Factors Predicting Failure of Internal Fixations of Fractures of the Lower Limbs: a Prospective Cohort Study

Barbara Prediger
Institute for Research in Operative Medicine (Witten/Herdecke University)
Thorsten Tjardes
Cologne-Merheim Clinic
Christian Probst
Hospital Gummersbach, Klinikum Oberberg GmbH
Anahieta Parvaresch
Institute for Research in Operative Medicine (Witten/Herdecke University)
Angelina Glatt
Institute for Research in Operative Medicine (Witten/Herdecke University)
Dominique Rodil Anjos
Institute for Research in Operative Medicine (Witten/Herdecke University)
Bertil Bouillon
Cologne-Merheim Clinic
Tim Mathes (tim.mathes@uni-wh.de)
Institute for Research in Operative Medicine (Witten/Herdecke University)

Research Article

Keywords: Prediction factors, failure, osteosynthesis, lower extremities, fractures

Posted Date: May 11th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-493067/v1

Abstract

Background

We assessed predictive factors of patients with fractures of the lower extremities caused by trauma. We examined which factors might increase failure rates. Furthermore, the predictive factors were set into context with other long-term outcomes, concrete pain and physical functioning.

Methods

We performed a prospective cohort study at a single level I trauma center. We enrolled patients with traumatic fractures of the lower extremities treated with internal fixation from April 2017 to July 2018. We evaluated the following predictive factors: age, gender, diabetes, smoking status, obesity, open fractures and peripheral arterial diseases. The primary outcome was time to failure (nonunion, implant failure or reposition), secondary outcomes were pain and physical functioning measured at follow up 6 months after initial surgery. For the analysis of the primary outcome we used a multivariate stratified (according fracture location) Cox proportional hazard regression model.

Results

We included 204 patients. Overall, we observed a failure in 33 patients (16.2%). Most of the failures occurred within the first 3 months. Obesity and open fractures increased the risk of failure and decreased physical functioning. None of the predictors had an impact on pain. Age, female gender and smoking of more than ≥ 10 package years increased failure risk numerically but statistical uncertainty was high.

Conclusion

We found that obesity and open fractures strongly increased the risk of failure. These seem promising candidates to be included in a risk prediction model and can be considered as a good start for clinical decision making across different types of fractures in the lower limb. However, large heterogeneity in the other analyzed factors suggest that for a precise personalized risk estimation, computer-based models incorporating a variety of detailed information (e.g. pattern of injury, x-ray and clinical data) and their interrelation might be needed to increase precision of prediction significantly.

Trial registration

NCT03091114

Background

Osteosynthesis, is the fixation of fractures or osteotomies by mechanical devices and usually describes the internal fixation of bone segments.

The aim of surgical fracture care with osetosynthetic devices is to restore the anatomic integrity of the injured bone, thereby allowing for early motion and/or weight bearing, i.e. training and rehabilitation of the injured limb or joint. Surgical fracture care fails with a rate of 10%-19% for several reasons [1–4]. Failure of an osteosynthesis usually results in prolonged treatment, revision surgery, worse functional outcome, pain, and thereby significantly increased cost, both for the health care system and for the society as well.

Generally any osteosynthesis is a trade off on a continuum between mechanical stability of the construct, residual motion of the fracture fragments, which is necessary to stimulate bone healing and the extend of soft tissue damage that has to be accepted to place the implants.

One can assume that any osteosynthesis failure is at least in part causally related to pre, intra- and postoperative decisions taken by the surgeon. The surgeon has to balance the individual patient prognostic and predictive factors against the mechanical necessities of bone healing physiology and his or her personal skill set to actually implement the intended osteosynthesis in the open reduction.

Given the complexity of the process of fracture healing and the broad variability of fracture patterns there is usually not enough explicit knowledge that provides a good basis for prognostics fracture healing pre-surgery. Given this absence of fact-based knowledge, many general parameters such as age or smoking status are considered as a basis for the surgeons' decision regarding an optimal therapeutic strategy. Most of these parameters have in common that they refer primarily not to bone physiology related conditions. Pathomechanically these parameters are usually not clearly traceable to the physiology of fracture healing. This gap of causality necessarily introduces a high degree of uncertainty for any clinical decision. Nevertheless, several studies have identified factors relevant for osteosynthesis failure in lower extremity fractures [5–10].

The objective of this prospective cohort study was to analyze predictive factors for treatment failure in patients having received an osteosynthesis of the lower extremity. Given the limited resources available to gather relevant predictive information in practice, the present study focuses on factors easily to identify, which might provide the opportunity for a simple individual risk estimation prior to surgery. In this way, we want get insights into factors that are possibly predictive across different types of limb fractures. In addition, the study should prove if it is sensible to develop a "simple" risk prediction model.

Furthermore, the predictive factors identified were set into perspective with long term pain and physical functioning.

Methods

Study design

We performed a prospective cohort study. We sampled all patients fulfilling the inclusion criteria consecutively. Prior to enrollment we registered the study (registry no. : NCT03091114) and received the approval by the ethic committee of University Witten/Herdecke. The study is reported in accordance with the ‚Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.

Patients and setting

Setting

All patients receiving surgical fracture care of the lower extremity between April 2017 and July 2018 at a level I trauma center in urban Germany were eligible for inclusion.

Eligibility criteria

Patients had to fulfill all of the following inclusion criteria.

- Age ≥ 18 years
- Internal fixation of an isolated traumatic tibial, femoral, calcaneal, malleolar or fibular fracture
- Sufficient German language skills and cognitive abilities to participate in follow up

Exclusion criteria:

- Periprosthetic fractures
- Fractures in context of a polytrauma

As there is no reliable evidence on factors, which might be relevant in terms of predictive value regarding osteosynthesis failure, we defined no further exclusion criteria.

Predictive factors

A prognostic factor can be defined as a measure that, among people with a given start point (here osteosynthesis of lower extremities), is associated with a subsequent endpoint [11], while a predictive factor is a subtype of a prognostic factor that predicts an outcome in treated patients, i.e. success of treatment (here failure of the internal fixation).

We chose potentially relevant predictive factors based on a literature review and an expert discussion [5–10]. We chose predictive factors for which we anticipated applicability across different types of lower limb fractures.

We included the following predictive factors in the model:

- Age
- Gender
- Diabetes
- Smoking status
- Obesity

- Open fractures
- Peripheral arterial disease

We collected all data on predictive factors from the clinical information system and patient interviews.

Outcome (measures) and follow-up

Definition and measurement

We defined time to failure (nonunion, implant failure or loss of reposition) as the primary outcome. We analyzed the following secondary outcomes:

- Physical functioning, as given by three items from the SF-36 questionnaire (difficulty in climbing one stair, difficulty in climbing more stairs, difficulties in stooping; each item offering three answer categories: much difficulties, some difficulties or no difficulties resulting in a possible score of 0 to 9)
- Subjective fracture related pain (given on a numeric rating scale (NRS) 0–10)

Data collection and follow-up

We collected outcomes with a questionnaire sent via post. Non-responders received a reminder invitation by SMS and we tried to reach them by a phone call in case there was no response three weeks after we sent out the questionnaire initially. In addition, we checked the clinical information system for occurrence of failure treated in our center. We planned to exclude failures because of surgical errors, but in none of the implant failures, a surgical error was recognized.

We assessed outcomes 6 months after surgery. Last patient out was July the 31st. Cut-off date for data collection was November the 30th. This means the follow-up period was reduced according to the cut-off date for data collection for patients we recruited in the last 3 months. For the last patient (i.e. the minimum follow-up period) the follow-up was 3 months. We decided to accept a follow-up of shorter than 6 months, even though definition of healing is usually referred to 6 months. However, we analyzed failure with a Cox regression. Consequently, this did not count patients with a shorter follow-up than 6 months no failure but it means that the observation time is censored.

Sample size

Studies suggest that five outcomes per variable are necessary in multivariate models of binary data [12]. This means, at least 35 events should be observed overall. We assumed a failure rate of 12%. Consequently, we planned including 292 patients in the final analysis. We included seven variables in the multivariate model.

Data management and statistical analysis

Data management

We entered all data in a standardized case report form. One investigator made all entries and a second verified the entries.

Statistical analysis

For the analysis of the primary outcome we used a multivariate stratified (according fracture location) Cox proportional hazard regression model. We entered all predictive factors simultaneously in the model to quantify the independent influence of each factor adjusted for all other factors. To get deeper insights we performed a subgroup analysis according to the localization (femur vs below the knee).

The influence of the predictive factors on physical functioning and pain was assessed using multivariate analysis of variance (MANOVA). For this analysis, we replaced missing values using multiple imputation. We calculated 95% confidence intervals (CIs) for all effect estimates.

Results

Population

We recruited 204 patients. For 26 (12.7%) we had no data on failure (2 died, 24 could not be reached e.g. moved and 2 for other reasons). In the analysis of pain and physical functioning, we included 172 (84%) patients (in addition to the lost patients above, 6 more did not respond any question on patient reported outcomes).

Table 1 shows the baseline characteristics.

Table 1
baseline characteristics

Predictive factor	
Age (mean ± SD)	51.39 (± 17.05)
Female	90 (44.1%)
BMI (mean ± SD)	26.01 (± 5.85)
Obesity (BMI ≥ 30)	37 (18.1%)
Smoker	75 (36.8%)
Smoking intensity (package years, mean ± SD)	18.62 (± 17.66)
Smoker type (≥ 10 package years)	47 (23%)
Diabetes (yes/no)*	11 (5.4%)
Peripheral arterial disease	5 (2.5%)
Open fracture	29 (14.2%)
Localization	
Tibia	88 (43.1%)
Femur	49 (24.0%)
Malleolus	27 (13.2%)
Calcaneus	17 (8.3%)
Fibula	23 (11.3%)
* type I and II not differentiated; BMI: body mass index; SD: standard deviation	

Primary outcome: failure

Table 2 shows the results of the multivariate analysis. Figures 1 and 2 show the unadjusted survival curves for BMI and open fracture, respectively.

Table 2
Cox regression model of predictive factors for failure

Predictive factor	Hazard Ratio (95% confidence interval)
Age (≥ 65 vs < 65)	1.51 (0.63 to 3.60)
Female (yes vs no)	1.25 (0.55 to 2.81)
BMI (≥ 30 vs < 30)	2.54 (1.12 to 5.80)
Package years (≥ 10 vs < 10)	1.19 (0.53 to 2.70)
Open fracture (yes vs. no)	5.36 (2.25 to 12.75)
Diabetes (yes vs. no)	1.07 (0.24 to 4.86)
Peripheral arterial disease (yes vs. no)	2.44 (0.29 to 20.72)

Overall, we observed a failure in 33 patients (16.2%). Of these, 16 had an implant failure, 8 an additional surgery for reposition and 17 a nonunion. Four of the 33 failure patients received antibiotics for treating wound infection. Most of the failures (compare Figs. 1 and 2) occurred within the first 3 months. Obesity and open fractures increased the risk of failure.

Age, female gender and smoking of more than ≥ 10 package years increased failure risk but statistical uncertainty was high for these factors. Diabetes was not associated with a higher risk of failure. Explorative subgroup analysis suggested that the negative influence of BMI was large in femur fractures but that the effect was uncertain in fractures below the knee (adjusted HR 6.18; 95%CI 1.42 to 26.95 vs adjusted HR 0.77 95%CI 0.24 to 2.44). The influence of the other factors was similar in both localizations (data not shown).

Secondary outcome: pain

Table 3 shows the results of the MANOVA. After 6 months, 27% of patients had no pain. Average pain after 6 months was 2.43 (95%CI 2.08 to 2.79) and the median pain was 2 (inter-quartile-range 2–4). All variables had a marginal impact on pain.

Table 3
Variables influencing pain

Variable	Regression coefficient (95% confidence interval)*
Intercept	2.89 (1.76 to 4.00)
Age (≥ 65)	-0.04 (-0.92 to 0.84)
Female	-0.02 (-0.71 to 0.68)
BMI (≥ 30)	-0.36 (-0.51 to 1.24)
Package years (≥ 10)	0.06 (-0.72 to 0.82)
Diabetes (yes)	0.79 (-0.70 to 2.28)
Peripheral arterial disease (yes)	0.48 (-1.60 to 2.56)
Open fracture (yes)	0.57 (-0.36 to 1.51)
Localization (femur)	-0.54 (-1.37 to 0.29)
*minus indicates a positive impact (reduction in pain)	

Secondary outcome: physical functioning

Results of the MANOVA for physical functioning are presented in Table 4.No difficulties in any physical task (climbing one stair, climbing more stairs, stooping) after 6 months were reported by 20% of patients. The median physical functioning score was 6 (lower quartile: 5; upper quartile: 8). Expectedly, physical functioning was reduced by the same factors that increased failure rates (BMI and open fracture). In addition, patients with peripheral arterial diseases reported more difficulties with physical functioning.

Although, this targeted sample size was not reached, we nearly satisfied the number of observations needed (33 instead of 35) per variable because the failure rate was higher than expected.

Table 4
Variables influencing physical functioning

Variable	Regression coefficient (95% confidence interval)*
Intercept	6.97 (6.13 to 7.81)
Age (≥ 65)	-0.16 (-0.80 to 0.48)
Female	-0.44 (-0.95 to 0.07)
BMI (≥ 30)	-0.70 (-1.38 to -0.03)
Package years (≥ 10)	-0.18 (-0.84 to 0.48)
Diabetes (yes)	-0.10 (-1.21 to 1.01)
Peripheral arterial disease (yes)	-1.80 (-3.38 to -0.21)
Open fracture (yes)	-0.80 (-1.54 to -0.07)
Localization (femur)	0.14 (-0.56 to 0.82)

*minus indicates a negative impact (more difficulties)

Discussion

Key findings

The present study prospectively assessed the impact of a set of variables on adverse outcomes of surgical fracture therapy over a 6 months period. Similarly, the outcome parameters are those the surgeon usually gets to know during follow up visits of his patients. The data can increase the clinical information on which the surgeon has to form his personal decision.

We found that open fractures and obesity in femoral fractures increased the risk of failure of osteosynthesis of lower limb fractures. For older age, female gender and arterial peripheral diseases we found that this might increase the failure risk moderately, however statistical uncertainty was high for these variables. Diabetes increased failure risk marginally and the effect estimate was highly imprecise.

None of the analyzed variables showed a clinical important impact on long-term pain.

The same variables which increased failure also reduced physical functioning, namely obesity and open fracture.

Limitations

The main limitation of our study is the small sample size. For this reason, the effect estimates for age, gender and peripheral arterial disease were uncertain or very uncertain. Another consequence of the small sample size is the statistical need for grouping the different fracture localizations. This might have obscured factors, which are important for only one or some certain localizations (e.g. fibula).

Interpretation of results in view of other evidence

Our results are in agreement with previous studies on failure and re-operation. As in our study most of these studies found that, BMI (weight and height) and features of the fracture are important predictors for failure of the osteosynthesis (1–4).

As in our study other studies found a varying effect depending on localization and high nonunion rates in the lower leg and in obese patients in femoral neck fractures [4]. There were many femoral neck fractures in our study likewise. Reason for the association of BMI and failure may include technical difficulties to reach the bone and increased soft tissue damage. In addition, worse perfusion might hinder healing and increase risk of infection. Furthermore, we suppose that the BMI might be a surrogate for the mechanical load. The reason, that this association with BMI becomes not obvious in these study in fractures below the knee might be that a large share of these fractures were sport or work injuries, i.e. occurred in non-obese patients.

Until today, the learning process orthopedic trauma surgery is still primarily based on individual learning from the patients a surgeon has treated. Given the currently available opportunities for clinical learning and learning based on, usually entity specific, scientific publications, the surgeon is caught in a dilemma which is defined by the often limited applicable evidence on the one hand and the cognitive limits of case based learning on the other hand. Information of predictive factors could support clinical decision making. However, in this and previous studies, even the influence of localization and severity of the fracture was heterogeneous [1, 3, 5, 9, 13]. In particular, the effect size and consequently the clinical importance differed strongly. The findings of this study, and previous studies on this topic raise the questions if evidence from “simple” prediction models and standard implementation approaches (e.g. clinical practice guidelines) could be a valuable approach for getting evidence into trauma care in general, i.e. can support the surgeons’ pre - and intra- operative decision making process significantly. In the view of the possible variations of fractures, the diversity of classifications systems and their manifold possible resulting classifications (e.g. AO classification), this heterogeneity seems quite impossible to handle using traditional approaches. Combining detailed clinical data with radiological and laboratory data might increase the accuracy of prediction. However, because of the heterogeneity of fractures and the large amount of possible relevant information, these require processing big data and these data have to be usable in clinical routine. One future possibility, which might overcome this problem might be developing standardized heuristics/algorithms (i.e. artificial intelligence based decision support systems) and implementing these using real-time clinical decision support systems. However, these have little attention so far in the literature on orthopedic trauma [14].

Of the considered factors we found no association with pain, suggesting that patient characteristics (e.g. age) or injury related factors (e.g. complexity of fracture) are not the most important determinants but that pre-existing pain, psychological factors and socioeconomic factors might have a stronger impact, as seen in the literature [15, 16]. We neither found clinical important determinants for failure risks and physical functioning with exception to those that generally decrease mobility (obesity and comorbidity) [15]. Thus, it appears that it is not very important to consider the effect of these variables on pain and physical functioning in the decision process on the individually appropriate osteosynthesis.

Generalizability

We recruited patients only in one urban level I trauma center. This might reduce the generalizability of our results because the patient population might be different in other regions and other centers.

We applied broad inclusion criteria and our center covers a broad urban as well as rural catchment area. Therefore, it can be assumed that our patient population is quite representative for the “general” lower limb fracture population regarding cause of accident, patient characteristics and fracture characteristics [4, 17]. Moreover, we cannot exclude that the results may vary between different centers. We believe that center associated variables (e.g. surgical skills) probably have an effect on absolute failure rates but have only little effect on the relative risks for a factor (e.g. the relative risk of open factures across different centers is similar). However, in particular, time to surgery could have an influence on results and might differ in other countries and less urban regions.

But even larger cohorts will likely not provide information that will allow for clear cut clinical decisions, i.e. data that do provide true decision support for the surgeon, because what is considered a predictive factor is based on a ‚negative‘ statement, i.e. predictive factors are used to identify constellations that might prevent the success of a therapeutic strategy. Predictive factors do tell the surgeon what better not to do in a given constellation.

Conclusion

In this prospective cohort study, we found preoperatively measurable factors, which appear promising for predicting the failure risk of an internal osteosynthesis in a traumatic lower limb fracture. In particular, obesity and open fractures increased the risk of failure. In addition, older age, female gender and peripheral arterial disease tend to increase the failure rate. Our results suggest that the combination of a few patient characteristics (e.g. age, BMI, morbidity), localization of the fracture and severity of the fracture might be candidates to predict failure, because they are predictive across different types of fractures at the lower limb Considering the diversity of fractures and fracture classifications, a formalized computer based risk classification could probably increase reliability and feasibility of using fracture related information for predicting failure, which is sufficient to support clinical decision making. A mobile device based risk prediction model combining patient characteristics and such computer processed fracture information (e.g. x-ray data), might enable the estimation of the precise individual risk at bedside and would therefore be a convenient tool for routine use.

Abbreviations

BMI: Body-Mass-Index

Declarations

Funding

This research received funding from the internal grant program (project PreFac) of the Faculty of Health at Witten/Herdecke University, Germany.

Conflicts of interest/Competing interests

All authors declare that they have no competing interests.

Availability of data and materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Code availability

Not applicable.

Authors' contributions

TM, BP and BB were involved in study design. BP, TT and TM were involved in analyses and interpretation of data and drafting of the article. BP, AG, AP and DRA were involved in data acquisition and critical revision of the article. TT, CP and BB were involved in critical revision of the article.

Ethics approval

The study was approved by the ethic committee of University Witten/Herdecke. The study was performed in agreement with the Declaration of Helsinki and ICH-GCP.

Consent to participate

Written informed consent was received from all participants prior to inclusion.

Consent for publication

Not applicable.

Acknowledgements

None.

References

1. Hoffmann MF, Jones CB, Sietsema DL, Tornetta P, 3rd, Koenig SJ: **Clinical outcomes of locked plating of distal femoral fractures in a retrospective cohort**. *J Orthop Surg Res* 2013, **8**:43.
2. Ricci WM, Streubel PN, Morshed S, Collinge CA, Nork SE, Gardner MJ: **Risk factors for failure of locked plate fixation of distal femur fractures: an analysis of 335 cases**. *J Orthop Trauma* 2014, **28**(2):83-89.
3. Rodriguez EK, Boulton C, Weaver MJ, Herder LM, Morgan JH, Chacko AT, Appleton PT, Zurakowski D, Vrahas MS: **Predictive factors of distal femoral fracture nonunion after lateral locked plating: a retrospective multicenter case-control study of 283 fractures**. *Injury* 2014, **45**(3):554-559.
4. Zura R, Xiong Z, Einhorn T, Watson JT, Ostrum RF, Prayson MJ, Della Rocca GJ, Mehta S, McKinley T, Wang Z *et al*: **Epidemiology of Fracture Nonunion in 18 Human BonesEpidemiology of Fracture Nonunion in 18 Human BonesEpidemiology of Fracture Nonunion in 18 Human Bones**. *JAMA Surgery* 2016, **151**(11):e162775-e162775.
5. Henry P, Wasserstein D, Paterson M, Kreder H, Jenkinson R: **Risk Factors for Reoperation and Mortality After the Operative Treatment of Tibial Plateau Fractures in Ontario, 1996–2009**. *J Orthop Trauma* 2015, **29**(4):182-188.
6. O'Halloran K, Coale M, Costales T, Zerhusen T, Jr., Castillo RC, Nascone JW, O'Toole RV: **Will My Tibial Fracture Heal? Predicting Nonunion at the Time of Definitive Fixation Based on Commonly Available Variables**. *Clin Orthop Relat Res* 2016, **474**(6):1385-1395.
7. Pincus D, Veljkovic A, Zochowski T, Mahomed N, Ogilivie-Harris D, Wasserstein DJJoot: **Rate of and risk factors for intermediate-term reoperation after ankle fracture fixation: a population-based cohort study**. *J Orthop Trauma* 2017, **31**(10):e315-e320.
8. Schemitsch LA, Schemitsch EH, Kuzyk P, McKee MDJJoot: **Prognostic factors for reoperation after plate fixation of the midshaft clavicle**. *J Orthop Trauma* 2015, **29**(12):533-537.
9. Thevendran G, Wang C, Pinney SJ, Penner MJ, Wing KJ, Younger ASE: **Nonunion Risk Assessment in Foot and Ankle Surgery: Proposing a Predictive Risk Assessment Model**. *Foot & Ankle International* 2015, **36**(8):901-907.
10. Westgeest J, Weber D, Dulai SK, Bergman JW, Buckley R, Beaupre LAJJoot: **Factors associated with development of nonunion or delayed healing after an open long bone fracture: a prospective cohort study of 736 subjects**. *J Orthop Trauma* 2016, **30**(3):149-155.
11. Riley RD, Hayden JA, Steyerberg EW, Moons KGM, Abrams K, Kyzas PA, Malats N, Briggs A, Schroter S, Altman DG *et al*: **Prognosis Research Strategy (PROGRESS) 2: prognostic factor research**. *PLoS medicine* 2013, **10**(2):e1001380-e1001380.
12. Vittinghoff E, McCulloch CE: **Relaxing the Rule of Ten Events per Variable in Logistic and Cox Regression**. *American Journal of Epidemiology* 2007, **165**(6):710-718.
13. Pavlou M, Ambler G, Seaman SR, Guttmann O, Elliott P, King M, Omar RZ: **How to develop a more accurate risk prediction model when there are few events**. *BMJ* 2015, **351**.
14. Perry WM, Hossain R, Taylor RA: **Assessment of the Feasibility of automated, real-time clinical decision support in the emergency department using electronic health record data**. *BMC Emergency*

Medicine 2018, **18**(1):19.

15. Mathes T, Pape-Köhler C, Moerders L, Lux E, Neugebauer EAM: **External Validation and Update of the RICP—A Multivariate Model to Predict Chronic Postoperative Pain**. *Pain Medicine* 2017, **19**(8):1674-1682.
16. Glare P, Aubrey KR, Myles PS: **Transition from acute to chronic pain after surgery**. *The Lancet* 2019, **393**(10180):1537-1546.
17. Higgins TF, Klatt JB, Beals TC: **Lower Extremity Assessment Project (LEAP) – The Best Available Evidence on Limb-Threatening Lower Extremity Trauma**. *Orthopedic Clinics of North America* 2010, **41**(2):233-239.

Figures

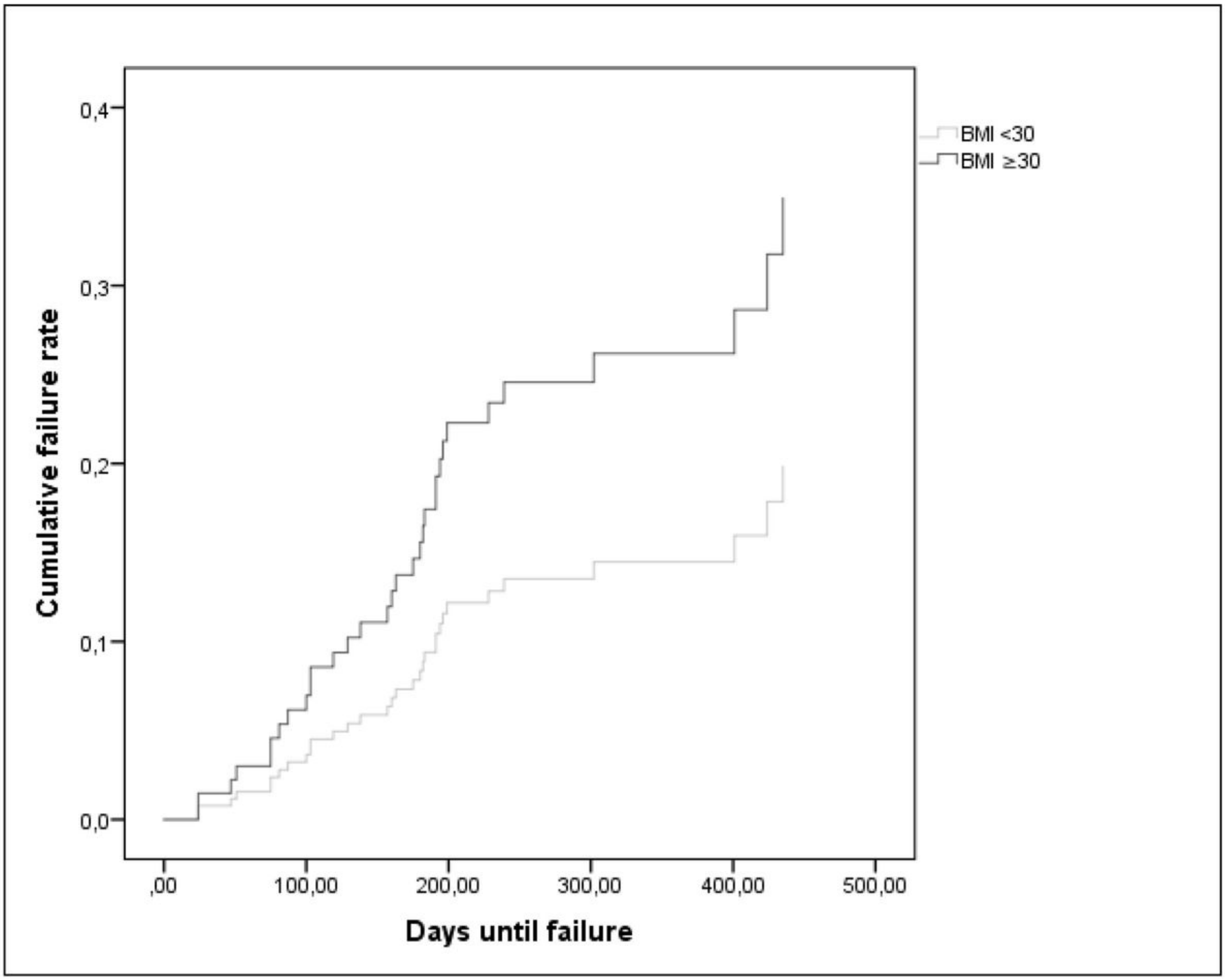

Figure 1

survival plot for BMI

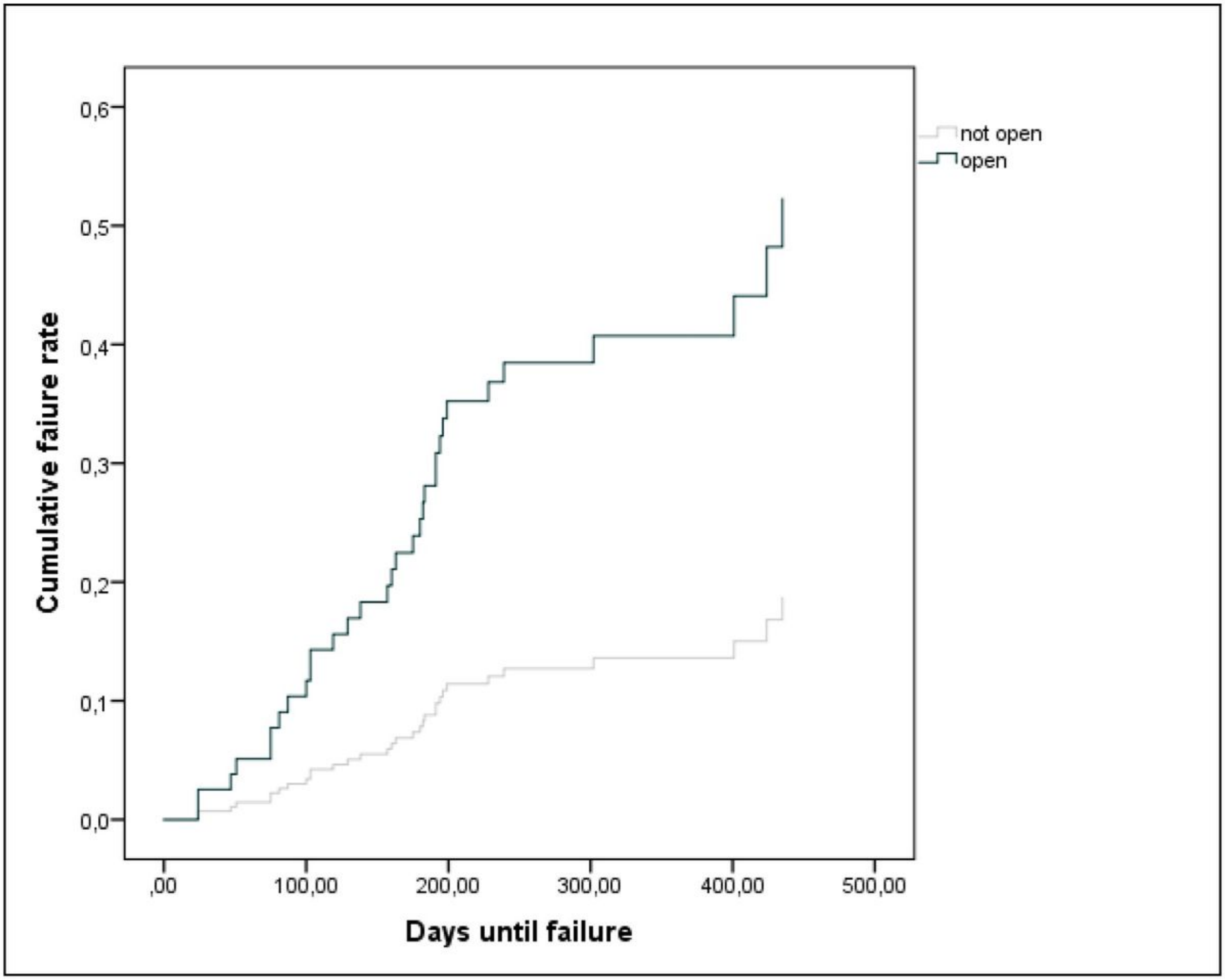

Figure 2

survival plot for open fracture