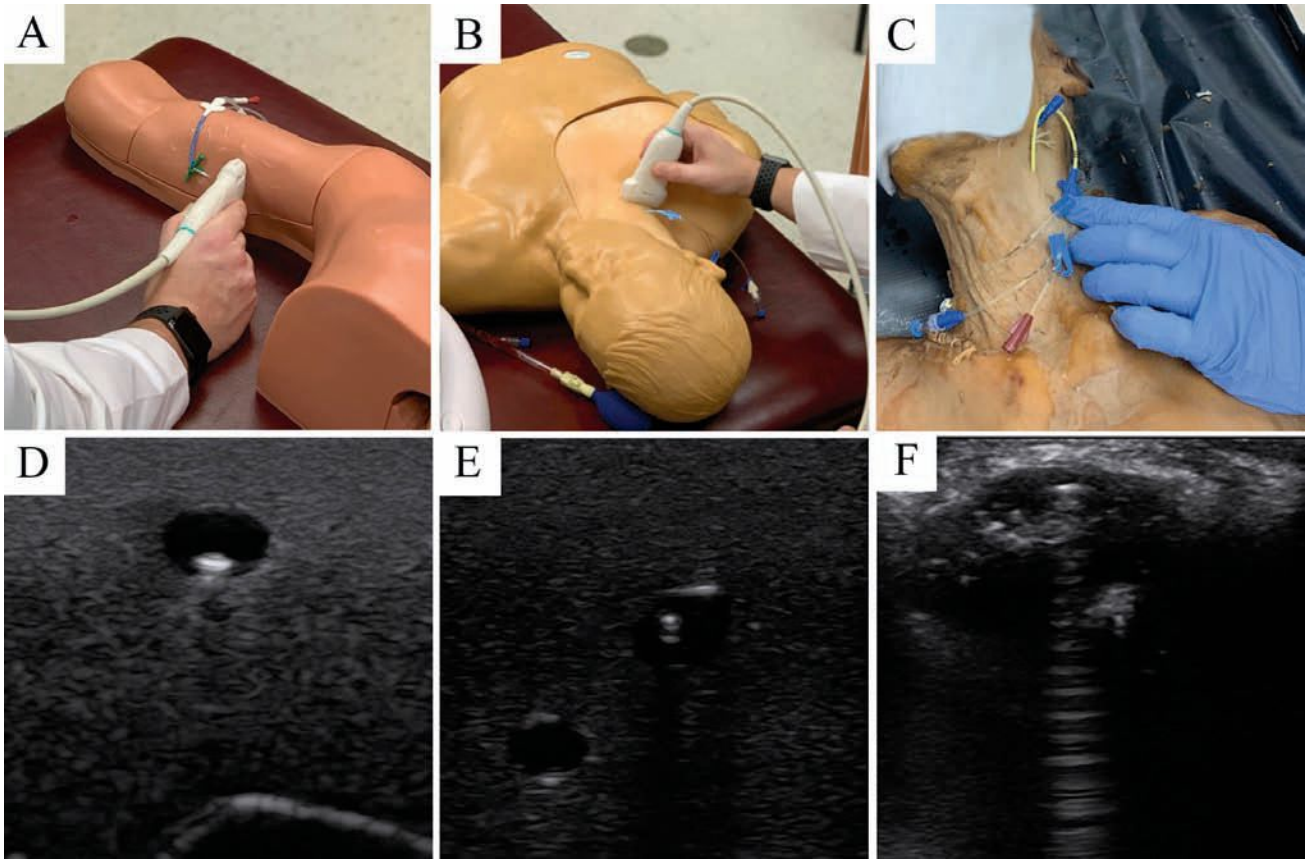


Figure 1. Ultrasound Training Models Used for the Needle-Guided Training Procedures of the Current Study
A: PICCLineMan Training Model (Simulab Corporation). B: Gen II Ultrasound Central Line Training Model (CAE Healthcare). C: Thiel-embalmed cadaver. D: Ultrasound image showing a needle in the basilic vein using the PICCLineMan Training Model. E: Ultrasound image showing a needle in the internal jugular vein using the Gen II Ultrasound Central Line Training Model. F: Ultrasound image showing a needle in the internal jugular vein using the Thiel-embalmed cadaver.

Pulsatility of the artery can be simulated with a manual hand pump or an automated pump and can be demonstrated using color Doppler ultrasound. The model allows for full thread guide wires, dilators, and catheters without resistance.

The Thiel-embalmed cadaver was used for both PICC line and central line training. The target vessels included the basilic and internal jugular veins (Figure 1F). Because these vessels were empty and collapsed, they were filled with ultrasound gel at the procedure sites for better visualization.

For the PICC line procedure with the cadaver, a longitudinal, superficial 3-cm cut was made along the medial aspect of the biceps brachii about 5-7 cm superior to the antecubital fossa to expose the basilic vein. Right angle forceps were used to pass a string deep to the vein. The basilic vein was then tied off at its most inferior point of exposure. A PICC line catheter was cut to 3 cm in length and inserted into the exposed basilic vein. The catheter was then sutured to the skin. Ultrasound gel was heated for 10 seconds in a microwave to decrease its viscosity. The gel was loaded into a syringe that was connected to the catheter and was inserted into the basilic vein. As the ultrasound gel was injected into the vein through the catheter, ultrasound was used to monitor the filling of the basilic vein 7-10 cm superior to the exposed vein. Once the vein was inflated, the injection was stopped. On average, it took 15-20 mL of gel to inflate the vessel.

For the central line procedure with the cadaver, a 3-cm longitudinal cut was made directly anterior to the mastoid process. The tissues were

dissected and retracted to visualize the internal jugular vein and carotid arteries. At the most superior point of exposure, right angle forceps were used to pass a string deep to the internal jugular vein. The string was then used to tie off the vein so that the ultrasound gel could not pass superiorly. A central line catheter was cut to 3 cm in length and inserted into the exposed internal jugular vein. The catheter was then sutured in place to the skin. Ultrasound gel was again heated in a microwave for 10 seconds to decrease its viscosity. The gel was then loaded into a syringe and connected to the catheter so the gel could be injected into the internal jugular vein. Once the vein was inflated, the injection was stopped. On average, it took 20-30 mL of gel to inflate the vessel.

Before participating in the needle-guided procedures laboratory, medical students had mastered basic ultrasonography techniques and applications during their clinical ultrasound coursework.[34] Before each training session of the current study, a review of the basic indications, contraindications, and techniques to perform the ultrasound-guided procedures was provided. The learning objectives, management of procedures, possible complications, and clinical relevance of the exercise were also outlined. The introduction was followed by a quick demonstration that allowed students to gain familiarity with the models, Thiel-embalmed cadaver, and equipment used during the training session. Students performed the PICC line and central line procedures with the phantoms and cadaver using sterile techniques and equipment. Students used real-time ultrasonography to scan the models and cadaver, identify target structures, and perform the procedure.

After the needle-guided procedures training laboratory, students were asked to complete a 14-question paper survey about their perceptions of the importance of the models and Thiel-embalmed cadaver for education and future practice. The survey was created specifically for the current study; it was voluntary and anonymous and did not collect demographic information. Twelve items were Likert-scale questions (strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree) and evaluated student agreement or disagreement with statements about understanding of the procedures, their comfort level with performing the ultrasound needle-guided procedures after using the models and cadaver, and their capability of performing the procedures in a clinical setting (Table). The survey also asked about challenges in interpreting the ultrasound images on the different training models and the benefits of using models and cadavers for development of their clinical skills. The last two survey items were open-ended questions that asked the following: What is one thing that you found useful about the cadaver training model? and Is there another procedure that you would like to practice using the cadaver model?

Frequency and percentage were reported for survey responses; agree and strongly agree responses and disagree and strongly disagree responses were grouped under a single agree or disagree category. Wilcoxon signed rank tests were used to test whether the level of agreement differed from "neither agree nor disagree" for each question. Pearson correlation coefficients were used to assess the linear relationships between feeling capable of performing on a cadaver and in a clinical setting for both the PICC line and central line procedures. Wilcoxon signed rank tests were used to test for differences in the perception of difficulty of image interpretation among models, a cadaver, and a real person. SAS version 9.4 software (SAS Institute, Inc) was used to conduct the analyses. A $P<.05$ was considered statistically significant.

Results

All students (100%, 13/13) agreed that practicing vascular access on a cadaver improved their understanding of both the PICC line and central line procedures (Table and Figure 2). The majority of students (92%, 12/13) felt capable of performing the PICC line and central line procedures on a cadaver after completing the training, but only 69% (9/13) felt capable of performing the PICC line procedure in a clinical setting and 85% (11/13) of performing the central line procedure in a clinical setting. All students (100%, 13/13) disagreed that it was challenging to interpret ultrasound images on either of the commercial models, but only 54% (7/13) disagreed that it was challenging to identify

Table 1. Likert-Scale Survey Question Responses of Second-Year Medical Students (N=13) Participating in a Voluntary Ultrasound Needle-Guided Training

Survey Item	Likert Responses, No. (%)			Mean (SD)
	Disagree*	Neither Agree Nor Disagree	Agree**	
Practicing vascular access on a cadaver has improved my understanding of the PICC line procedure	0	0	13 (100)	4.9 (0.3)
Practicing vascular access on a cadaver has improved my understanding of the central line procedure	0	0	13 (100)	5.0 (0)
I feel capable of performing the PICC line procedure on a cadaver	0	1 (8)	12 (92)	4.5 (0.7)
I feel capable of performing the PICC line procedure in a clinical setting	0	(31)	9 (69)	4.0 (0.8)
I feel capable of performing the central line procedure on a cadaver	0	1 (8)	12 (92)	4.6 (0.7)
I feel capable of performing the central line procedure in a clinical setting	1 (8)	1 (8)	11 (85)	3.9 (0.8)
I find it challenging to interpret an ultrasound image on the PICC line model	13 (100)	0	0	1.0 (0)
I find it challenging to interpret an ultrasound image on the central line model	13 (100)	0	0	1.0 (0)
I find it challenging to interpret an ultrasound image of upper limb veins on a cadaver	7 (54)	1 (8)	5 (38)	2.0 (1.2)
I find it challenging to interpret an ultrasound image of upper limb veins on a real person	10 (77)	0	3 (23)	2.5 (1.5)
The use of a cadaver for guided injections was beneficial for the development of my clinical skills	0	1 (8)	12 (92)	4.7 (0.6)
A cadaver is a useful tool to learn and practice skills associated with vein cannulation	0	2 (15)	11 (85)	4.7 (0.8)

*Includes disagree and strongly disagree responses. **Includes agree and strongly agree responses. Abbreviation: PICC, peripherally inserted central catheter.

structures on the cadaver using ultrasonography. The majority of participants (85%, 11/13) agreed that the Thiel-embalmed cadaver was a useful tool to learn and practice vein cannulation.

There was high positive, but not significant, correlation between feeling capable of performing the PICC line on a cadaver and performing the procedure in a clinical setting (r=0.44, P=.11). There was a strong positive correlation between feeling capable of performing the central line procedure on a cadaver and in a clinical setting (r=0.63, P=.03). Students felt it was easier to perform the procedure and interpret the image on PICC and central line models than on the cadaver and a real person (all P<.001). Students felt it was equally challenging to identify veins on a cadaver and a real person (P =.27). There was no variation in how each student perceived the difficulty of the PICC line and the central line procedures; all indicated strongly disagree.

For the open-ended question regarding what was most useful about the cadaver training model, 11 of the 13 written responses mentioned the difference between real anatomy and the models, which were considered "too ideal." For the question about what other procedures students would like to practice using the cadaver model, students mentioned chest tubes (n=3), arterial access (n=2), lumbar puncture (n=2), thoracentesis (n=1), and joint injections (n=1).

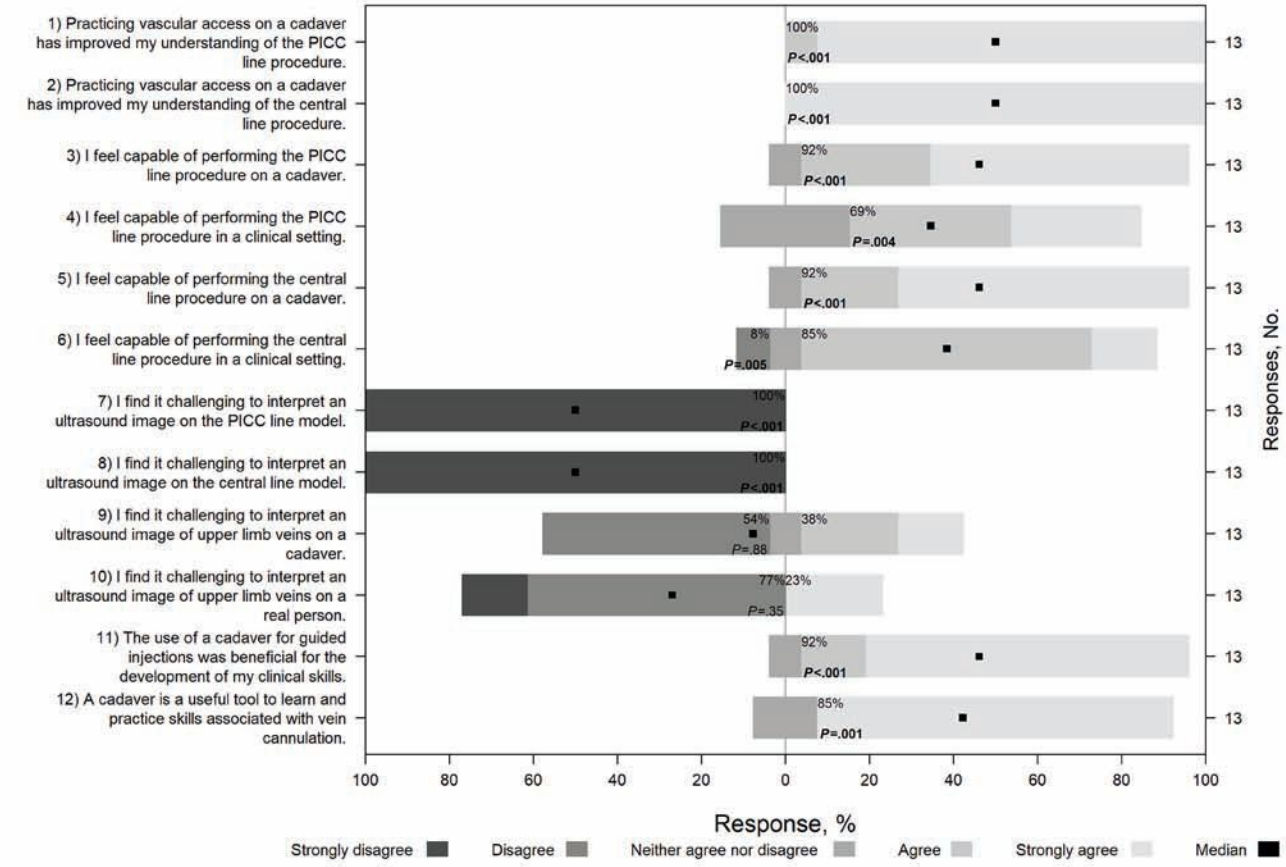


Figure 2. Survey Responses of Second-Year Medical Students Participating in a Voluntary Ultrasound Needle-Guided Training Session
Abbreviation: PICC, peripherally inserted central catheter.

Discussion

Using modern tools to incorporate procedural skills training and ultrasound simulation into preclinical medical education may improve clinical practice and decision-making by increasing confidence and competence with ultrasound needle-guided procedures.[37, 38] The goal of the procedural training in the current study was to evaluate student perception and potential benefits of using soft-embalmed human cadavers for ultrasound needle-guided training. We hypothesized that a Thiel-embalmed cadaver could be used as a clinical training tool and that it would yield effective learning and adequate clinical performance of needle-guided procedures for future physicians. Our results suggested that the majority of participating second-year medical students felt the Thiel-embalmed cadaver contributed to better understanding of clinical procedures and increased their capability of performing those procedures in a real clinical setting. Students commented that the Thiel-embalmed cadaver "gives more of a real feel compared to models," "gives feel for human tissue," and provides a "real life experience."

Even though there was no difference in how students perceived the difficulty of the PICC line and central line procedures, results indicated a difference in their perceived capability of performing these procedures in a clinical setting. We did not expect students to feel more capable of performing the central line procedure in a clinical setting since it is a more challenging and invasive procedure than the PICC line procedure.[39] This result was likely caused by differences in the procedures: the PICC line procedure involves smaller vessels and requires more practice for ultrasound guidance using models,

while the central line is associated with more complications in real clinical encounters.

Our results also suggested that students became competent in ultrasound imaging interpretation and procedural skills after completing the training session. The majority of students could interpret ultrasound images identifying vascular structures without difficulty after the training. The ability to interpret ultrasound images while performing the PICC line and central line procedures is an important aspect of medical training, and it can have an impact on physician competence and patient safety. In a review of the role of medical simulation, physicians trained with simulation-based techniques outperformed and were more competent than traditionally trained physicians for a specific procedure.[40] Further, using simulation-based education increased patient safety.[40] Thus, models are important for early medical training because they build student confidence with invasive procedures and increase comfort level when performing needle guidance before practicing on a cadaver. Students in the current study felt it was easier to perform the procedures and interpret the images on the models than the cadaver, which suggests cadavers are more realistic and better prepare the students for future clinical practice. Our results also showed a strong positive correlation between students feeling capable of performing the PICC line and central line procedures on the cadaver and in a clinical setting, which suggested the training that included the Thiel-embalmed cadaver increased their confidence in performing these procedures in real life.

The training exercise of the current study allowed medical students to use actual PICC line and central line equipment on the models and Thiel-embalmed cadaver, which added a realistic feel to the procedural exercise and contributed to the positive student perceptions. In an open-ended response, one student wrote the cadaver training model was useful for "looking at the vasculature on an actual body and being able to thread instruments through," which supports the uniqueness of this training experience. The training format also included ultrasonography of a real person's vasculature to better understand the anatomy for ultrasound needle guidance. As a result, students felt it was equally challenging to identify veins on a cadaver and a real person, which supports our hypothesis that a Thiel-embalmed cadaver can be used as a clinical training tool to yield effective learning and adequate clinical performance of needle-guided procedures.

Procedural training, such as that provided to students in the current study, is one of the key requirements for producing competent physicians. To assess the acquisition of a procedural clinical skill, ultrasound milestones can be used. These milestones are competency-based developmental outcomes that mark a progression toward independent practice,[37] and medical students should complete them before graduation.[41] Generally, a milestone outcome, such as a procedural skill, can only be developed with repeated practice.[41] Therefore, increasing student comfort with needle-guided procedures is an important milestone since ultrasound-guided techniques for central venous cannulation may reduce the risk of misplacement and complications.[42]

The main limitation of the current study was its small size; only 13 students from one institution participated. We deliberately kept the number of students small because we were unsure of how many needle sticks were possible in the Thiel-embalmed cadaver before the puncture site would degrade. Future studies should include multiple cadavers and recruit a larger group of students or residents. Another limitation was that training involved only two procedures, the PICC line and central line. In future studies, we are planning on using soft-embalmed cadavers for thoracentesis, paracentesis, and lumbar puncture procedures.

Conclusion

In the current study, the ultrasound models and Thiel-embalmed cadaver provided students with a unique training opportunity, and the majority agreed the training helped them improve their practical skills associated with vein cannulation using ultrasound imaging. These results suggest a Thiel-embalmed cadaver can be used as a clinical training tool for learning needle-guided procedures. Therefore, new cadaver-based ultrasound training exercises during preclinical medical education

should be developed and used to enhance student understanding and learning of invasive procedures and to facilitate higher confidence in the clinical setting.

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Disclosure

None reported. **MM**

Anatomical and Radiographic Characterization of the Lateral Patellofemoral Ligament of the Knee

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FIRST IN WHOLE PERSON HEALTHCARE

These newly identified radiographic landmarks for the attachment of the lateral patellofemoral ligament (LPFL) may have important clinical implications and may be used to assist surgeons in reconstructing the LPFL when indicated.



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Abstract

The purpose of the current study was to describe the femoral and patellar insertions of the lateral patellofemoral ligament (LPFL) and to determine their location relative to known anatomic and radiographic landmarks. In this descriptive laboratory study, 10 cadaveric knees were dissected, and the patellar and femoral insertions of the LPFL were identified. Each specimen was examined radiographically. The average center of the femoral insertion of the LPFL was calculated in reference to radiographic landmarks.

Introduction

Symptomatic medial instability of the patellofemoral joint is an uncommon clinical entity that can occur after surgical release of the lateral retinaculum of the knee.[1-3] Further, diagnosis and treatment of medial subluxation of the patella is difficult, and various surgical treatments have been proposed, such as lateral retinacular repair and isometric lateral patellofemoral ligament (LPFL) reconstruction.[4, 5] The knee structures responsible for restraining the medial displacement of the patella include the iliotibial band (ITB), the LPFL, and the lateral patellotibial ligament.[6, 7] The lateral stability of the patella, on the other hand, is maintained by the medial patellofemoral ligament (MPFL), medial patellotibial ligament, and medial patellomeniscal ligament, of which the MPFL provides the major restrictive force.[8]

The gross anatomy of the LPFL and MPFL and their biomechanical participation in the patellofemoral joint are well studied.[7-16] For the lateral structures, two distinct fascial layers—superficial and oblique—have been identified within the lateral retinaculum.[6] Deep to the retinaculum, two transverse bands exist, one extending from the ITB to the patella (the patellotibial band) and the other from the femur to the patella (the epicondylopatellar band).[6] At the lateral aspect of the distal femur, the most superficial layer of the retinaculum is a deep fascial layer, and deep to it exists the obliquely oriented fibers described as arciform fibers.[17] Deep to the arciform fibers are the fibers extending directly from the lateral aspect of the quadriceps tendon and the ITB. The deepest two layers are the ITB-patella fibers and the LPFL.[7, 14] Merican et al[7] described the LPFL as a thickening of the joint capsule and noted that there was also a thickening of

the joint capsule extending to the lateral meniscus. In their study investigating the strength of the intermediate structures of the lateral retinaculum, they also identified three distinct structures in the deep lateral retinaculum, namely the ITB-patella, LPFL, and lateral patellomeniscal ligaments.[7]

Current techniques for LPFL reconstruction include testing before definitive graft placement to identify an isometric point for the graft. To our knowledge, reconstruction of the LPFL based on anatomic insertions at the femur and patella has not been previously described, and radiographic landmarks for the femoral LPFL insertion are currently unknown.[4, 5, 18, 19] Such information would be useful to surgeons performing LPFL reconstruction to confirm anatomic placement of the reconstruction soft tissue graft. Therefore, the purpose of the current study was to describe the femoral and patellar insertions of LPFL and to determine their location relative to known anatomic and radiographic landmarks.

Methods

Dissection of the LPFL was performed on 10 embalmed cadaveric knees. The cadavers were randomly selected from the anatomy teaching laboratory at A.T. Still University's Kirksville College of Osteopathic Medicine (ATSU-KCOM). Standard embalming procedures were used, and all cadavers had undergone double embalming preservation, first with an embalming solution at the funeral home followed by an embalming solution containing 26.25% isopropanol, 11.75% ethylene glycol, 8.5% phenol, 1.25% formaldehyde, 1.25% methanol, and 51% water in the Anatomy Department at ATSU-KCOM. Cadavers were infused with embalming solution through a cannulated right carotid artery and were filled passively for 48 hours. The cadavers were kept at room temperature (approximately 21°C) in the teaching laboratory. The local institutional review board considered the current study exempt.

Dissection procedures were carried out in a consistent manner between specimens. The skin and superficial fascia about the knee were removed. A medial arthrotomy was performed, extending from the quadriceps tendon to the patellar tendon insertion at the tibia. The patellar tendon was released from the tibial tuberosity and reflected superiorly. All attachments to the superior portion of the patella were then removed, leaving only the patellar tendon distally and the lateral retinaculum attached to the patella. The quadriceps muscles were reflected superiorly to the mid-femur, allowing for transection of the femur.

The lateral retinaculum is composed of a dense connective tissue sheath that forms the lateral portion of the joint capsule.[7] Associated with the lateral retinaculum are multiple distinct bundles of connective tissue forming three ligaments: the patellar portion of the ITB, the LPFL, and the lateral patellotibial ligament.[7] The patellar portion of the ITB is the most superficial of the ligaments and is composed of thickened bands of deep fascia that contain laterally oriented fibers that insert onto the lateral aspect of the patella.[7] The ITB attachment to the lateral aspect of the patella was released followed by a complete removal of the iliotibial tract. Removal of the entire iliotibial tract allowed for better visualization of the lateral retinaculum and isolation of the LPFL.

The LPFL, which is immediately deep to the patellar portion of the ITB, originates on the lateral epicondyle of the femur and inserts on the lateral patella.[7] Gross inspection of the ligament confirmed that it appeared to be a thickened band of fibers within the lateral retinaculum and joint capsule. The portions of lateral retinaculum attached to the LPFL were released both superiorly and inferiorly from the patella and femur, which allowed isolation of the LPFL and made it the only soft tissue attachment from the femur to the patella (Figure 1).

Disarticulation of the femorotibial joint was performed to allow for inspection and proper imaging. The anterior and posterior cruciate ligaments, the medial and lateral collateral ligaments, and the meniscotibial ligaments were transected. The muscles of the posterior compartment of the thigh were detached from their distal attachments and reflected superiorly to mid-femur. The proximal attachment of the gastrocnemius was released from the posterior femur and reflected distally. The popliteal nerves and vessels were transected and reflected superiorly and inferiorly. The femur was transected about 20 cm proximal to the distal femoral condyles, and the patellofemoral portion—the patella, distal femur, and LPFL—was removed from the specimen.

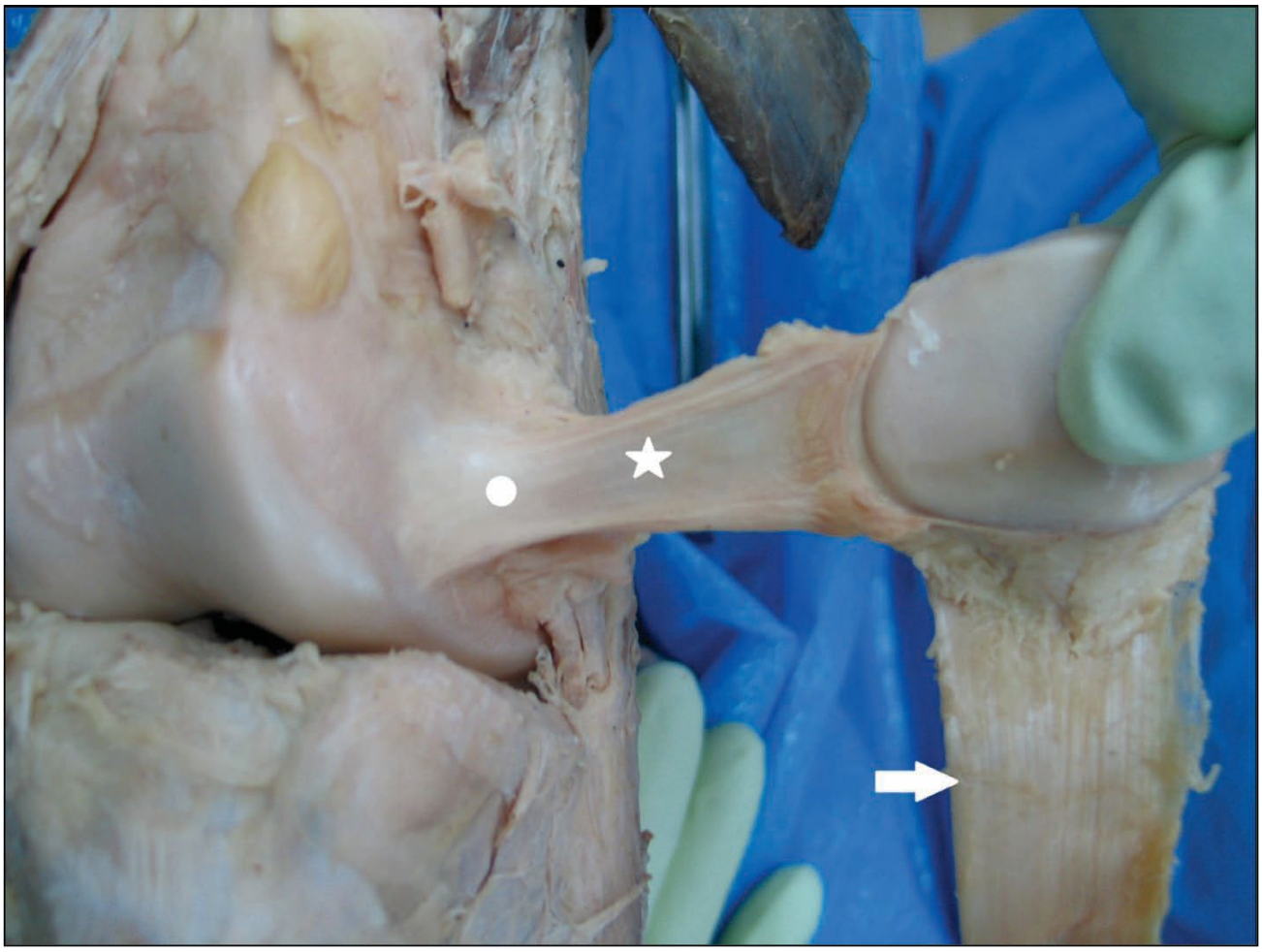


Figure 1. Anatomic dissection of the lateral patellofemoral ligament (LPFL). The LPFL (white star) was consistently identified with insertions at the lateral border of the patella and near the lateral femoral epicondyle (white dot). Also pictured is the patellar tendon (arrow) after release from the tibial tuberosity.

To image each specimen, the patella was everted to extend the LPFL (Figure 1). The patella was fixed in a clamp device, which allowed photographs to be taken at the same distance for each specimen. A metric ruler was incorporated into the image to allow image analysis and to verify measurements. The image obtained with the camera showed the attachment of the LPFL to the patella. In eight specimens, the LPFL was detached from the lateral femoral insertion, marked using a felt tip pen, and photographed using digital photography.

The eight intact patellofemoral specimens were used for radiographic imaging of the femoral insertion of the LPFL. The visual center of the LPFL femoral attachment was approximated and marked with a radiopaque metal pin. Using live fluoroscopy, each specimen was rotated to obtain a "perfect lateral" knee radiograph, in which the posterior condyles were precisely overlapped on the image. Radiographs were obtained and stored to a digital picture archiving and communication system (PACS). The radiopaque markers were identified, and measurements from the center of the LPFL to the corticomedullary line anteriorly, inferiorly, and posteriorly were obtained using the metal pin as a reference. Using PACS imaging software, the average radiographic center of the femoral attachment of the LPFL was calculated. The average center of the femoral insertion of the LPFL was calculated in reference to specific radiographic landmarks, namely, Blumensaat's line and the posterior surface of the femoral cortex.

To account for size variation, regression analysis was used to determine whether the insertion of the LPFL could be identified by the anterior-posterior distance of the distal femoral shaft at the junction of

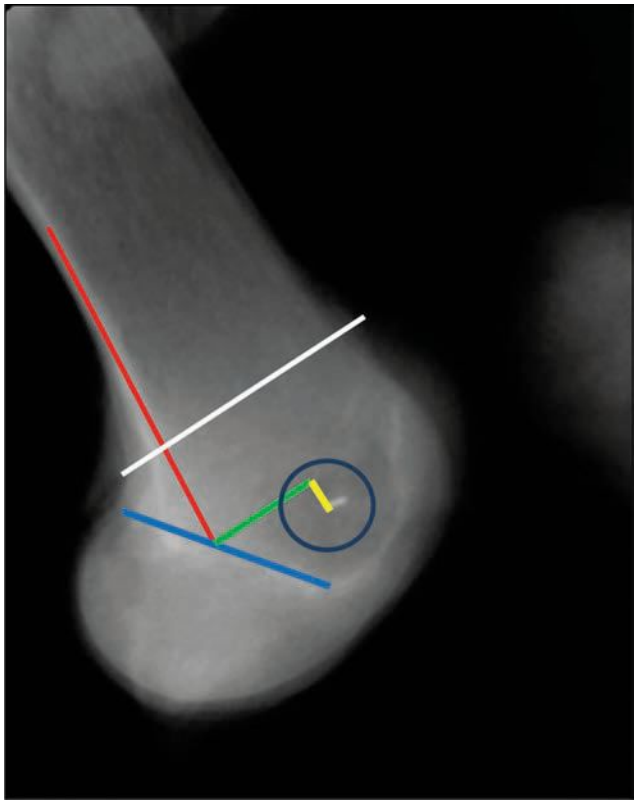


Figure 2. Lateral radiograph of the distal femur and landmarks for identification of the insertion of the lateral patellofemoral ligament (LPFL). The insertion of the posterior femoral cortical extension line (red line) and Blumensaat's line (blue line) serve as the starting point for identification of the LPFL insertion (blue circle). Using regression analysis, the anteroposterior distance of the distal femoral shaft at the junction of the posterior femoral condyles perpendicular to the axis of the femur (white line) was correlated with the anterior distance (green line) and the distal distance to the LPFL insertion point (yellow line).

the posterior femoral condyle and the femoral shaft (Figure 2, white line). Specifically, the anterior distance from the junction of the posterior femoral cortical extension line and Blumensaat's line to the LPFL insertion point (green line) and the distal distance to the LPFL insertion point (yellow line) were calculated using the following equations:

$$\text{Green line} = 0.86*\text{white line} - 39.68$$

$$\text{Yellow line} = \sqrt{-0.03*\text{white line}^2 + 2.92*\text{white line} - 195.12}$$

The coefficient of determination (R^2) was used to determine the predictability of the regression model.

Results

The patellar insertion of the LPFL was found to consistently encompass the entire lateral margin of the patella. The average radiographic center (Figure 2) of the femoral insertion of the LPFL (blue circle) on a lateral radiograph was 13.9 mm (95% CI, 9.9-17.8 mm) anterior (green line) and 5.3 mm (95% CI, 2.5-8.0 mm) distal (yellow line) to the intersection of a line extending from Blumensaat's line (blue line) and the posterior femoral cortex (red line).

The regression analysis for size variation found coefficients of determination of 0.71 for the green line and 0.74 for the yellow line.

Discussion

The purpose of the current study was to describe the femoral and patellar insertions of LPFL and to determine their location relative to known anatomic and radiographic landmarks. We identified a relatively consistent radiographic femoral insertion of the LPFL, which was correlated with the anteroposterior diameter of the distal femur on the lateral view of the knee.

Lateral patellar dislocation is a common injury that occurs at a rate of 5.8 to 77 per 100,000 individuals and has a similar incidence as that of anterior cruciate ligament ruptures in young athletes.[20] The mechanism of patellar dislocation most commonly involves a valgus moment of the knee joint with external tibial rotation under eccentric contraction of the quadriceps.[20] This injury can occur in athletes during a planting and pivoting movement. Often, the patella will spontaneously reduce with forceful extension of the knee. Redislocation is frequent at a rate of 14%-55%, and 50% of patients experience symptomatic pain.[20] Patient complaints are medial peripatellar knee pain caused by damage of the medial structures, specifically the MPFL, that stabilize the patella leading to pain or instability. Without associated injuries, conservative treatment of the patella region is recommended for first-time dislocations.[20]

The MPFL is the primary restraint to lateral translation of the patella and accounts for 53%-67% of the medial restraining force, especially in the first 30° of knee flexion prior to patellar

engagement in the femoral trochlea.[20, 21] Incidentally, the MPFL is injured in 94% of lateral patellar dislocations and most commonly at the femoral attachment.[22] The anatomy of the MPFL is well described as 55 mm long and ranging from 3-30 mm in width. The location of the femoral attachment has been noted to be 9.5 ± 1.8 mm proximal and 5.0 ± 1.7 mm posterior of the center of the medial epicondyle.[18-22]

Surgical reconstruction of the MPFL is often prescribed for patients who have poor outcomes from conservative treatment. Studies investigating MPFL reconstruction suggest excellent outcomes and low recurrence rates. For instance, a meta-analysis of eight studies that involved 186 MPFL reconstructions (mean patient age=24 years) showed a low recurrence rate, and the authors noted that MPFL reconstruction provided "favorable clinical and radiographic outcomes."[23] Buckens et al[24] reviewed 14 studies (level of evidence III and IV) and also found low recurrence rates and favorable outcomes. Based on the available data, however, the authors noted that the current research was heterogenous and without long-term outcomes data.[24] Despite these limitations, they suggested MPFL reconstruction was superior to extensor mechanism realignment procedures and older stabilization techniques.[24] Others have also recommended MPFL reconstruction, noting that osseous realignment should be rethought and that MPFL reconstruction is probably a more patient friendly option.[20, 24]

Medial instability of the patella is a much less common clinical finding. This diagnosis is difficult and relies on a careful history and thorough physical examination. Patients often describe a history of arthroscopic or open release of the lateral retinaculum of the knee. Knee function is markedly impaired, and patients may have had previous surgical procedures to correct instability of the extensor mechanism with subsequent scar tissue formation, synovitis, and possibly muscle atrophy.[4] Diagnostic criteria include the ability to passively subluxate or dislocate the patella medially while reproducing the patient's symptoms.[2]

Treatment of medial patellar instability is difficult and includes operative and nonoperative options. Repair and reconstruction of the lateral stabilizing ligaments have been previously described, but an anatomic reconstruction of the LPFL has not been presented in the literature. Hughston et al[2] described various surgical techniques for the treatment of medial patellar subluxation. For instance, they suggested direct lateral retinacular repair with and without vastus lateralis repair could be performed if retinacular tissue was sufficient.[2] When insufficient lateral retinacular tissue was present, one of three procedures were suggested to reconstruct the patellotibial ligament.[2] The first method involved the detachment of a 3-4 cm strip of iliotibial band, leaving the distal insertion intact at Gerdy's tubercle.[2] The second method involved detachment of the lateral one-fourth of the patellar tendon from the tibial tubercle and subsequent reattachment to the lateral tibial tubercle.[2] The third method was a combined technique involving an anastomosis of a strip of ITB and lateral patellar tendon.[2] Another surgical technique was described by Tietge et al[25] and used a 4-5 cm × 1 cm partial-thickness quadriceps tendon graft. For this technique, an isometric point is identified using a commercially available isometer at the lateral femoral epicondyle.[25]

Recently, a surgical reconstruction of the lateral patellofemoral ligament with a gracilis tendon allograft has been suggested.[26, 27] One of the pitfalls of the procedure was a failure to accurately identify the site of the femoral attachment of the lateral patellofemoral ligament.[27] Correct identification of this site using radiographic landmarks described in the current study could aid in avoiding this pitfall.

With better understanding of the anatomical structure of the lateral aspect of the knee, reconstructive surgery is becoming a more valid choice of treatment for medial patellar subluxation. Although LPFL reconstruction has been previously described, correlations to anatomical descriptions of the ligament have not been well documented.[25] The known lateral patellar stabilizing structures are the ITB, the LPFL, and the lateral patellomeniscal ligament; and distinct superficial and oblique fascial layers have been identified in the lateral retinaculum.[6]

Two transverse bands of tissue exist deep to the retinaculum, one extending from the ITB to the patella and the other from the femur to the patella, which are known as the patellotibial and epicondylopatellar bands, respectively.[6]

The current study had sampling bias as a limitation. All knee specimens were obtained from cadavers at a gross anatomy laboratory, and all cadavers were donated through the body donation program.

Conclusion

In the current study, we identified a relatively consistent radiographic femoral insertion of the LPFL at on a lateral radiograph at 13.9 mm (95% CI, 9.9-17.8 mm) anterior and 5.3 mm (95% CI, 2.5-8.0 mm) distal to the intersection of a line extending from Blumensaat's line and the posterior femoral cortex (red line). To our knowledge, radiographic landmarks had not been established for the LPFL insertion before our study. Such landmarks have been proposed for the MPFL; Redfern et al[28] suggested the radiographic insertion was 0.5 mm anterior to the distal posterior cortex and 3 mm proximal to the apex where it meets Blumensaat's line. Our results suggested the consistent radiographic femoral insertion of the LPFL was size-referenced to the anteroposterior diameter of the distal femur on the lateral view of the knee. These newly identified radiographic landmarks for the attachment of the LPFL may have important clinical implications and may be used to assist surgeons in reconstructing the LPFL when indicated.

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Disclosure

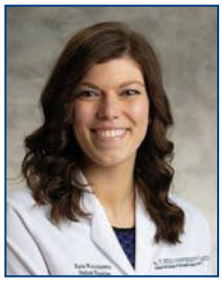
None reported.

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Educational Value of Ultrasonography Used as a Diagnostic Tool by Medical Students at a Student-Run Free Clinic

by Catherine Wlodarkiewicz, MA, OMS III, James Adams, DO & Tatyana Kondrashova, MD, PhD

Results of the current preliminary study suggested beneficial outcomes for patients from a rural and underserved area and for medical students from the use of ultrasonography at student-run free clinics.



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Abstract

At A.T. Still University's Kirksville College of Osteopathic Medicine, Still Caring Health Connection is a student-run organization that hosts free clinic nights for the underserved. The clinics are beneficial for patients and medical students because patients receive needed medical attention and medical students get early clinical exposure. During the clinics, medical students use portable ultrasound machines to guide diagnoses. When surveyed about their use of ultrasound on clinic nights, most students responded positively.

Introduction

Educational Value of Student-Run Free Clinics

Student-run free clinics (SRFCs) are common in medical schools because they allow medical students to take responsibility for management of the clinics while also providing disease-specific treatment to the patients.[1] In general, the goals for SRFCs are to provide medical care to underserved populations and create learning experiences for students because they can apply course content to an actual patient. Currently, more than 75% of U.S. medical schools have SFRCs.[2, 3] In one study,[2] students and faculty agreed that these clinics are a valuable part of medical education. Specifically, they allow students to gain valuable clinical experiences during the first two years of medical school,[4] and those experiences often complement the didactic material they are exposed to in the curriculum.[5] Another benefit of SRFCs is that they promote interprofessional collaboration. Typically, a variety of health professions students (eg, medical, dental, nursing) participate in the clinics, and such collaboration is critical in real-world patient care. From a medical student perspective, learning to work with healthcare providers from different disciplines is a valuable experience, especially before clinical rotations.

Educational Value of Ultrasonography for Future Primary Care Physicians

Ultrasound is a core skill that is being used with increasing frequency in many clinical specialties because of its utility for point-of-care diagnostics.[7] Therefore, bedside ultrasonography has become more prominent in patient care, and more medical schools are including ultrasound training earlier in undergraduate medical education.[8] The inclusion

of ultrasound training in the curriculum enhances the anatomical and clinical training of students and increases their preparedness for future practice.[9, 10] In one study,[3] early exposure to ultrasound in a patient-centered curriculum was feasible and seemed to improve the physical examination skills of students. Another study suggested that ultrasound surpassed the abilities of auscultation through a stethoscope, whether performed in an outpatient clinic or a trauma situation, making it the stethoscope of the future.[11] Other studies suggested that students using ultrasound imaging had greater diagnostic accuracy than those using physical examination skills alone.[12, 13] However, a limitation of ultrasound imaging is that it is operator-dependent. Undergraduate medical students should be taught this technology so they are familiar with ultrasound techniques and competent with image interpretation. Further, ultrasound training in basic science courses and clinical clerkships allows medical students to stay informed about developments in medicine while preparing them to apply those developments to future patient care.[11, 14-16]

Value of Ultrasonography in Rural Areas

In this descriptive study we report preliminary results of the integration of portable ultrasonography in SRFCs. Because of advancements in medical technology, medical ultrasound devices are becoming more portable and affordable, which allows their use in diverse patient populations, such as rural and underserved areas where other diagnostic imaging tools may not be easily accessible.[17] The use of portable ultrasound machines in uninsured and underserved populations can provide much-needed access to diagnostic imaging and could, in some cases, save lives. Further, SRFCs are an ideal clinical setting where portable ultrasound and ultrasound competency are extremely valuable. To our knowledge, there is no published data on the use of ultrasonography as a diagnostic tool in SRFCs, and the educational value of ultrasonography has not been assessed in this context. Therefore, the purpose of the current study was to evaluate medical student perception of the incorporation of ultrasound technology into an SRFC and to determine their level of comfort with using ultrasonography and interpreting ultrasound images. We hypothesized that the educational value of ultrasonography in the SRFC would be beneficial for development of clinical decision-making skills because the ultrasound images would provide greater clinical confidence from immediate visual validation of the diagnosis.

Methods

Student-Run Free Clinic

At A.T. Still University's Kirksville College of Osteopathic Medicine (ATSU-KCOM), Still Caring Health Connection (SCHC) is a student-run medical and dental school organization that strives to give back to the local community and benefit its underserved population by hosting various healthcare events, such as free clinic nights. During these clinic nights, patients indicate which services provided by the clinic they wish to receive, such as diabetes or lipid panels, osteopathic manipulative treatment, or dental screenings. Supervised by attending physicians, the medical and dental students evaluate, diagnose, and treat the clinic patients. Through these clinic encounters, medical students are able to practice numerous skills learned in the medical school curriculum. Further, students are encouraged to perform more complete, rather than focused, physical examinations as a means of reinforcing and practicing clinical skills. For example, students practiced taking a patient history, performing a physical and ultrasound exams, they tested blood pressure, blood glucose and HA1C, learn how to present a patient to a physician, etc. Clinic nights also provide students with an opportunity to apply ultrasound skills obtained through ATSU-KCOM's clinical ultrasound curriculum.[6] Ultrasound education has been part of the curriculum at ATSU-KCOM for 10 years and is fully integrated into the first two years.[6]

For the current study, first-year and second-year medical students participated in the free SCHC clinic nights. All clinics had at least three faculty physicians on site, and they supervised students during the patient encounters. During physical examinations, students identified whether the use of ultrasonography could guide and confirm the initial diagnosis. The following portable ultrasound machines were available for student use: a Vscan with dual probe handheld portable ultrasound



Figure 1. Portable ultrasound units used in the student-run free clinics.

(GE Healthcare) and a Mindray 7 (Shenzhen Mindray Bio-Medical Electronics Co., Ltd.) (Figure 1). A Vscan with dual probe has two transducers in one probe and is hand-sized. A Mindray 7 is the size of a laptop.

Students participating in the clinics had a working knowledge of ultrasound techniques and applications from their clinical ultrasound coursework. At ATSU-KCOM, the Clinical Ultrasound course is taught in four semesters during the first two years.[6] During SCHC clinics, students filled out an ultrasound patient log to record the areas and the type of ultrasound scan performed. The log also indicated whether the student's initial diagnosis was confirmed or not confirmed by the volunteer radiologist on site. Recorded scanning regions included the abdomen, the neck for thyroid gland and carotid arteries, echocardiography, obstetrical ultrasound, and musculoskeletal ultrasound imaging of the wrist and ankle.

Survey

To evaluate medical student perception of the incorporation of ultrasound technology into an SRFC and to determine their level of comfort with using ultrasonography and interpreting ultrasound images, a 12-item paper survey was created specifically for the current study. Students who performed ultrasound examination during patient encounters at the SCHC clinics completed the survey. It contained seven Likert scale questions and five open-ended questions. The Likert scale questions included in the survey were the following: (1) I felt confident using portable ultrasound units to guide my diagnosis; (2) I felt prepared to use the portable ultrasound unit as a diagnostic tool for my patient; (3) The portable ultrasound unit was helpful in guiding my diagnosis; (4) It was easy to identify structures using a portable ultrasound unit; (5) I enjoyed using ultrasound as a diagnostic tool for my patient encounter; (6) Using the portable ultrasound unit improved my clinical reasoning skills; and (7) I received enough training before using the portable ultrasound unit. A standard Likert scale (strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree) was used to evaluate agreement or disagreement. The open-ended survey questions asked about benefits of using portable ultrasonography, patient response to the use of portable ultrasonography, and possible curricular implications. The open-ended questions included in the survey were the following: (1) What were your thoughts regarding the use of a portable ultrasound unit to guide your diagnosis? (2) How do you feel the use of portable ultrasound impacted your patient encounter? Positively? Negatively? (3) How did your patient respond to your use of a portable ultrasound unit? (4) What components of the Clinical Ultrasound course were most relevant to your patient encounters at the free clinic? (5) What would you like to see added to the Clinical Ultrasound course that would have been helpful for your patient encounters at the free clinic?

The A.T. Still University-Kirksville Institutional Review Board considered the current study exempt. Students were informed that they provided their consent by completing the survey. All data were collected anonymously, and participation in the survey did not affect student grades in any way.

Results

Student Perception of Incorporation of Ultrasonography into SRFC

Because the COVID-19 pandemic caused our SCHC clinics to close to meet social distancing guidelines and stay-at-home orders, data from only seven students were collected. Therefore, here we present those preliminary results and hope to complete the study at a future date.

For the Likert survey responses, 71% (5/7) of students felt confident using portable ultrasound units to guide diagnosis, 43% (3/7) felt prepared to use the

portable ultrasound unit as a diagnostic tool for the patient, and 100% (7/7) indicated the portable ultrasound unit was helpful in guiding diagnosis. The majority of students (86%, 6/7) thought it was easy to identify structures using a portable ultrasound unit, 100% (7/7) enjoyed using ultrasound as a diagnostic tool for the patient encounters, and 100% (7/7) indicated using the portable ultrasound unit improved their clinical reasoning skills. All (100%, 7/7) indicated they received enough ultrasound training before using the portable ultrasound unit.

Educational Value of Ultrasonography During SRFC

The open-ended question responses supported the Likert scale responses. For the question about the use of portable ultrasound to guide diagnosis, one student wrote, "It was helpful to rule out an obvious fracture and also, to give my patient's father more satisfaction in our treatment and diagnosis." Other students wrote, "It was really helpful to rule out some differential diagnosis," and "It helped us come to a conclusive diagnosis."

For the questions about how the use of portable ultrasound impacted the patient encounters and how the patients responded to the use of portable ultrasound, students wrote comments like, "[it] helped us discover it was likely a fibrous cyst," and "It was nice to show them what we're seeing and showed them we can rule out some bad diagnoses." Other students wrote, "The patient seemed to appreciate getting results right then and there," and "The patient's father seemed happy to have a diagnostic test done when no x-ray was available." The students' written comments suggested that most patients responded to the use of ultrasonography very positively. Students wrote, "He seemed to like getting results rapidly," "The patients loved it and loved being explained what's on the screen," and "They liked that we were able to perform an ultrasound exam." One student suggested a possible negative patient outcome from portable ultrasound in the following comment: "the patient abdominal exam prompted the identification of an unknown U.S. abnormality. Might result in additional imaging the patient cannot afford."

The following are examples of what students wrote in response to the question about the most relevant components of the Clinical Ultrasound course at the free clinic: "Knowing how to use an ultrasound, what to look for"; "How to orient probe. How to get oriented to structures on screen"; "The repeated practice of identifying normal anatomy and where to look"; "Recognizing the different components of a joint and evaluating for any abnormalities"; and "The shoulder, ankle, and uterus/ovary components were most useful." Students also indicated that cardiac and gynecological ultrasound laboratories were very helpful in preparing them for the patient encounters.

A common comment from students in response to the question about what they would like to see added to the Clinical Ultrasound course to make it more helpful for patient encounters at the free clinic was that they wanted to "use portable ultrasound machines in lab. This will get us more accustomed to new/different machines." The most frequent comment to this survey question was related to their desire to have "more practice on ID of pathology within each organ system."

Discussion

The purpose of the current study was to evaluate medical student perception of the incorporation of ultrasound technology into an SRFC and to determine their level of comfort with using ultrasonography and interpreting ultrasound images. Survey results suggested medical students were receptive to incorporating portable ultrasound into the SRFC and that portable ultrasound units were helpful in guiding diagnoses. Most students felt confident using the portable ultrasound units, which suggested they were competent at obtaining and interpreting ultrasound images. Because it can impact physician competence and patient safety, the ability to accurately identify and interpret ultrasound images is an important aspect of medical training, and medical students need to feel comfortable with these skills.

All students agreed that the use of ultrasonography was beneficial to the development of their clinical reasoning skills and agreed that the portable ultrasound units had a positive impact on their patient encounters. Further, reported student confidence using portable ultrasound units and their comfort identifying anatomical structures suggested the students had been well prepared by

their ultrasound curriculum to apply their knowledge in a clinical setting. Taken together, these findings suggested that SRFCs can be a valuable educational tool for medical students to fill the gap between formal training and real-world experience.

Student responses to the open-ended survey questions indicated that they were overwhelmingly positive about the incorporation of ultrasonography as a diagnostic tool into SRFCs and into ATSU-KCOM's curriculum overall. The use of ultrasound technology during the free clinic encounters helped patients better understand their health status and improve their overall experience. These results suggest that ultrasound technology should be incorporated to a greater extent in rural medicine given that this clinical setting typically has limited access to other forms of imaging and a larger proportion of uninsured patients.

In general, SRFCs can be a valuable and distinct aspect of medical education, especially considering they provide valuable opportunities for students interested in primary care. Further, first-year students can benefit from the unique learning environment of SRFCs as they are mentored by second-year students and attending physician volunteers about aspects of patient presentation, physical examination, and ultrasonography skills. These clinics are also vital for creating academic/community partnerships between the medical school and the local community by providing free medical services. Using ultrasonography as a diagnostic tool at SRFCs is also beneficial because it improves student proficiency and level of comfort in their diagnoses while providing care to underserved populations.

The current study had several limitations. Because the COVID-19 pandemic caused our SCHC clinics to close to meet social distancing guidelines and stay-at-home orders, data from only 7 students were collected. Therefore, our findings are preliminary and should be interpreted with caution.

Conclusion

Results of the current preliminary study suggested beneficial outcomes for patients from a rural and underserved area and for medical students from the use of ultrasonography at SRFCs. Patients received needed medical care, and medical students received clinical exposure early in their medical education. Our results suggested the first-year and second-year medical students were able to apply the skills they had learned through the ultrasound curriculum at ATSU-KCOM and could use these skills to scan actual patients in a clinical setting. Further, using portable bedside ultrasound equipment helped students adapt to changing medical technologies, improved their clinical reasoning skills, and enabled them to become well-rounded and knowledgeable physicians of the future.

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Disclosure

None reported. **MM**

Current Endovascular Treatment of Acute Ischemic Stroke

by Kunal Bhatia, MD, Sachin Bhagavan, MD, Navpreet Bains, DO, Brandi French, MD, Farhan Siddiq, MD, Camilo R. Gomez, MD & Adnan I. Qureshi, MD

Endovascular therapy for management of acute ischemic stroke has evolved tremendously over the recent years and is currently considered standard of care in selected patients with large vessel occlusion within the anterior circulation.



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Abstract

Acute ischemic stroke is one of the leading causes of death and long-term disability in the United States. Intravenous thrombolysis with recombinant tissue-type plasminogen activator (rt-PA) has been the mainstay of acute therapy. However, multiple randomized clinical trials have been published that have shown higher rates of recanalization and improved functional outcomes with endovascular therapy compared with intravenous rt-PA in patients with ischemic stroke from large vessel occlusion. This article provides an update and discusses the role of endovascular therapy in management of acute ischemic stroke.

Introduction

Stroke is the leading cause of serious long-term disability and the fifth most common cause of death in the U.S. Ischemic stroke accounts for approximately 87% of all strokes in the U.S.[1] For almost two decades, prompt administration of intravenous fibrinolytic treatment with recombinant tissue plasminogen activator (rt-PA), within 4.5 hours of the onset of symptoms in eligible patients, has been the standard of care in management of acute ischemic stroke.[2] Despite improvement in functional outcomes at three to six months in patients who receive rt-PA,[3-5] the efficacy of IV rt-PA in achieving recanalization continues to be limited (Table 1). Limitations of rt-PA include - a narrow therapeutic time window (within 3 - 4.5 hours), resistance of an old or large thrombus to fibrinolysis, risks of systemic and cerebral hemorrhage and lower rates of recanalization in patients with proximal vessel occlusion.[4,7,12,13] This led to evolution of endovascular approaches devised to reduce clot burden, improve vessel recanalization, and hence improve functional outcomes. Table 2 describes the most commonly used terms in endovascular management of acute ischemic stroke.

Clinical Evidence

In 2013 three randomized controlled trials of endovascular treatment of acute ischemic stroke with primarily intra-arterial (IA) fibrinolysis and/or first generation-mechanical embolectomy devices were published: The Interventional Management of Stroke III (IMS III),[13] Magnetic Resonance and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE)[14] and Local versus Systemic Thrombolysis for Acute Ischemic Stroke (SYNTHESIS

Table 1. Results of Treatment with IV rt-PA in Acute Ischemic Stroke

Rate of recanalization	20 – 46%[6]
Rate of death or disability	47 – 61%[4,7-10]
Percentage of eligible patients who fail to receive rt-PA	18-25%[11]

rt-PA – Recombinant tissue plasminogen activator

Table 2. Description of Selective Stroke Terminology

Time Last Known well	The time prior to hospital arrival at which the patient was last known to be without the signs and symptoms of the current stroke or at his or her baseline state of health.
Endovascular Treatment	Catheter based approach that may include administration of intra-arterial thrombolytic, and/or mechanical clot retrieval (thrombectomy).
The National Institute of Health Stroke Scale (NIHSS)	A 42-point score that objectively quantifies severity of neurological impairment from acute stroke.
Recanalization	Complete or partial restoration of cerebral blood flow as determined on pre and post cerebral angiography.
Alberta Stroke Program Early CT Score (ASPECTS)	A 10-point quantitative topographic CT scan score to determine early ischemic changes (<3 hours from symptoms onset) in anterior circulation stroke.
Modified Rankin Score (mRS)	A 6-point disability score most widely used in stroke clinical trials to document outcome measure.
Functional Independence	Defined by a mRS score of 0 – 2
Symptomatic Intracerebral Hemorrhage (sICH)	Radiographic appearance of hemorrhage associated with neurological deterioration post thrombolytic/endovascular therapy.

EXPANSION).[15] The results showed that endovascular therapy was non superior to the standard treatment with intravenous rt-PA alone with similar safety outcomes and no significant differences in functional independence. On further analysis it was observed that patient selection criteria used in the these trials (included patients with minor ischemic stroke with NIHSS < 6), lack of arterial occlusion confirmation on imaging (CT or MR angiography), delayed time of endovascular intervention, mechanical thrombectomy as a sole endovascular treatment option and use of old generation thrombectomy devices/stent retrievers; may have contributed towards a lack of clinical benefit of endovascular therapy as compared to medical management.[16]

Learning from the shortcomings of these trials, in 2015 five landmark randomized controlled trials demonstrated improved clinical outcomes and rates of recanalization of occluded artery with use of new generation mechanical thrombectomy devices (stent retrievers) in acute ischemic stroke with large vessel occlusion in the anterior circulation (Table 3). This led to a paradigm shift in the management of acute ischemic stroke and formed the basis for updating the American Heart Association (AHA)/American Stroke Association guidelines in 2015, establishing the use of endovascular therapy in patients with acute ischemic stroke with a large vessel occlusion.[2] Later a meta-analysis, comprising data from 1,287 patients was performed by the Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials (HERMES) collaborators.[22] The results showed that the proportion of patients achieving functional independence at 90 days (defined as modified Rankin Score of 0–2) was 46.0% in the intervention group (mechanical thrombectomy) compared with 26.5% in the control group (odds ratio: 2.35; 95% confidence interval [CI]: 1.85 to 2.98; p <0.0001). These findings further emphasized the benefit of endovascular treatment for management of acute ischemic stroke in anterior circulation large vessel occlusion over medical management and helped paved the way for establishing endovascular therapy as a standard of care for management of acute ischemic stroke in select patient population.

Table 3. Summary of five major Randomized Controlled Trials of Endovascular Therapy in Acute Ischemic Stroke

	MR CLEAN[17]	ESCAPE[18]	SWIFT PRIME[19]	EXTEND-IA[20]	REVASCAT[21]
No of patients	500	316	196	70	206
Age (years)	≥18	≥18	18-80	≥18	18-85
NIHSS inclusion criteria	≥2	>5	8-29	None	≥6
Treatment Arm	IV rt-PA + IA UK/rt-PA/device	Stent retriever ± IV rt-PA	Stent retriever ± IV rt-PA	Stent retriever ± IV rt-PA	Stent retriever ± IV rt-PA
Control Arm (Standard care)	± IV rt-PA	± IV rt-PA	± IV rt-PA	± IV rt-PA	± IV rt-PA
IV rt-PA use	87%	72.7%	100%	100%	68%
Median time from stroke onset to groin puncture (min)	260	200	224	210	269
Use of Stent retriever	81.5%	86.1%	89%	77%	95%
Rate of recanalization [TICI 2b/3a]	59%	72.4%	88%	86%	66%
Functional Independence (mRS 0-2)	32.6% vs. 19.1%	53.0% vs. 29.3%	60.0% vs. 35%	71% vs. 40%	43.7% vs. 28.2%
Mortality/sICH	No significant difference in death or sICH	Mortality at 90 days: 10.4% (treatment arm) vs.19% (control arm). No significant difference in sICH	No significant difference in death or sICH	No significant difference in death or sICH	No significant difference in death or sICH

MR CLEAN - Multicenter Randomized Control Trial of Endovascular treatment for Acute Ischemic Stroke; ESCAPE - Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times; SWIFT PRIME- Solitaire FR With the Intention for Thrombectomy as Primary Endovascular Treatment of Acute Ischemic Stroke; EXTEND-IA - Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial ; REVASCAT - Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting Within 8 Hours of Symptom Onset; NIHSS - National Institutes of Health Stroke Scale; IV rt-PA - intravenous tissue plasminogen activator; IA - intra-arterial; UK – urokinase; TICI - Thrombolysis in Cerebral Infarction scale; mRS - modified Rankin scale; sICH – Spontaneous intracerebral hemorrhage.

Neuroimaging

As a rule, all patients suspected of having acute ischemic stroke should obtain neuroimaging on first arrival to a hospital before initiating any specific therapy. As per the 2019 AHA/ASA guidelines, both non-contrast CT (NCCT) and magnetic resonance (MR) imaging (MRI) is effective to exclude underlying hemorrhage and determine whether the patients with acute ischemic stroke are candidates for thrombolytic or endovascular therapy.[23] However, NCCT head is preferred as the initial imaging test due to low cost, wide spread availability and faster speed of acquisition of images. The Alberta Stroke Program Early CT Score (ASPECTS)- a 10-point quantitative, topographic CT score is a simple and reliable method of assessing the extent of ischemic changes on NCCT which aids in rapid identification of patients who would benefit from endovascular therapy.[24] Furthermore, for patients who meet criteria for endovascular therapy, a non-invasive intracranial vascular study – CT angiogram (CTA) or MR angiogram (MRA) of the head and neck; is strongly recommended during the initial imaging evaluation of acute stroke patients, without delaying administration of intravenous rt-PA (Figure 1).[23] Obtaining CTA or MRA of head and neck allows rapid identification of large vessel occlusion, presence of collaterals, clinically significant vascular disease

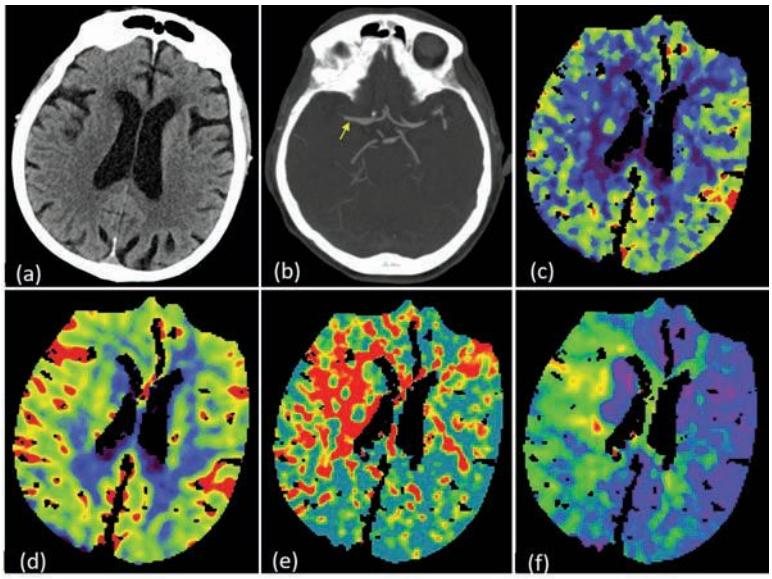


Figure 1. 75-year old female presented with sudden onset left sided weakness with left facial droop. Time of onset of symptoms was 3.5 hours prior to coming to the hospital. Patient did not receive IV rt-PA as she was on Xarelto due to underlying atrial fibrillation. NIHSS score on admission was 7. NCCT head was negative for any intracranial bleed or early signs of ischemia (a). CTA head and neck showed occlusion (yellow arrow) of the right proximal M1 segment of MCA (b). CT perfusion study showed a large penumbra [reduced regional cerebral blood flow (c) with preserved regional cerebral blood volume (d), elevated mean transmit time (MTT) (e) and elevated Tmax (f)].

(e.g., atherosclerotic stenosis) as well as the aortic arch and great vessel anatomy. When evaluating patients with acute ischemic stroke within 6 hours of last known normal with large vessel occlusion and an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of ≥6, selection for mechanical thrombectomy based on CT and CTA or MRI and MRA is recommended in preference to obtaining additional imaging such as perfusion studies. However, in selected patients with AIS within 6 to 24 hours of last known normal who have large vessel occlusion (LVO) in the anterior circulation; obtaining CT perfusion (CTP), Diffusion Restriction Imaging (DWI-MRI), or MRI perfusion (MR-perfusion) is recommended to aid in patient selection for mechanical thrombectomy, but only when patients meet eligibility criteria from one of the trials (DAWN or DEFUSE)[25,26] [Table 3] that showed benefit from mechanical thrombectomy in this extended time window [Class of recommendation I, Level of Evidence A].[23] With recent advances in the management of acute ischemic stroke, multi-modal CT protocols including CT, CTA, and CTP are being made available increasingly in many centers which can help in quick decision making before attempting endovascular therapy.

Patient Selection Criteria

As per the most recent American Heart Association (AHA)/American Stroke Association guidelines published in 2019,[23] selected patients with acute ischemic stroke with onset of symptoms between 0-6 hours, should undergo mechanical thrombectomy (with a stent retriever) if they meet all of the following criteria [Class of recommendation I, Level of Evidence A]:

1. Pre-stroke modified Rankin Score (mRS) of 0 to 1 (functional independence)
2. Patients ≥ 18 years
3. Stroke severity on NIHSS ≥ 6
4. Computed tomography (CT) brain without evidence of large infarct suggested by Alberta Stroke Program Early CT Score (ASPECTS) of ≥ 6
5. Imaging proven causative occlusion of the Internal carotid artery (ICA) or proximal segment (M1) of middle cerebral artery (MCA).
6. Treatment can be initiated (groin puncture) within 6 hours of symptom onset.

In 2018 two major randomized controlled trials were published: DAWN (DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo), [25] and DEFUSE 3 (The Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke); [26] which showed encouraging findings resulting in extending the time window for endovascular therapy in acute ischemic stroke within 6-24 hours from symptom onset. The DAWN trial used clinical-core mismatch, which is a mismatch between the severity of clinical deficit (NIHSS) and infarct volume on diffusion-weighted magnetic resonance imaging (MRI) or perfusion CT imaging (CTP), as an eligibility criteria to select patients with large anterior circulation vessel occlusion for treatment with mechanical

Table 4. Summary of DAWN and DEFUSE -3 Eligibility Criteria

DAWN Criteria (6 to 24 hours)[25]	DEFUSE-3 (6 to 16 hours)[26]
• Age ≥ 18 years • NIHSS ≥ 10 • Prestroke mRS ≤ 1 • Occlusion of the intracranial ICA and/or MCA-M1 segment as evidenced by MRA or CTA • Clinical Imaging Mismatch (CIM) defined as one of the following on MR-DWI or CTP: ➢ 0 – < 21 cc core infarct, NIHSS ≥ 10, age ≥ 80 years ➢ 0 – < 31cc core infarct, NIHSS ≥ 10, age < 80 years ➢ 31 – ≤ 51cc core infarct, NIHSS ≥ 20, age < 80 years	• Age 18-90 years • Baseline NIHSS ≥ 6 • Only slight or no prestroke disability: baseline mRS score ≤ 2 • Cervical/Intracranial ICA occlusion (with/without tandem MCA lesions) or M1 segment on CTA/MRA • Target Mismatch profile: ➢ Infarct volume (ischemic core) < 70 cc ➢ Ratio of volume of ischemic tissue to initial infarct volume ≥ 1.8 ➢ Absolute volume of potentially reversible ischemic (penumbra) > 15 cc

DAWN - DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo; DEFUSE 3 - The Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke; NIHSS - National Institute of Health Stroke Scale; mRS - Modified Rankin Scale; MCA - Middle Cerebral Artery; ICA -Internal Carotid Artery; MRA - Magnetic Resonance Angiography; CTA - Computed Tomography Angiography; MR-DWI - Magnetic Resonance-Diffusion Weighted Imaging; CTP - Computed Tomography Perfusion

thrombectomy between 6 and 24 hours from last known normal. The study demonstrated a benefit in functional outcome at 90 days in the treatment group (mechanical thrombectomy plus standard care) as compared to standard care alone (mRS score 0–2, 49% vs 13%; adjusted difference, 33% [95% CI, 21–44]. Whereas, the DEFUSE-3 trial used perfusion-core mismatch and maximum core size as imaging criteria to select patients with large anterior circulation occlusion 6 to 16 hours from last known normal for mechanical thrombectomy. The results showed a benefit in functional outcome at 90 days in the endovascular-therapy group as compared to the medical-therapy group alone (mRS score 0–2, 44.6% versus 16.7%; RR, 2.67 [95% CI, 1.60–4.48]; P<0.0001). Current guidelines recommend mechanical thrombectomy (preferably with a stent retriever) in selected patients with acute ischemic stroke within 6 to 16 hours of last known normal who have large vessel occlusion in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria (Table 4) [Class of recommendation I, level of evidence A].

Other Indications for Endovascular Treatment

Vertebrobasilar Circulation Stroke

Approximately 20% of all ischemic strokes occur in the vertebrobasilar circulation, which includes acute basilar artery occlusion (BAO),and upto 80-90% of patients with acute basilar artery occlusion have a fatal and poor outcome.[27] Unlike anterior circulation ischemic stroke, data on use of endovascular therapy and its efficacy in achieving successful revascularization in large vessel occlusion within vertebrobasilar circulation is sparse. However, small single-centre studies have shown good functional outcomes following basilar thrombectomy ranging from 30% to 48% and lower mortality (approximately 30 percent) than expected when compared with outcomes among patients who did not receive endovascular therapy.[28-30] Due to lack of randomized controlled trials on endovascular treatment in patients with basilar artery occlusion, management of such patients should be guided by the severity of the symptoms, time of onset of symptoms, age, clinical status of the patient and presence of collaterals after careful evaluation of non-invasive vessel imaging.

Tandem Occlusions

Tandem occlusions, defined as simultaneous occurrence of an intracranial large vessel occlusion and a high-grade stenosis or occlusion of the ipsilateral proximal internal carotid artery (at the level of the cervical internal carotid artery), accounts for 10–20% of large vessel strokes.[31,32] Previous studies have shown that patients with tandem occlusion (cervical ICA-MCA) have a lower likelihood of recanalization and poor outcomes as compared to isolated MCA occlusion after treatment with intravenous thrombolysis.[32,33] Consequently,

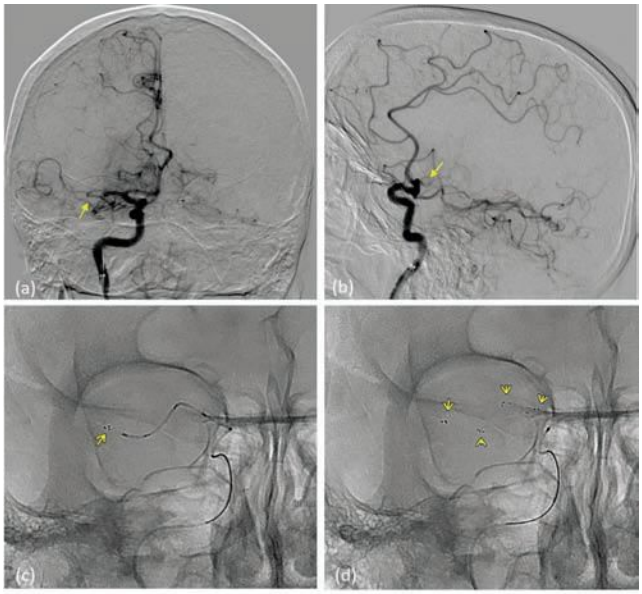


Figure 2. (a) and (b) - Selective right internal carotid injection showing occlusion (yellow arrow) in the proximal M1 segment of right MCA on axial (a) and lateral (b) projections. (c) and (d) - The solitaire revascularization device is seen deployed (yellow arrows highlighting the radiopaque markers) through the micro-catheter and across the occluding thrombus.

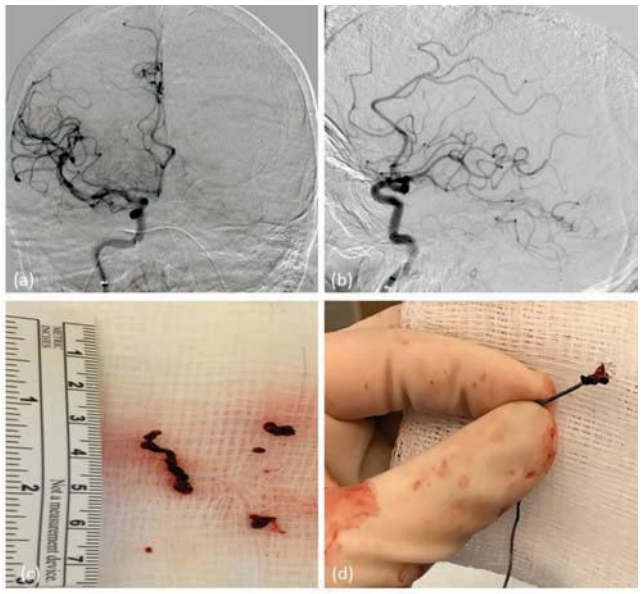


Figure 3. (a) and (b) – Selective Right Internal carotid injection showing complete recanalization of the previously occluded right middle cerebral artery M1 segment [TICI 3] with flow visualized in both superior and inferior divisions of middle cerebral artery. (c) and (d) – Shows the clot fragment retrieved after a combination of manual aspiration and removal of stent retriever.

endovascular treatment has evolved as a more effective treatment option with or without prior intravenous rt-PA. However, there is uncertainty regarding the best approach (anterograde vs. retrograde) for treating tandem occlusions in acute ischemic stroke due to lack of randomized multicenter trials evaluating the different approaches and its effect on clinical outcomes. In a systematic review by Mbabuike et al.[34] patients with acute ischemic stroke with tandem occlusions, a distal to proximal revascularization approach appeared to be more practical and effective with an advantage of decreased time to reperfusion and hence better functional outcome. The optimum approach for management of tandem occlusions and choice of therapy for management of proximal occlusion should be ascertained on an individual case to case basis after careful evaluation of the clinical severity, age, presence or absence of collaterals and bleeding risks.

Cerebral Angiography

Endovascular access is obtained through the common femoral artery in most cases. However, in patients with severe ilio-femoral arterial occlusions, unfavorable aortic arch anatomy, extremely tortuous vessels; alternate routes like trans-radial or trans-brachial can be used. After achieving access, a standard diagnostic catheter can then be used to engage the carotid arteries at which time digital subtraction angiography (DSA) is performed to visualize the cerebral vessels focusing on the specific artery of interest, its distal branches, site of occlusion and presence or absence of collaterals (Figure 2 and Figure 3). Other supplementary catheters like micro-catheter to pass the site of occlusion and large bore catheters for aspiration can then be utilized depending on the vessel caliber and site of occlusion.

Endovascular Recanalization Techniques

Endovascular therapy for management of acute ischemic stroke from a large vessel occlusion, has evolved rapidly over the years due to availability of newer generation thrombectomy devices and advancements in the catheter technology. Historically, intra-arterial fibrinolytic therapy with use of recombinant pro-urokinase in the vessel of interest, to achieve clot lysis, was used to achieve recanalization.[35,36]

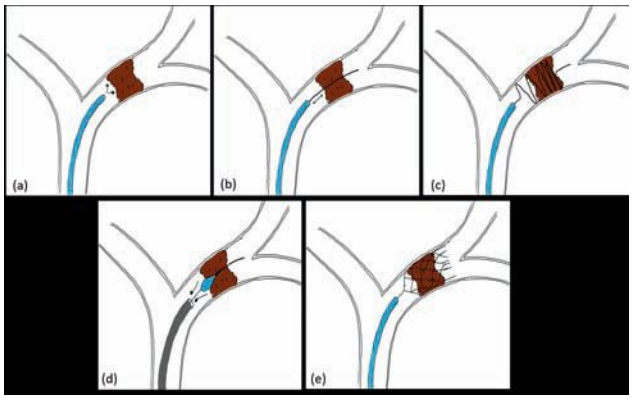


Figure 4. Illustration of different endovascular approaches used for management of acute ischemic stroke. (a) Intra-arterial rt-PA, (b) Microwire manipulation, (c) Merci retriever, (d) Penumbra Aspiration, (e) Solitaire stent retriever.

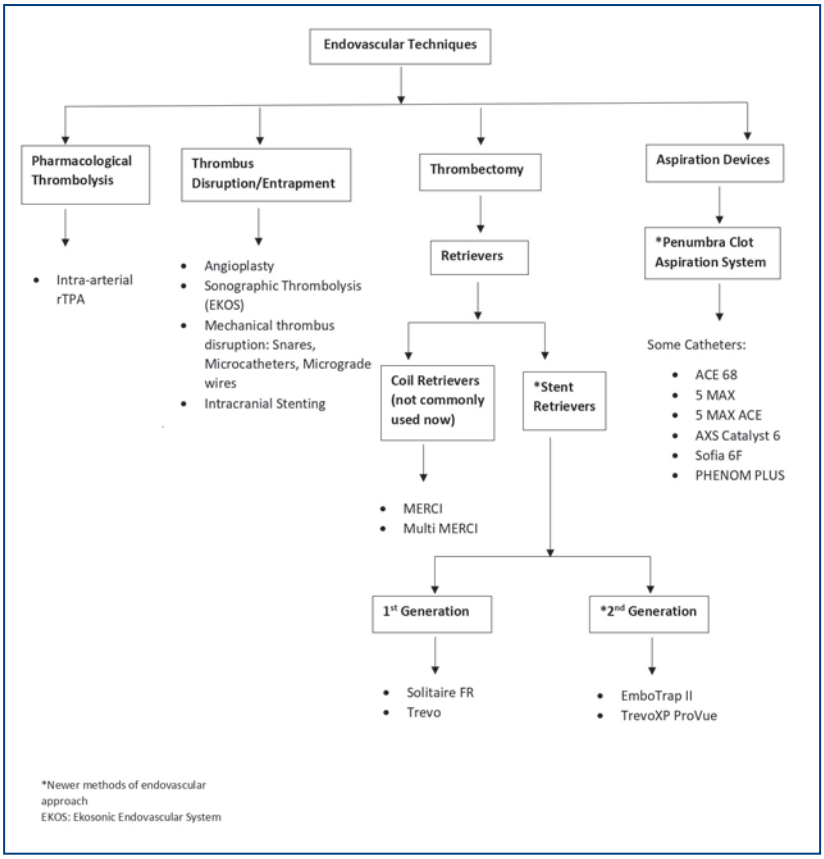


Figure 5. Summary of the different endovascular treatment options available currently. rTPA – Recombinant tissue plasminogen activator; EKOS – Ekosonic endovascular system; * - Newer generation thrombectomy devices.

Neurointerventionalists than began attempting mechanical thrombus disruption by repeated probing of the thrombus by a micro guidewire, microcatheter or snares. This when combined with use of intra-arterial fibrinolytic therapy leads to an increase in the surface area on which fibrinolytic agents can act, thus increasing efficacy of thrombolytic therapy [Figure 4 (a) and (b)]. [37-39] However, there is a risk of clot fragmentation and distal embolization with this approach leading to suboptimal rates of reperfusion. Intracranial stenting within the occluded segment using the Enterprise vascular reconstructive device (Codman, Raynham, Massachusetts, USA) was also tested as a potential tool to achieve mechanical clot disruption and partial restoration of blood flow in acute ischemic stroke.[40,41] However, its use has been limited due to concomitant use of dual antiplatelets during the procedure and risks of bleeding.

Mechanical Thrombectomy Devices

The Merci retriever (Concentric Medical, Mountain View, California, USA), was the first stroke device to be approved by the FDA for mechanical thrombectomy in acute ischemic stroke patients. The Merci device (Mechanical Embolus Removal in Cerebral Ischemia) works primarily by advancing through the occlusion/thrombus using a micro-catheter and deploying distal to the thrombus [Figure 4 (c)]. This is followed by withdrawal of the Merci retriever with the thrombus captured by its helical loops, alongside the micro-catheter, using manual aspiration with a large syringe to reverse the flow and further aspirate any clot debris. However, thrombectomy with Merci device was associated with lower rates of recanalization ranging between 46%-55%.[42,43]

The next generation of mechanical thrombectomy devices, stent retriever, brought a paradigm shift in the endovascular management of acute ischemic stroke. Solitaire (ev3 Endovascular, Plymouth, Minnesota, USA) and Trevo Pro (Stryker Neurovascular, Kalamazoo Michigan, USA) are the most common stent retrievers used in the recent thrombectomy trials that showed a higher recanalization rates and a shorter

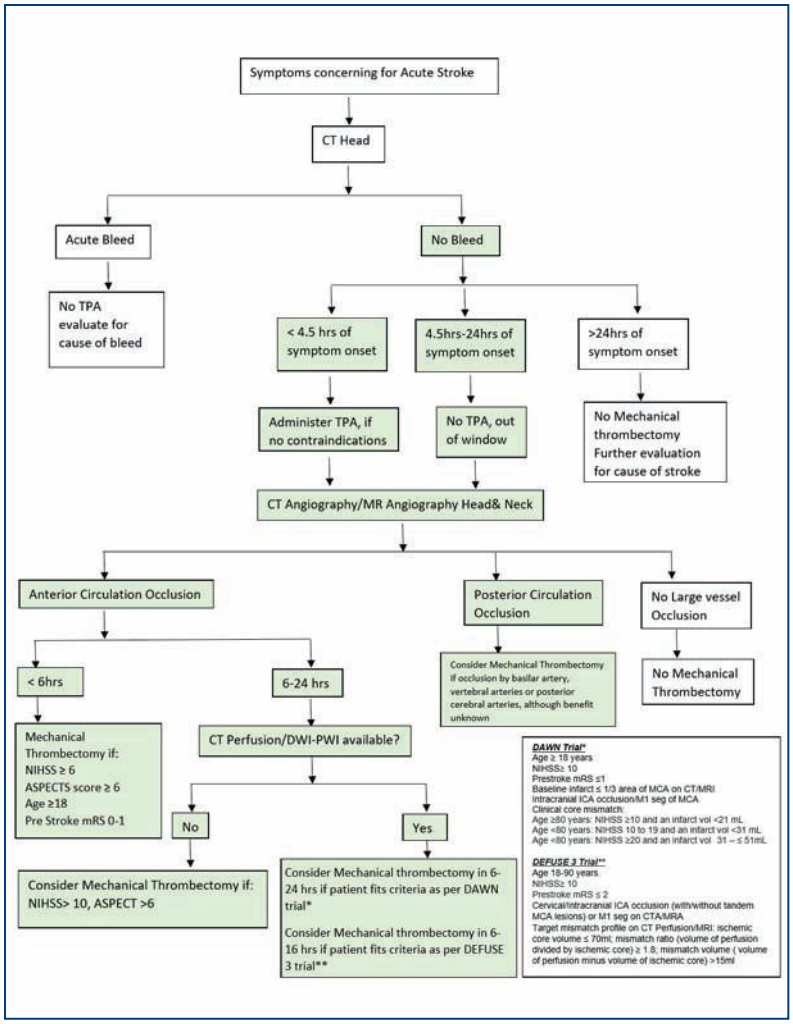


Figure 6: Flowchart summarizing the imaging and patient selection criteria for endovascular therapy in patients with acute ischemic stroke. NIHSS - National Institute of Health Stroke Scale; mRS - Modified Rankin Scale; ASPECTS -Alberta Stroke Program Early Computed Tomography Score; MCA- Middle cerebral artery; ICA – Internal carotid artery; DWI/PWI – Diffusion weighted perfusion imaging.

time to treatment in ischemic stroke from large vessel occlusions.[17-21,25,26] Stent retrievers are re-sheathable, re-constrainable, self-expanding stents mounted on a wire and are deployed within the thrombus through a microcatheter. The radial force of the stent compresses the thrombus against the vessel wall allowing restoration of the blood flow immediately. Leaving the device in place, for up to 5 mins, promotes engagement of the device with thrombus. The micro-catheter and stent are then withdrawn gently under continuous aspiration using a large syringe through the guiding-catheter to prevent the development of an embolism [Figure 4 (e)]. The use of stent retrievers is indicated in preference to the coil retrievers such as Merci device for mechanical thrombectomy [23]

More recently, large caliber aspiration catheters have been made available [ACE 68, 5MAX, 5MAX ACE (Penumbra Inc., Alameda, CA, USA), AXS Catalyst 6 (Stryker), Sofia 6F (MicroVention, Aliso Viejo, CA, USA)] that can be advanced easily in the cerebral vasculature and can be placed at the level of thrombus over a microcatheter and is used to aspirate the thrombus directly using a syringe or Penumbra aspiration pump that is part of the Penumbra thrombectomy/ aspiration system [Figure 4 (d)].[44]

Figure 5 summaries the different endovascular revascularization strategies available currently. In general, the technical goal of the thrombectomy procedure should be reperfusion to a modified Thrombolysis in Cerebral Infarction (mTICI) grade 2b/3 angiographic result [2b= antegrade reperfusion of more than half of the previously occluded target artery ischemic territory, 3= complete antegrade reperfusion of the previously occluded target artery ischemic territory with absence of visualized occlusion in all distal branches],[45] to maximize the probability of a good functional clinical outcome [Figure 3 (a) and (b)]. The use of adjunctive salvage techniques, including IA fibrinolysis, may be reasonable to achieve mTICI 2b/3 angiographic results if completed within 6h of symptom onset.[23]

Choice of Anesthesia

Both general anesthesia and conscious sedation can be used during endovascular therapy in acute ischemic stroke patients. However, the choice between general anesthesia and conscious sedation should be individualized based on clinical characteristics, tolerance of procedure and patient risk factors. A recent meta-analysis showed that use

of general anesthesia may be associated with poorer outcomes as compared to conscious sedation in the setting of endovascular therapy.[46] However, general anesthesia may be preferable in patients with depressed level of consciousness, respiratory compromise, and uncooperative or agitated patients for airway protection.

Post Procedure Care

All patients who undergo endovascular therapy for acute ischemic stroke should be admitted to neurological critical care units for closer monitoring. Low threshold should be kept for obtaining a non-contrast CT head to detect hemorrhagic transformation, particularly in patients who develop neurological decline post procedure. There is no consensus regarding the appropriate timing of obtaining follow up CT head and can range from immediately post procedure to 24 hours.

There is very limited data available to guide BP management during and after the procedure in patients who undergo mechanical thrombectomy. The ESCAPE protocol states that SBP ≥150 mm Hg is probably useful in promoting and keeping collateral flow adequate while the artery remains occluded.[18] The DAWN protocol recommends maintaining SBP <140 mm Hg in the first 24 hours in subjects who are reperfused after mechanical thrombectomy.[27] According to current AHA guidelines, it might be reasonable to maintain BP at a level < 180/105 mm Hg in patients who undergo mechanical thrombectomy with successful reperfusion.[23]

Vascular groin complications can arise from use of multiple or large bore catheters and should be monitored regularly. A standardized protocol should be followed diligently by the nursing staff and physicians for assessment of vascular complications and maintenance of hemostasis at the puncture site either with use of manual compression or vascular closure devices. Other post-procedural complications can include cardiac arrhythmias, temperature dysregulation, respiratory failure, hemorrhagic transformation, malignant cerebral edema, stroke evolution, and vessel re-thrombosis.

Conclusion

Endovascular therapy for management of acute ischemic stroke has evolved tremendously over the recent years and is currently considered standard of care in selected patients with large vessel occlusion within the anterior circulation. Figure 6 depicts a flowchart summarizing the imaging and patient selection criteria for endovascular therapy in patients with acute ischemic stroke. Diagnostic advancements in imaging with availability of multi model imaging protocols including CT perfusion, MR-DWI and MR-perfusion has made it possible to extend the time window for endovascular therapy up to 24 hours in select patient population, leading to improved functional outcomes. Recognition of large vessel related stroke and timely transfer of patients to specialized stroke centers with endovascular intervention capabilities, can help improve patient outcomes and improve stroke related morbidity.

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Disclosure

None reported. **MM**

Sleep in the Elderly

by Prathusha Tatineny, MD, Fariha Shafi, MD, Ashraf Gohar, MD & Abid Bhat, MD

Older people have difficulty in falling asleep and staying asleep due to frequent arousals. It is important to know how sleep patterns change as we age and, at the same time, to recognize primary sleep disorders among the elderly people.



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Abstract

Aging is associated with several changes in sleep patterns. Older adults have increased prevalence of primary sleep disorders including insomnia, sleep disordered breathing, restless legs syndrome, REM sleep behavior disorder, and circadian rhythm disturbances. These can be further compromised by sleep disturbances secondary to medical or psychiatric disorders, and medication side effects. This review discusses age-related changes in sleep architecture, etiology, clinical presentation, and treatment options of various sleep disorders in the elderly.

Introduction

Sleep is an important aspect for health and wellness across the lifespan. The number of people in the United States who are 65 years or older is steadily increasing, and is expected to double over the next 25 years to about 72 million. By 2030, roughly one in five people in the US will be over the age of 65.[1] Sleep physiology changes with the age, and many sleep disorders increase in the elderly. As many as 50% of older adults, compared to 15.9 to 22.3% of the general population, complain about sleep problems.[2] In the elderly population, a large contributing factor to poor sleep is the high prevalence of medical and psychiatric comorbidities in addition to the issue of polypharmacy. Sleep complaints when persistent, can lead to daytime sleepiness, which can lead to morbidity in elderly people, such as impaired cognition, disorientation, delirium, as well as increased risk of falls. Patients with sleep disorders are often more likely to develop cardiovascular and cerebrovascular disorders, and individuals with a history of these medical disorders are often at a high risk of developing sleep disorders. Sleep disturbance in the elderly should be considered a multifactorial geriatric health condition, requiring consideration of multiple risk factors and a comprehensive treatment approach.[3] In this review, we will focus on common sleep disorders, along with the diagnostic and specific treatment options to help improve quality of life in the elderly population.

Sleep Changes with Aging

As part of the natural aging process, sleep becomes more fragmented and lighter with an increase in the number of EEG arousals and awakenings which result in reduced sleep efficiency and total sleep time.[4] Several changes occur in both sleep architecture as well as sleep parameters throughout the lifespan.[5] (Table 1.) The percentage of stage N1 and stage N2 along with time spent awake during the night increases with aging while there is a reduction in sleep efficiency and slow-wave sleep percentage. The elderly tend to

Table 1. Age-Related Changes to Sleep Architecture

	Increased	Decreased
Sleep Parameter	Sleep Latency	Sleep efficiency
	Time awake after sleep onset (WASO)	Total sleep time
	Number of arousals from sleep	Slow wave sleep

go to bed earlier and wake up earlier when compared to young adults. The shift in sleep times is due to the circadian rhythm generated by the pacemaker that is located in the suprachiasmatic nucleus (SCN) of the hypothalamus. Aging is associated with a decrease or malfunction in sensitivity of the SCN to environmental cues to adjust circadian rhythm to a natural 24-hour day/night cycle. Melatonin levels also diminish with age and reach levels similar to daytime concentrations which may contribute to the increased prevalence of sleep-related disorders with aging.[6] The amplitude of circadian rhythms, including those of body temperature and hormones including cortisol, are reduced in the elderly.[7] Sleep homeostasis also declines with aging. The age-related decrease in total sleep time and sleep efficiency may be partially due to the reduced homeostatic sleep pressure with aging.[8,9] The age-related changes mentioned above are mostly relevant to older adults who are in excellent health. However, a significant percentage of older adults have multiple comorbidities, including osteoarthritis, cardiovascular disease, pulmonary disorder, psychiatric illnesses, diabetes mellitus, gastroesophageal reflux and cancer.[10] The increased use of medications along with an increase in prevalence of primary sleep disorders may also have a detrimental effect on sleep. It is therefore reasonable to say the sleep problems reported in elderly people are usually multifactorial and are not necessarily explained by age alone.

Common Age-Related Sleep Disorders

Insomnia

There is a high prevalence of reported sleep disturbances in the elderly. Foley and colleagues reported up to 43% of older adults with complaints of initiating or maintaining sleep.[11] Multiple factors increase the risk of developing insomnia in older adults. (Table 2.) For example, sleep complaints may be caused by behavioral and environmental issues. Many individuals older than 65 years are retired and may not feel the need to follow a regular sleep-wake schedule. In addition, people who are institutionalized may be at a higher risk of sleep disturbance due to social isolation and decreased daily activity. A number of primary sleep disorders including restless leg syndrome, periodic limb movement disorder, sleep apnea, and rapid eye movement sleep disorder can present as insomnia. Also, many medications (e.g., beta blockers, bronchodilators, anticholinergics, antihypertensives, antidepressants, and stimulants) cause or exacerbate insomnia.[12]

Due to the high prevalence and negative consequences of insomnia in older adults, screening for insomnia and other sleep disorders should be included in the routine clinical evaluation. It is important for clinicians to take a detailed history from patients and their bed partner, asking for insomnia symptoms, sleep-wake patterns, other sleep related questions, daytime functioning, and previous treatments.[13] As in younger adults, use of the sleep diary and/or structured sleep questionnaires (e.g., Insomnia Severity Index, Pittsburg Sleep Quality index) is appropriate in older adults. Elderly people with significant vision or hearing impairment and problems with manual dexterity may have difficulty with completing these diagnostic methods. Objective assessments of sleep such as polysomnography and wrist actigraphy are usually not indicated in the routine evaluation of insomnia but may be utilized to rule out other sleep disorders including sleep disordered breathing, disruptive nocturnal movements, and circadian rhythm sleep-wake disorders.[14] The treatment of insomnia in the elderly population must include maintaining a regular sleep-wake schedule, optimizing treatment of comorbid medical and psychiatric conditions, and eliminating medications contributing to insomnia. Several studies suggest behavioral/psychological treatment should be the first-line treatment for insomnia in older adults.[15] Cognitive therapy of insomnia(CBTi) is a multicomponent process that involves cognitive and behavioral techniques like stimulus control therapy, sleep restriction therapy, cognitive restructuring, relaxation techniques, and sleep hygiene education.[16] Pharmacotherapy should be exercised with caution in the elderly due to reduced metabolism, as well as, drug-to-drug interactions in patients that take multiple medications. Longer acting benzodiazepines should

Table 2. Causes of poor sleep in the Elderly Subjects

Physiologic	Age related changes in sleep efficiency
Medical Disorders	Cardiopulmonary disorders, Arthritis, Chronic pain syndrome, Neurodegenerative disorders Gastroesophageal reflux disorder
Psychiatric Disorders	Depression, Anxiety Disorder
Behavioral	Excessive napping, Use of caffeinated beverages, including alcohol
Medications	Diuretics, Beta-blockers, Anti-depressants
Primary sleep disorders	Insomnia, Restless Legs Syndrome, Sleep disordered breathing, REM sleep behavior disorder

be avoided due to risks of daytime sedation, falls, and confusion.[17] Due to a shorter duration of action, most non-benzodiazepines (zolpidem, eszopiclone and zaleplon) are believed to carry a lower risk of side effects. However, these should be avoided in older adults with dementia and cognitive impairment.[18] Other FDA approved agents include melatonin receptor agonist, such as ramelteon which has shown efficacy in older adults for sleep initiation insomnia.[19] Diverse categories of antidepressants (including trazodone, tricyclic antidepressants, and mirtazapine) and first-generation anti-histamines (diphenhydramine) have been used for the treatment of insomnia. In the absence of an underlying depressive disorder, antidepressants should be avoided in the elderly because they can also increase the risk of falls and cause orthostatic hypotension. Melatonin is an endogenous hormone secreted by the pineal gland and has been used in people with insomnia in different doses and strengths. Melatonin decreases subjective sleep latency in some studies but may cause headaches and drowsiness.[20] Melatonin preparations are not regulated by the FDA.

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is characterized by instability of the upper airway during sleep via recurrent pharyngeal collapse which results in reduced (hypopnea) or absent(apnea) airflow.[21] OSA increases with advancing age, with prevalence estimates varying depending on the definition used. OSA prevalence in older adults may be as high as 70% in men and 56% in woman as compared to the prevalence estimates of 15% in men and 5% in women in the general adult population.[22] The increase in prevalence has been attributed to the structural changes to the upper airway, including lengthening of soft palate and upper airway fat pad deposition.[23] Elderly people are more likely to present with excessive daytime sleepiness and nocturia while witnessed apneas and snoring may not be reported as frequently.[24, 25]

Although there has been controversy about whether sleep disordered breathing has health consequences in older adults, recent studies indicate a significant health risk of sleep disordered breathing in older adults.[26, 27] In a six-year follow-up in a population-based cohort of 394 noninstitutionalized elderly subjects (ages 70-100 years, median 77 years, 57% men), Munoz et al. found that severe obstructive sleep apnea (Apnea Hypopnea Index (AHI) index of greater than 30) at baseline had an increased risk of ischemic stroke in the elderly.[28] Whether sleep disordered breathing increases the risk of hypertension in older adults remains uncertain given the conflicting findings in the literature. In a cross-sectional analysis, sleep disordered breathing was not associated with systemic hypertension in subjects age 60 years or older.[29] Conversely, a French study reported that an AHI of 30 or greater was independently associated with incident hypertension, after three years, in normotensive older adults.[30] A longitudinal study of incident congestive heart failure showed that each 10 unit increase in the AHI led to a 13% increase in heart failure in men, but not in woman.[31] The diagnosis of sleep apnea requires overnight sleep study and previously necessitated an overnight stay at an in-lab sleep facility. The Centers for Medicare and Medicaid Services has also approved portable at home sleep apnea testing (HSAT) for subjects with suspicion

of sleep disordered breathing. Home sleep testing is generally recommended for patients with moderate to high clinical probability of sleep apnea. Ambulatory monitoring can be successfully completed in older adults, but factors such as adequate visual acuity, arthritis and other functional limitations may need to be addressed.

As with younger adults, continuous positive airway pressure (CPAP) therapy is the treatment of choice in older patients. Before instituting any specific treatment, certain general measures are recommended including weight loss, smoking cessation, avoidance of alcohol and sedatives before bedtime, avoidance of supine sleep position and maintaining nasal patency. The major limiting factor for CPAP use is patient adherence: approximately 40 to 50% are adherent.[32] Older age by itself does not affect CPAP adherence.[33] Adherence to CPAP therapy in older adults may be impaired by factors such as medical and mood disorders, cognitive impairment, impaired manual dexterity, nocturia, and lack of a supportive partner. The benefits of CPAP therapy are noticeable in older population, with improvement in cognition, memory, executive function, sleep quality and cardiovascular function.[34] For Medicare to cover CPAP therapy long-term, the patient must use CPAP for a minimum of four hours a night on 70% of the nights for at least one month during the initial three-month trial. In addition, they require a face-to-face encounter with the ordering physician to document clinical response at sometime between months one and three. Individuals who have failed or refused CPAP therapy for obstructive sleep apnea may be considered for oral appliances. These devices are effective in treating snoring and mild to moderate obstructive sleep apnea but may not be appropriate in older adults who are edentulous. Common side effects include dry mouth, increase salivation, tooth soreness and temporomandibular joint discomfort. As with younger adults, upper airway surgery is not particularly effective for older patients and may be associated with especially high morbidity in the elderly.[35]

Sleep-Related Movement Disorders

Restless legs syndrome, also known as Willis-Ekbom disease, is characterized by an urge to move the legs often accompanied by abnormal leg sensation, resulting in sleep initiation and/or sleep maintenance problems.[36] Restless legs syndrome (RLS) may be idiopathic or secondary to other medical conditions including iron deficiency anemia, chronic renal disease and peripheral neuropathy. Medications including SSRIs, tricyclic antidepressants, lithium along with excess caffeine intake and tobacco smoking can worsen symptoms in RLS patients. Restless leg syndrome is common in older people, with an estimated prevalence of 10-35% among those over 65 years of age.[37] The majority of people with RLS also present with periodic limb movements (PLMs) in sleep that are characterized by repetitive, stereotyped movements of the big toe and ankle and occasionally of the knee and hip. However, PLMs occur in the absence of RLS approximately 70% of the time. [38] This syndrome is diagnosed with polysomnography by recording bursts of electromyographic activity that recur at regular periods in the affected muscles. Although PLMs may be asymptomatic and require no treatment, the findings of PLMs in patients with unexplained insomnia may warrant appropriate treatment. The pathogenesis of RLS is unclear, but appears to involve abnormalities in the dopaminergic neural transmission.[39] Iron replacement therapy should be considered for RLS treatment when serum ferritin levels are lower than 50 μg/L. If there is no response to iron supplementation or the initial ferritin is >50μg/L, RLS is usually treated with dopaminergic agents such as ropinirole or pramipexole. Patients should be warned about side effects including sleep attacks and compulsive behaviors. In some cases, augmentation can occur that leads to reemergence and worsening of RLS symptoms. Alpha-2-delta calcium channel ligands such as gabapentin, gabapentin enacarbil, and pregabalin are also effective therapies for RLS with data showing decreased augmentation with pregabalin.[40] Benzodiazepines and opioids may be used in refractory cases but caution is warranted while using these medications in the elderly population.

Rapid Eye Movement Sleep Disorder

Rapid eye movement sleep disorder (RBD) is a parasomnia that occurs during REM sleep and is characterized by dream enacting behavior. Affected people may display a variety of movements, which in extreme cases can be harmful to the patient or bed partner. These behaviors/movements can include talking, shouting, thrashing limbs, punching, while remaining in REM sleep. RBD is most prevalent among older adult males.[41] Although the etiology of RBD is unclear, acute onset of RBD has been associated with the use of tricyclic antidepressants, fluoxetine, monoamine oxidase inhibitors, and withdrawal

from alcohol or sedatives.[42] Chronic RBD has been associated with neurodegenerative disorders such as Parkinson's disease, Lewy body dementia, and multiple system atrophy. Interestingly, symptoms of REM sleep behavior disorder may precede a diagnosis of Parkinson's disease for years.[43] RBD is diagnosed with polysomnogram to detect loss of muscle atonia during REM sleep in the setting of proper clinical context. Patient education, including removing potentially hazardous objects from the bedroom and placing the mattress on the floor to prevent falling from the bed is important to prevent sleep-related injury. RBD is often treated with clonazepam, a long-acting benzodiazepine, which is shown to reduce or eliminate abnormal motor behavior in approximately 90% of RBD patients.[44] Melatonin is an alternative therapy and is usually better tolerated in the elderly population and therefore may be used as a first-line agent in this group.[45]

Circadian Rhythm Sleep-Wake Disorders

Circadian rhythm sleep-wake disorders (CRSWD) occur when the timing of sleep is disrupted due to an altered circadian rhythm or mismatch between an individual's circadian rhythm and required sleep-wake schedule. The sleep-wake cycle is controlled by the suprachiasmatic nucleus (SCN) in the hypothalamus. This brain region controls the internal circadian pacemaker, which is synchronized to the hour of the day by both external cues and internal cues. Light is the most important external queue while the core body temperature and melatonin are the internal cues. Circadian rhythms become weaker and less responsive to the external stimuli with advancing age. Advance sleep-wake phase schedule (ASWPS) is the most common circadian rhythm sleep-wake disorder in older adults. Elderly people with ASWPS tend to become sleepy early in the evening (typically between 1900 and 2000 h) and wake up early in the morning (typically around 0300 to 0400 h). Many of these adults feel pressure from societal norms to stay up later in the evening, despite being sleepy and despite continuing to wake up early in the morning. This can lead to limited sleep resulting in daytime sleepiness. ASWPS can easily be misdiagnosed as insomnia and it's important to differentiate between the two diagnoses because the treatment approach differs. Circadian rhythm disorders are treated with bright light therapy where the patient is exposed to light at specific times which helps to realign the sleep-wake schedule.

Sleep and Dementia

Sleep disturbances are common (25-40%) in patients with Alzheimer's dementia.[46] Patients with neuro-degenerative disorders, including Lewy body dementia (LBD) or Parkinson's disease (PD) may have sleep disorders including REM sleep behavior disorder (RBD). Sleep disordered breathing is the most common sleep disorder in individuals with vascular dementia while patients with Alzheimer's dementia present more commonly with symptoms of insomnia and excessive daytime napping.[47] The polysomnographic findings in patients with Alzheimer's disease include a decrease in sleep efficiency, increase in N1 sleep, increase in awakening frequency, and a reduction in sleep spindles and K complexes.[48] Individuals with dementia are also at risk for irregular sleep-wake rhythm disorder (ISWRD) where the person sleeps in fragmented episodes during the day and night. Pharmacological agents for the treatment of dementia may also disrupt sleep. Individuals taking acetylcholinesterase inhibitors to slow down the cognitive decline in Alzheimer's dementia may lead to increased nighttime arousals and nightmares.[49] Behavioral interventions including a daily consistent routine for bed and wake times should be instituted. Naps may be planned but should be brief and consistently done at the same time every day. Bright light therapy has been shown to increase sleep efficiency and total sleep time in individuals with dementia.[50]

Conclusion

In conclusion, there are changes to sleep architecture throughout the lifespan that are considered normal. Older people have difficulty in falling asleep and staying asleep due to frequent arousals. It is important to know how sleep patterns change as we age and, at the same time, to recognize primary sleep disorders among the elderly people. Careful assessment of sleep including a comprehensive sleep history, and relevant testing, should be conducted to evaluate the patient's complaints. Treatment should address both the primary sleep problem and any comorbidities thereby optimizing the chance for improvement in quality of life and functioning in older adults.

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Disclosure

None reported. **MM**

MSMA NEW MEMBER SPOTLIGHT

M. SLADE STRATTON, MD

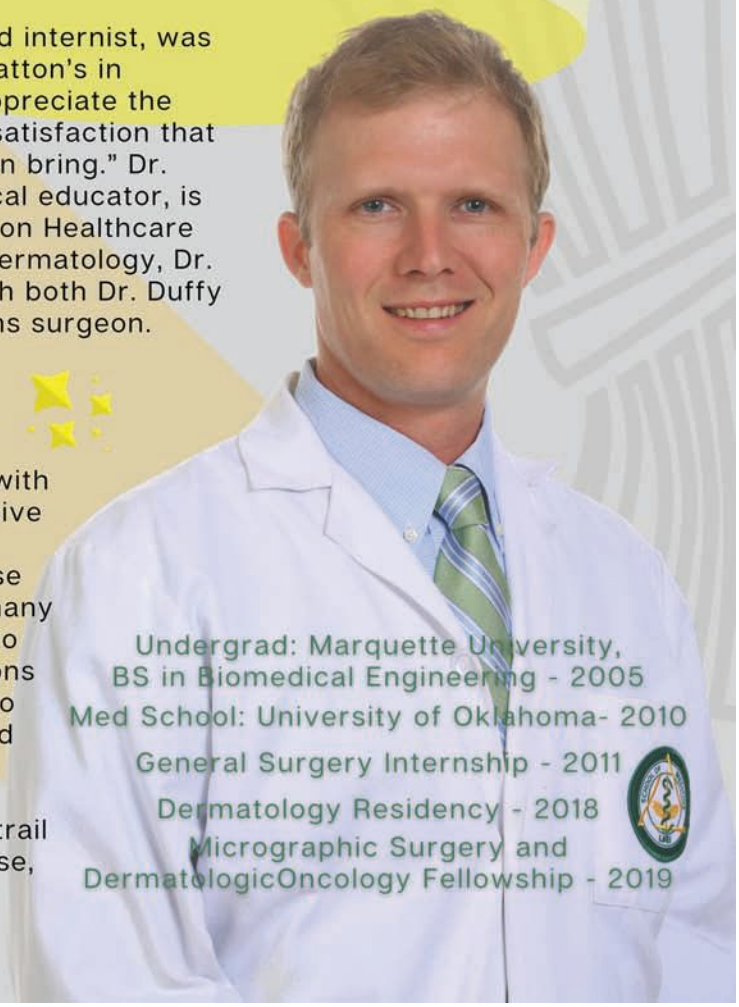
Slade Stratton, MD, grew up in rural Oklahoma in a medical family, with both is father and grandfather being pediatricians, and his mother teaching nursing. He was raised around doctors and patients and “couldn't see myself doing anything else.” You might say he was born into medicine. Dr. Stratton pursued an undergraduate degree in engineering in 2005 and, still, he knew he would become a doctor. Dermatology later became his calling.

“There's a great combination of long-term continuity with patients and outpatient surgery in dermatology,” states Stratton. As a surgical intern in the Navy, he discovered that being a hospital doctor wasn't for him, yet his love for outpatient surgery and cutaneous procedures grew strong. The Navy, as he puts it, “provides a unique opportunity in medicine to delay answering the omnipresent question, ‘what do I want to be when I grow up?' ”

Dr. Dan Duffy, now a nearly-retired internist, was a close friend and mentor of Dr. Stratton’s in medical school. “He helped me to appreciate the personal rewards and professional satisfaction that long-tem continuity with patients can bring.” Dr. Duffy, a national, professional medical educator, is also founder of American Academy on Healthcare Communications. Before choosing dermatology, Dr. Stratton had careful discussions with both Dr. Duffy and another friend, a practicing Mohs surgeon.

“The most challenging, and rewarding, part of dermatology practice,” Dr. Stratton says, “is navigating shared decision making with patients. Treatment and reconstructive decisions with skin cancers can be difficult for many patients to traverse and, in dermatology, there can be many options. I really think it's important to help patients make informed decisions while framing risk/benefit analysis to a patient's level of sophistication and values.”

Dr. Stratton enjoys long-distance trail running and fly fishing. He, his spouse, and three children live in St. Louis, where he practices dermatologic surgery at Epiphany Dermatology.





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