RESEARCH AND STATISTICAL ANALYSIS PLAN
Internal review board ID: HUS/624/2024
Date of the document: 2/1/2025

RISK FACTORS FOR TREATMENT FAILURE IN HUMERAL SHAFT FRACTURES

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INTRODUCTION

Humeral shaft fractures can be treated either nonsurgically or surgically with good and comparable outcomes at one year. However, up to 30% of nonsurgically treated patients have problems with the fracture healing leading to later surgery. The functional outcomes in these patients undergoing later surgery are inferior to those who heal uneventfully with the primary treatment. Although surgically treated patients have significantly less problems with fracture union compared with nonsurgically treated patients, they have elevated risk for infection and iatrogenic radial nerve palsy. The reported infection risk with plate osteosynthesis is around 3%, and with intramedullary nailing around 1.5%. The risk of radial nerve injury during surgery is 4%. Current literature regarding risk factors for treatment failure in the patients with humeral shaft fractures is controversial and scarce especially in surgically treated patients. This study aims to identify the risk factors for treatment failure both in nonsurgically and surgically treated patients in the largest cohort of humeral shaft fracture patients to date.

MATERIALS AND METHODS

This retrospective study is conducted in Helsinki and Tampere University hospitals. Hospital registry is used to identify adult patients with humeral shaft fractures treated in the units. For the Helsinki University hospital, the included patients were treated between 2006 and 2016, and for the Tampere University hospital between 2001 and 2022.

Separate analysis of the risk factors for treatment failure in nonsurgically and surgically treated patients will be carried out. The definition of treatment failure for nonsurgically treated patients will be a need of later surgery due to fracture healing problems and for surgically treated patients, a secondary surgery due to treatment failure. A secondary analysis will assess the risk factors for later surgery due to fracture nonunion both in nonsurgically and surgically treated patients.

Additionally, risk factors for other unfavorable outcomes such as wound infections and secondary radial nerve palsy will be explored if deemed statistically feasible.

Our data consists of following variables:

- Patient-related variables
    - Age at the time of trauma
    - Gender
    - Underlying comorbidies
    - ASA classification
    - Overweight
    - Smoking
    - Alcohol consumption
    - Under the influence of alcohol upon arrival
    - Use of other substances

- Injury-related variables
    - AO type and group
    - Fracture site (proximal, mid, distal)
    - Open fracture (Gustilo-Andersson classification)
    - Periprosthetic fracture
    - Additional injuries
    - Trauma energy (low or high)
- Treatment-related variables
    - Primary treatment
    - Treatment changes
    - Fracture nonunion/union with the primary treatment

STATISTICAL ANALYSIS PLAN

Our statistical analysis is based on predictive approach, and we will follow guidelines from Harrell et al. and Heinze et al. We will use logistic regression since our outcome is binary in all models. Baseline variables included in the predictive analysis: age, gender, comorbidities, ASA classification, BMI, smoking, alcohol consumption/under influence upon arrival, AO type, fracture site, trauma energy. All baseline variables will be added simultaneously to the logistic model. Variable missingness is assessed. We assume Missing Completely at Random (MCAR) for any missing data and multiple imputation is used. Imputation is done if missingness is less than 20%. Variables with higher than 20% missingness are excluded from primary analyses but included in the secondary analyses. For each the overall pseudo-R2 is estimated and used to interpret the applicability of baseline predictors. Variable importance is also assessed using Wald chisquared test minus degrees of freedom. Calibration plots will be printed for all three models. Multiplicity is not considered since we are not focused on single regression coefficients nor we have specific multiple testing. When appropriate, 95% confidence intervals will be calculated, and associated p-values calculated. Analysis is done with RStudio using rms package.

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