

Complications and Functional Outcomes after Subcapital Humerus Fractures

Protocol ID	SURF Study protocol
Short title	SURF study
EudraCT number	<i>Not applicable</i>
Version	6
Date	February 12, 2020
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Subsidising party	<i>Not applicable</i>
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Laboratory sites <if applicable>	<i>Not applicable</i>
Pharmacy <if applicable>	<i>Not applicable</i>

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

AE	Adverse Event
CA	Competent Authority
CMS	Constant Murley Score
DASH	The Disabilities of the Arm, Shoulder and Hand score
DSMB	Data Safety Monitoring Board
E.G.	Exempli Gratia (for example)
EQ5D	EuroQol5D questionnaire
FAC	Functional Ambulation Categories
FJS	The Forgotten Joint Score
GDPR	General Data Protection Regulation; in Dutch: Algemene Verordening Gegevensbescherming (AVG)
IC	Informed Consent
PHF	Proximal humerus fractures
PSQI	Pittsburgh Sleep Quality Index questionnaire
(S)AE	(Serious) Adverse Event
SANE	Single Assessment Numeric Evaluation
Sponsor	The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.
SUSAR	Suspected Unexpected Serious Adverse Reaction
UAVG	Dutch Act on Implementation of the General Data Protection Regulation; in Dutch: Uitvoeringswet AVG
WMO	Medical Research Involving Human Subjects Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen

SUMMARY

Rationale: Proximal humerus fractures are commonly seen and the incidence rate is expected to increase. Proximal humerus fractures are strongly associated with osteoporosis and are most frequently observed in the geriatric population. Thirteen percent of proximal humerus fractures are subcapital humerus fractures which are often treated non-operatively. However, little is known about outcomes after non-operative treatment of subcapital humerus fractures and few studies have reported a follow-up time of 2 years or longer.

Objective: The primary objective is to assess functional shoulder outcome scores and complications after non-operative treatment of subcapital humerus fractures among adults and older adults at least 2 years after the fracture. The secondary objectives are:

1. To assess which factors (e.g. age, comorbidities, ambulation ability, independency in activities of daily living, trauma mechanism) are associated with a difference of more than 10 points between the Constant Murley Score of the affected and contralateral shoulder in patients with a subcapital humerus fracture treated non-operatively.
2. To describe the number of patients with a subcapital humerus fracture treated surgically and non-operatively.

Study design: A cross-sectional cohort study will be carried out at OLVG Hospital Amsterdam.

Study population: Patients with subcapital humerus fractures treated non-operatively will be asked to participate in the study. The study will evaluate the results of adults and older adult patients. The adult cohort encompasses patients between 18 and 65 years of age. The older adult cohort encompasses patients of at least 65 years of age. Both groups are required to have follow-up time of at least 2 years.

Main study parameters/endpoints: Primary outcome: the Constant Murley Score. The Constant Murley Score is a score ranging from 0 to 100 that quantifies shoulder function based on four domains: pain, activities in daily living, mobility and strength. A higher score represents a better shoulder function.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Participation requires physical efforts: the trip to the hospital, obtaining radiographs, undergoing a shoulder examination and the completion of the questionnaires. The duration of the shoulder examination will be 15 minutes, completing the questionnaires 25 minutes and having the radiographs taken 10 minutes. A potential risk associated with the study is radiation dosage applied in radiography. However, the dosage radiating from the X-ray source is very low and may not cause any adverse health effects: the radiation dosage of two radiographs is 0.08 mSv. As illustration, the annual background radiation in the Netherlands is ~2.5 mSv. There are no benefits for participating patients. Nevertheless, patients may appreciate having the shoulder examined and checked with additional radiographs. Participation will contribute to increase current knowledge and improve treatment for patients with subcapital humerus fractures.

1. INTRODUCTION AND RATIONALE

Worldwide 6% of all fractures are localized in the proximal humerus and the incidence rate is expected to increase (1,2). Proximal humerus fractures (PHF) are strongly associated with osteoporosis and are most frequently observed in the geriatric population, showing a peak incidence of 379 per 100.000 among females above 80 years of age (2,3). The mortality rate is 10% and it is considered as one of the major causes for social dependency among older adults (4). The most common causes of PHF in patients younger than 50 years of age are high-energy traumas and sports related injuries. PHF could have a high impact on daily life activities: patients may be unable to do sports or carry out their work. Treatment options include surgical intervention or non-operative management, depending on the type of fracture, fragment displacement and patient characteristics. Twenty percent of the cases require surgical intervention (5). However, a lack of consensus exists on correct indications (6,7). Thirteen percent of proximal humerus fractures are subcapital humerus fractures which are most frequently treated non-operatively (8,9). Previous studies have reported the outcomes of different surgical techniques, patients sustaining three- or four-part fractures and populations including patients of all ages (10). However, little is known about outcomes after non-operative treatment of subcapital humerus fractures and few studies have reported a follow-up time of 2 years or longer (11,12). It is hypothesized that non-operative treatment of subcapital humerus fractures are associated with good functional outcome scores and a low complication rate. In case satisfactory outcomes are reported surgical costs and intra- and postoperative complications could be prevented.

2. OBJECTIVES

The primary objective is to assess functional shoulder outcome scores and complications after non-operative treatment of subcapital humerus fractures among adults and older adults at least 2 years after the fracture. The secondary objectives are:

1. To assess which factors (e.g. age, comorbidities, ambulation ability, independency in activities of daily living, trauma mechanism) are associated with a difference of more than 10 points between the Constant Murley Score (CMS) of the affected and contralateral shoulder in patients with a subcapital humerus fracture treated non-operatively.
2. To describe the number of patients with a subcapital humerus fracture treated surgically and non-operatively.

It is hypothesized that the difference between the CMS of the affected shoulder and contralateral shoulder is less than 10 points.

3. STUDY DESIGN

A cross-sectional cohort study will be carried out at OLVG Hospital Amsterdam in the Netherlands.

4. STUDY POPULATION

4.1 Population (base)

Patients with subcapital humerus fractures treated non-operatively are eligible for the study. A subcapital humerus fracture is defined as a two-part surgical neck fracture, regardless of the degree of fragment displacement. Non-operative treatment includes sling immobilization followed by gradual mobilization. The study will evaluate the results of

adults and older adults. The adult cohort encompasses patients between 18 and 65 years of age. The older adult cohort encompasses patients of at least 65 years of age.

4.2 Inclusion criteria

Adults (18- 65 years of age):

Patients with subcapital humerus fractures treated non-operatively and a minimum follow-up length of 2 year will be included. In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. Men or women of between 18 and 65 years of age upon the first presentation at the Emergency Department.
2. Written informed consent to participate in the study

Older adults (at least 65 years of age):

Patients with a subcapital humerus fracture treated non-operatively and a minimum follow-up length of 2 year will be included. In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. Men or women of at least 65 years of age upon the first presentation at the Emergency Department.
2. Written informed consent to participate in the study

4.3 Exclusion criteria

Adults (18- 65 years of age):

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. Patients with less than 2 years of follow-up time (the mean time for bone consolidation is 2 years)
2. Patients presented to the emergency department more than 1 month after injury (a delay in adequate treatment may affect functional shoulder outcomes)
3. Patients with an open fracture
4. Patients with neurovascular injury
5. Patient with concomitant injuries of the affected shoulder
6. Incapacitated patients
7. Patients with a shoulder arthroplasty in the contralateral shoulder
8. Patients with a nerve injury and concomitant motor function impairment of the contralateral shoulder
9. Patients with a medical history of a proximal humerus or clavicle fracture in the contralateral shoulder
10. Patients with a severely decreased shoulder function due to any other medical condition of the contralateral shoulder at the time of the outpatient visit

Older adults (at least 65 years of age):

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. Patients less than 2 years of follow up time (the mean time for bone consolidation is 2 years)
2. Patients presented to the emergency department more than 1 month after injury (a delay in adequate treatment may affect functional shoulder outcomes)

3. Patients with an open fracture
4. Patients with neurovascular injury
5. Patients with concomitant injuries of the affected shoulder
6. Incapacitated patients
7. Patients with a shoulder arthroplasty in the contralateral shoulder
8. Patients with a nerve injury and concomitant motor function impairment of the contralateral shoulder
9. Patients with a medical history of a proximal humerus or clavicle fracture in the contralateral shoulder
10. patients with a severely decreased shoulder function due to any other medical condition of the contralateral shoulder at the time of the outpatient visit

4.4 Sample size calculation

The sample size was calculated based on the CMS (primary outcome) using statistical software PASS (17). For adults and older adults sample sizes were calculated. A difference of 10 points on the CMS is considered clinically relevant (13). It is hypothesized that the difference between the Constant Murley Score of the affected shoulder and contralateral shoulder is less than 10 points. In this study a clinically relevant difference is not to be expected between the affected shoulder and contralateral shoulder.

The sample size calculation was performed using the study of Launonen et al as reference (14). Launonen et al carried out a randomized controlled trial in which patients with a 2-part proximal humerus fracture were allocated to operative or non-operative treatment. A mean CMS score of 66.0 was observed with a standard deviation of 20.6 after 2 years. The standard deviation of 20.6 was obtained from the standard error of 3.4 based on 39 patients who completed the study. We performed a paired T-test and sample size calculation revealed that at least 34 patients should be included to indicate a difference of 10 point on the Constant Murley Score between the affected and contralateral shoulder. Results were calculated with a power of 80.8% and an alpha of 0.05. This sample size calculation is applicable for the adult and older adult cohort.

METHODS

4.5 Study parameters/endpoints

4.5.1 Main study parameter/endpoint

Primary outcome: the Constant Murley Score (15). The CMS is a score ranging from 0 to 100 to evaluate the function of both shoulders. A higher score represents a better shoulder function. The CMS consists of four domains: pain (0-15), activities in daily living (0-10), mobility (0-50) and strength (0-25). To determine mobility the pain-free range of shoulder abduction, forward flexion, external rotation and internal rotation is tested. The shoulder strength is measured at 90 degrees in abduction.

4.5.2 Secondary study parameters/endpoints

The following secondary outcomes will be reported for adults and older adults:

- Radiographic outcome: each X-ray image will be assessed by the radiologist for osteoarthritis, non-union (defined as the absence of consolidation 3 months after the initial trauma), fracture consolidation and avascular necrosis. Additionally, the humeral neck- shaft angle will be measured with the shoulder in external rotation.
- Complications: the need for surgical intervention due to failure of non-operative management, nerve injury, chronic pain syndrome, rotator cuff pathology, mal-union (defined as healing of the bone in an abnormal position), non-union and mortality after 1 year.
- The quality of life measured with the EuroQol5D (EQ5D) questionnaire.
- The sleep quality reflected by the Pittsburgh Sleep Quality Index (PSQI)
- The rate of the shoulder as a percentage of normal shoulder function measured with the Single Assessment Numeric Evaluation (SANE).
- The performance of daily activities measured with the Disabilities of the Arm, Shoulder and Hand score (DASH) questionnaire.

Two additional secondary outcomes will be reported for adults (18-65 years).

- Return to sports measured with the DASH score module sports.
- Return to work using the DASH score module work.

Two additional secondary outcomes will be reported for older adults (at least 65 years of age).

- The functional independency reflected measured with the Katz index.
- The ambulation ability of patients measured with the Functional Ambulation Categories (FAC).

4.5.3 Other study parameters

Retrospectively, the following baseline variables will be documented for adults and older adult patients: age, gender, body mass index (kg/m²), Charlson Comorbidity Index, dominant side, trauma mechanism (fall, fall from height, traffic accident), shoulder dislocation, AO/ OTA classification and Neer- classification (classified by the research fellow RS supervised by the shoulder surgeon MB), length of follow-up and the non-operative treatment protocol (16). The Charlson Comorbidity Index is a score depending on age and the following comorbidities: myocardial infarction, congestive heart failure, peripheral arterial disease, cerebrovascular disease (CVA or TIA), dementia, Chronic Obstructive Pulmonary Disease, connective tissue disease, peptic ulcer disease, liver disease, chronic kidney failure, diabetes, hemiplegia, tumor, leukaemia, lymphoma and AIDS..

Additional baseline study parameters will be included for older adult patients. These questionnaires are the Katz index of independence in Activities in Daily Living and the Functional Ambulation Categories (FAC). The Katz index of independence in Activities in Daily Living is a score from A to G reflecting the functional independency of patients. The Functional Ambulation Categories (FAC) is a 6-point scale representing the ambulation ability of patients.

Baseline variables will be collected from the electronic medical record. When data is not reported (e.g. mechanism of injury of dominant side), patients will be asked to provide this information during the outpatient visit. The number of missing values will be reported for each variable, however baseline variables will not be excluded.

4.6 Study procedures

The study will be carried out at OLVG Hospital Amsterdam, the Netherlands. Patients with a subcapital humerus fracture treated non-operatively will be identified by the hospital code "non-operative treatment of subcapital humerus fracture". Surgically treated patients will be identified by the hospital code "surgical treatment of subcapital humerus fracture". Patients eligible for the study are sent an information letter on behalf of the treating specialist. After patients have given informed consent the following questionnaires will be sent and asked to fill out: the EQ5D, PSQI, the SANE and the DASH. Return to sports measured with the DASH score module sports and return to work using the DASH score module work will solely be sent to the adult cohort. The Katz index of independence in Activities in Daily Living and the FAC will be sent to the older adult cohort and should be completed according to patients situation at the time of fracture.

Demographic variables, medical history and fracture characteristics are retrieved from the electronic medical record. Eligible patients will be contacted to schedule an outpatient visit for shoulder examination according to the CMS and for obtaining two shoulder radiographs (anterior-posterior and lateral view). During the outpatient visit both shoulders will be examined and patients are asked for shoulder pain and activities in daily living. To determine mobility, the pain-free range of shoulder abduction, forward flexion, external rotation and internal rotation is tested. The researcher will also complete the FAC questionnaire and KATZ index according to the patients current situation. The shoulder strength is measured at 90 degrees in abduction. Patients not willing to participate in the study can point out their motive in the letter and are asked to fill out the Oxford Shoulder Score and the questionnaires mentioned above. Mortality among the non-responders will be assessed by retrieving the number of deaths in the study population from the electronic medical record and the municipality register. To obtain the CMS a house visit may be scheduled for patients physically not able to visit the hospital.

4.7 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons.

4.8 Replacement of individual subjects after withdrawal

Individual subjects will be replaced after withdrawal, until the required sample size has been obtained.

4.9 Follow-up of subjects withdrawn from treatment

Captured data till the date of withdrawal will be used for analysis, unless the patient specifically requests otherwise.

4.10 Premature termination of the study

When only 10 or less study participants can be recruited the study will be terminated after 2 years.

5. SAFETY REPORTING

5.1 Temporary halt for reasons of subject safety

In accordance to section 10, subsection 4, of the WMO, the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardise subject health or safety. The sponsor will notify the accredited METC without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the accredited METC. The investigator will take care that all subjects are kept informed.

5.2 AEs, SAEs and SUSARs

5.2.1 Adverse events (AEs)

Given the cross-sectional study design, with no intervention and without additional follow up moments, this section is not applicable. Any complications related to the subcapital humerus fracture that occurred between trauma and data collection will be recorded as secondary outcome.

5.2.2 Serious adverse events (SAEs)

Not applicable (see 5.2.1).

5.3 Follow-up of adverse events

Not applicable

5.4 [Data Safety Monitoring Board (DSMB) / Safety Committee]

Not applicable

6. STATISTICAL ANALYSIS

Data will be analysed using IBM SPSS statistics version 22 for Windows. For both adults and older adults this statistical analysis will be performed. Descriptive statistics of patient characteristics will be presented in numbers with percentages, means with standard deviation or as median with range. Variables will be assessed for normality using the Kolmogorov-Smirnov test, histograms and boxplots. Normal distributed data will be displayed as means with standard deviation. Non-normally distributed data will be presented as median with (interquartile) range. It is hypothesized that the difference between the Constant Murley Score of the affected shoulder and contralateral shoulder is 0 to 10 points. The difference between the CMS of the affected shoulder and the contralateral shoulder will be presented as mean with standard deviation. The occurrence of complications and the different categories of the FAC and KATZ index will be described in numbers with percentages. The EQ5D, SANE, PSQI and DASH will be presented as mean with standard deviation. Radiographic outcomes will be described as numbers with percentages and the humeral neck-shaft angle as mean with standard deviation. Missing values will be accepted since radiographic assessment is one of the

secondary outcome measures. To determine whether the results are under- or over estimated, baseline variables will be compared between the group who obtained radiographs and who did not obtained the radiographs. For continues data an unpaired T-test will be used for normal distributed data and the Mann-Whitney U test for non- normal distributed data. The Chi-Square test will be used for categorical data. The EQ5D, PSQI and DASH will be compared to the norm values using a one Sample T- test. The KATZ index and the FAC will be compared between baseline and follow up using the Chi-Square test. A figure will be depicted to show the annual percentage of conservative and surgical treated patients expressed as percentage of all the patients with a subcapital humerus fracture. Logistic univariable analyses will be performed to indicate which variables are associated with a difference of more than 10 points between the CMS of the affected and contralateral shoulder. The dependent variable will be a difference of more than 10 points between the CMS of the affected and contralateral shoulder (yes/no). The independent variables will be fitted in a univariable logistic regression model. Each model will be carried separately. The independent variables among older adults are mechanism of injury, Charlson Comorbidity index, FAC index, Katz index, age and body mass index. The dependent variables among adults are Mechanism of injury, Charlson Comorbidity index, age and body mass index. Variables will not be added to the univariable model if more than 20% of the values within a variables are missing. Results will be presented as odds ratio with 95% confidence interval. Results showing a p-value at or below 0.05 are considered to be significant.

7. ETHICAL CONSIDERATIONS

7.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (64th version; World Medical Association General Assembly; Fortaleza, Brazil; November 27, 2013) and the Medical Research Involving Human Subjects Act (WMO).

7.2 Recruitment and consent

To present the treatment of subcapital humerus fractures chosen in the OLVG hospital a flowchart will be provided to indicate the number of non-operative and surgical treated patients. Therefore, both surgical and non-operative treated patients will be identified with the hospital codes "non-operative treatment of subcapital humerus fracture" and "surgical treatment of subcapital humerus fracture". Patients eligible for the study are sent an information letter and informed consent form on behalf of the Surgery and Orthopaedic unit. If patients are willing to participate in the study they are requested to sign the informed consent form. After two weeks patients will be contacted by telephone to deal with any potential questions and to verify their participation. Patients can also contact the research department by telephone or email. A research fellow will call each patient. The expected time period of inclusion is 3 months.

7.3 Objection by minors or incapacitated subjects (if applicable)

Not applicable

7.4 Benefits and risks assessment, group relatedness

No costs are associated with participation in the study. Participants will be compensated for travel expenses (including parking fees) and costs associated with the radiographs will be covered. Participation requires physical efforts: the trip to the hospital, obtaining radiographs, undergoing a shoulder examination and the completion of the questionnaires. The duration of the shoulder examination will be 15 minutes, completing the questionnaires 25 minutes and having the radiographs taken 10 minutes. A potential risk associated with the study is radiation dosage applied in radiography. However, the dosage radiating from the X-ray source is very low and may not cause any adverse health effects: the radiation dosage of two radiographs is 0.08 mSv. As illustration, the annual background radiation in the Netherlands is ~2.5 mSv. There are no benefits for participating patients. Nevertheless, patients may appreciate having the shoulder examined and checked with additional radiographs. Participation will contribute to increase current knowledge and improve treatment for patients with subcapital humerus fractures.

7.5 Compensation for injury

Since participants will not be exposed to health related risks. The METC will be contacted to apply for an insurance dispensation for participants.

7.6 Incentives (if applicable)

Not applicable

8. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

8.1 Handling and storage of data and documents

Patient data will be handled electronically using Castor Electronic Data Capture and are strictly confidential. Solely the research team will have access to these data and all data files will be secured with a digital code. Each participant will be assigned a study number which is used for data management and analysis. A separate subject identification code list will be created to link data to the study participants. Informed consent forms and questionnaires will be stored in separate binders in the archive closet provided with a study number. The key will be kept by the research co-ordinator of the department of orthopaedic surgery. The data will be stored electronically for at least 15 years on the research hard drive and in the archive at the Department of Joint Research. The software Sharepoint OLVG will be used to store data electronically. Data management will be conducted according to the General Data Protection Regulation.

8.2 Monitoring and Quality Assurance

Monitoring of the study will be conducted according to the OLVG hospital guidelines.

8.3 Amendments

Amendments are changes made to the research after a favourable opinion by the accredited METC has been given. All amendments will be notified to the METC that gave a favourable opinion.

A 'substantial amendment' is defined as an amendment to the terms of the METC application, or to the protocol or any other supporting documentation, that is likely to affect to a significant degree:

- the safety or physical or mental integrity of the subjects of the trial;
- the scientific value of the trial;
- the conduct or management of the trial; or
- the quality or safety of any intervention used in the trial.

All substantial amendments will be notified to the METC and to the competent authority.

Non-substantial amendments will not be notified to the accredited METC and the competent authority, but will be recorded and filed by the sponsor.

8.4 Annual progress report

The sponsor/investigator will submit a summary of the progress of the trial to the accredited METC once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial, serious adverse events/ serious adverse reactions, other problems, and amendments.

8.5 Temporary halt and (prematurely) end of study report

The investigator/sponsor will notify the accredited METC of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient's last visit.

The sponsor will notify the METC immediately of a temporary halt of the study, including the reason of such an action.

In case the study is ended prematurely, the sponsor will notify the accredited METC within 15 days, including the reasons for the premature termination.

Within one year after the end of the study, the investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited METC.

8.6 Public disclosure and publication policy

Research data can be published solely in approval of the research team and will be reported anonymously. Patient's approval is necessary in case radiographs will be published or used for educational purposes.

9. REFERENCES

1. Palvanen M, Kannus P, Niemi S, Parkkari J. Update in the Epidemiology of Proximal Humeral Fractures. *Clin Orthop Relat Res*. 2006;442(NA;):87-92. doi:10.1097/01.blo.0000194672.79634.78
2. Court-Brown CM, Caesar B. Epidemiology of adult fractures: A review. *Injury*. 2006;37(8):691-697. doi:10.1016/j.injury.2006.04.130
3. Launonen AP, Lepola V, Saranko A, Flinkkilä T, Laitinen M, Mattila VM. Epidemiology of proximal humerus fractures. *Arch Osteoporos*. 2015;10(1):2. doi:10.1007/s11657-015-0209-4
4. Clement ND, Duckworth AD, McQueen MM, Court-Brown CM. The outcome of proximal humeral fractures in the elderly. *Bone Joint J*. 2014;96-B(7):970-977. doi:10.1302/0301-620X.96B7.32894
5. Jawa A, Burnikel D. Treatment of Proximal Humeral Fractures. *JBJS Rev*. 2016;4(1):e31-e39. doi:10.2106/JBJS.RVW.O.00003
6. Beks RB, Ochen Y, Frima H, et al. Operative versus nonoperative treatment of proximal humeral fractures: a systematic review, meta-analysis, and comparison of observational studies and randomized controlled trials. *J Shoulder Elb Surg*. 2018;27(8):1526-1534. doi:10.1016/j.jse.2018.03.009
7. Tamimi I, Montesa G, Collado F, et al. Displaced proximal humeral fractures: when is surgery necessary? *Injury*. 2015;46(10):1921-1929. doi:10.1016/j.injury.2015.05.049
8. Court-Brown CM, Garg A, McQueen MM. The epidemiology of proximal humeral fractures. *Acta Orthop Scand*. 2001;72(4):365-371. doi:10.1080/000164701753542023
9. Court-Brown CM, Garg A, McQueen MM. The translated two-part fracture of the proximal humerus. Epidemiology and outcome in the older patient. *J Bone Joint Surg Br*. 2001;83(6):799-804. <http://www.ncbi.nlm.nih.gov/pubmed/11521917>. Accessed June 29, 2019.
10. Rangan A, Handoll H, Brealey S, et al. Surgical vs Nonsurgical Treatment of Adults With Displaced Fractures of the Proximal Humerus. *JAMA*. 2015;313(10):1037. doi:10.1001/jama.2015.1629
11. Hauschild O, Konrad G, Audige L, et al. Operative versus non-operative treatment for two-part surgical neck fractures of the proximal humerus. *Arch Orthop Trauma Surg*. 2013;133(10):1385-1393. doi:10.1007/s00402-013-1798-2
12. Bonifacio L, Syson P, Llanes J. Revisiting the outcome of displaced two-part fractures of the humeral neck in elderly patients after conservative treatment. *Malaysian Orthop J*. 2014;8(1):57-60. doi:10.5704/MOJ.1403.020
13. Kukkonen J, Kauko T, Vahlberg T, Joukainen A, Äärimaa V. Investigating minimal clinically important difference for Constant score in patients undergoing rotator cuff surgery. *J Shoulder Elb Surg*. 2013;22(12):1650-1655. doi:10.1016/j.jse.2013.05.002
14. Launonen AP, Sumrein BO, Reito A, et al. Operative versus non-operative treatment for 2-part proximal humerus fracture: A multicenter randomized controlled trial. Handoll H, ed. *PLOS Med*. 2019;16(7):e1002855. doi:10.1371/journal.pmed.1002855
15. Constant CR, Murley AH. A clinical method of functional assessment of the shoulder. *Clin Orthop Relat Res*. 1987;(214):160-164. <http://www.ncbi.nlm.nih.gov/pubmed/3791738>. Accessed June 23, 2019.
16. Neer CS. Displaced proximal humeral fractures. I. Classification and evaluation. *J Bone Joint Surg Am*. 1970;52(6):1077-1089. <http://www.ncbi.nlm.nih.gov/pubmed/5455339>. Accessed June 22, 2019.