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Early operative versus non-operative treatment of fragility fractures of the pelvis – a propensity matched multicenter study

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Abstract

Objective: To compare early operative treatment with non-operative treatment of fragility fractures of the pelvis regarding mortality and functional outcome.

Design: Retrospective

Setting: Two trauma centers

Patients and Methods: 230 consecutive patients 60 years of age or older with an isolated low-energy fracture of the pelvis and with a follow-up of at least 24 months. In center 1, treatment consisted of a non-operative attempt and early operative fixation if mobilization was not possible. In center 2, all patients were treated non-operatively.

Main Outcome Measurements: Primary outcome was mortality. Secondary outcomes were in-hospital complications. Patients that survived were contacted by phone and a modified Majeed Score was obtained to assess functional outcome at final follow-up

Results: At final follow-up (mean 61 months, SD 24), 105/230 (45.7 %) patients had died. One year after the initial hospitalization 34/148 patients (23%, 95% CI: 17% to 31%) of the ear1y operative group and 14/82 patients (17%, 95% CI 10% to 27%) of the non-operative group had died (p=0.294). Non-operative treatment had a protective effect on survival during the first two years (hazard ratio of the non-linear effect: 2.86, 95% CI 1.38 to 5.94, p<0.001). Patients in the early operative treatment group who survived the first two years, had a better long-term survival. The functional outcome at the end of follow-up as measured by a modified Majeed score was not different between the two groups (early operative: 66.1, SD 12.6 vs. non-operative: 65.7, SD 12.5, p=0.910).

Conclusion:

Early operative fixation of patients who cannot be mobilized within three to five days was associated a higher mortality rate and complication rate at 1 year but with a better long-term survival after more than two years. Hence, patients with a life expectancy of less than 2 years may not benefit from surgery with regard to survival.

Level of Evidence: III

Key Words: pelvis fractures; fragility fractures; osteoporosis; mortality; operative treatment; complications; outcome; aged.

Introduction

Fragility fractures of the pelvis (FFP) have had an increased incidence within the geriatric population. They frequently are a result of a low energy trauma in the presence of osteoporosis [1]. The mean cumulative risk of sustaining a pelvis fracture between the age of 65 and 90 years is 6.9 % in women and 2.8 % in men. It is likely that the incidence of FFPs will triple during the next 20 years [2,3].

Most of these fractures are stable and can be successfully treated by non-operative treatment [4]. However, all-cause mortality and in-hospital complications reported for non-operative treatment of FFP can be as high as from hip fractures [5–7]. Hence, especially percutaneous surgical techniques have been suggested as a valuable alternative to non-operative treatment [8–10]. Operative treatment is thought to reduce pain and to facilitate mobilization in patients with FFPs [11,12]. Even though complications and overall mortality remain high among geriatric patients with a FFP when treated operatively [13], a benefit of surgical over non-operative treatment with regard to mortality has been suggested [14]. However, most studies on this topic did not account for the selection bias frequently seen with comparisons of operative and non-operative treatment in elderly patients: it is often the patients' morbidity that triggers the decision for non-operative treatment and not the other way around.

The aim of this study was to compare non-operative treatment to early operative intervention with respect to mortality and functional outcome. Our hypothesis was that early operative fixation of patients who cannot be mobilized within three to five days would have a beneficial effect on survival.

Materials and Methods

Patients

This retrospective multicenter propensity matched case-control study with a prospective follow-up was approved by the local ethics committee (Kantonale Ethikkommission Zürich, Switzerland. KEK-ZH-Nr. 2017-01440).

Based on previous studies we estimated the 1-year mortality in the non-operative group to be around 24 % [15]. Assuming a decrease in 1-year mortality down to 15 % and aiming for an 80% power one would need to include 237 patients in the study.

391 consecutive patients 60 years of age or older who were treated for a low-energy fracture in one of the two study centers between 01/2008 and 12/2015 were evaluated. Patients who had concomitant fractures of the acetabulum or the lower extremity, who were not included by the national social insurance mortality database (e.g. tourists) or who had expressed objection to the use of their data for research purposes were excluded (Patient flow chart, Figure 1). In addition, patients who were by language or cognitive impairment not able to understand the Majeed questionnaire were excluded from the functional outcome assessment. All patients evaluated required a minimum of 24 months follow-up.

Intervention

Two treatment concepts were compared: In center 1 (*early operative group*), treatment consisted of an initial non-operative attempt including analgesic medication including opioids and physiotherapy without weight-bearing restrictions. If patients were not able to ambulate with a walker or crutches under analgesic medication within three to five days, early operative fixation was performed. As a standard, sacral fractures were addressed by percutaneous sacro-iliac screw fixation, if possible in S1 and S2 (6.5-cannulated steel screws) [9,10]. In case of bilateral sacral fractures, bilateral sacro-iliac screws were placed in S1 and S2 or spino-pelvic posterior instrumentation was performed. If displaced more than a shaft width or if the patient reported localized inguinal pain, anterior ring fractures were stabilized by either plate or ramus screw fixation and in case of comminution of the anterior pelvic ring a subcutaneous internal anterior fixation (INFIX) was used. Open reduction and plate fixation was reserved for fractures with gross displacement.

In center 2 (*non-operative group*), all patients were treated non-operatively by means of analgesic therapy including opioids and physiotherapy. This regimen mainly included an early mobilization accompanied and carefully instructed by the physiotherapist. Full weight bearing was never restricted. Depending on the level of pain, mobilization was initiated with a walker and advanced to crutches or cane. Whenever possible, patients were also mobilized on an anti-gravity treadmill (AlterG, Fremont, CA, USA) for 30 minutes per day.

Outcome

Primary outcome was mortality. In addition to a time-to-event approach of mortality at last follow-up, 1-year and 2-year mortality were assessed. Survival status was retrieved from a national social insurance mortality database (Alters- und Hinterlassenen-Versicherung) that provides survival data for each permanent resident in Switzerland.

Secondary outcomes were in-hospital complications including hospital-acquired infections (e.g. pneumonia and urinary tract infections), thromboembolic events, postoperative delirium and duration of the hospitalization. Those patients that had survived were contacted by phone and a modified Majeed Score was obtained to assess functional outcome at final follow-up [13,16,17].

Statistical Analysis

Statistical analysis was performed with R for windows 3.5.0 [18]. Descriptive statistics included mean and standard deviation (SD) for the continuous variables, median and interquartile range (IQR) for ordinal variables, as well as number and percentage of total for the categorical variables.

Kaplan-Meier plots were used to visualize the survival probability in both treatment groups. Median survival and median follow-up times were displayed including 95% confidence intervals (CI). If Kaplan-Meier curves crossed, time-varying treatment effects were assumed. To quantify the effect of the non-operative treatment, Cox proportional hazard models were fitted. Time-varying treatment effects of non-operative treatment were assumed to be non-linear over time, $g(t) = \log(t+1)$. The treatment regime might have been influenced by factors such as age, gender, or American Society of Anesthesiologists Classification (ASA) [19], therefore these variables were accounted for in the analysis through the estimation of a propensity score. Propensity score matching is a statistical technique that tries to estimate the effect of an intervention by accounting for covariates that may predict receiving the treatment. This is done by adjusting for potential confounders that were found by simply comparing outcomes among patients that received the treatment versus those that did not.

In a first approach, the treatment effect was estimated without any adjustment for confounding. In a second approach, the propensity score was used to adjust for confounding in the Cox model, in a third approach the propensity score was used for matching each patient with early operative treatment to a patient with non-operative treatment. Balance after matching was assessed using the standardized mean difference (SMD). The SMD is a statistical parameter measuring effect sizes and is defined as the mean divided by the standard deviation of a difference between two random values each from one of two groups. If the SMD is < 0.1, the variable can be considered balanced across treatment groups [20].

Results of the Cox models are presented graphically, with estimated hazard ratios, 95% CIs, and p-values. Missing data were reported as such for each outcome parameter.

The study was reported according to the STROBE guidelines for observational studies.

Results

In total, 230 patients with a mean age of mean 81 years (range, 60 to 98 years) were included in the final analysis (Patient flow chart, Figure 1). Of the 230 patients, 148 patients were included in the early-operative group and 82 in the non-operative treatment group. Early operative fixation was performed in 60/148 (41%) of the patients in the early operative treatment group, for the rest the initial non-operative attempt was successful and continued. Of the 60 patients eventually treated by operative fixation, 33 received unilateral percutaneous sacro-iliac screw fixation and 24 bilateral sacro-iliac screw fixation. Two patients were stabilized by posterior spino-pelvic instrumentation and two by posterior plate fixation. The anteriopr pelvic ring was stabilized by plate fixation through a modified Stoppa approach in 8 cases, by ramus screws in 5 cases, and by an INFIX in 4 cases. Most of the patients in both groups were female (81% and 89%, respectively). Forty-four percent of the patients in the non-operative and 52 % of the early-operative had an ASA score greater than 3 ($p=0.297$, Table 1).

The median follow-up time was longer for patients in the early operative group (69 months, 95%CI: 60 to 85 months) than for patients in the non-operative group (44 months, 95% CI: 41 to 53 months).

Unadjusted comparison of secondary outcomes

Patients in the early-operative group were hospitalized for mean 12 days (SD 9) compared to the non-operative group with 8 days (SD 4, $p<0.001$). Thirty-six of 148 patients in the early-operative group (24%) and 19 (23%) in the non-operative group were able to return to home.

Complications during the hospitalization were more likely to occur in the early operative group compared to the non-operative group ($p=0.005$, Table 2).

Mortality

At final follow-up (mean 61 months, SD 24), 105/230 (45.7 %) patients had died. One year after the initial hospitalization 34/148 patients (23%, 95% CI: 17% to 31%) of the early operative group and 14/82 patients (17%, 95% CI 10% to 27%) of the non-operative group had died (p=0.294).

Kaplan-Meier analysis of the unadjusted survival status in the early operative and the non-operative treatment group showed a crossing of the survival curves at two years (Figure 2).

Hence, the time varying treatment effect was calculated in three different ways: without adjustment, with propensity-score adjustment and with matching. The matched sets of patients were balanced with respect to SMD (SMD < 0.1). Details can be found in Table 1, Figure 3 shows the estimated treatment effects for non-operative treatment.

Non-operative treatment was associated with better survival during the first two years. However, patients in the early operative treatment group who survived the first two years, had a better long-term survival. This means that survival was better in the non-operative group during the first two years and worse after that.

Functional outcome

To determine the functional outcome at final follow-up up (mean 61 months, SD 24), a modified Majeed score was used (maximum achievable points was 76). Forty (27%) of the patients with early operative treatment and 15 (18%) of the patients with non-operative treatment were available for final follow-up assessment of the Majeed score. On average, the Majeed score was 66.1, SD 12.6 (87 % of achievable maximum) for the early operative group and 65.7, SD 12.5 (86 % of achievable maximum) for the non-operative group (p=0.910).

Discussion

The aim of this study was to compare non-operative treatment of FFPs to early operative intervention with respect to mortality and functional outcome. Our hypothesis, that early operative fixation of patients who cannot be mobilized within three to five days would have a beneficial effect on 1-year survival was not confirmed. The survival rates were similar during the first two years. However, in those patients who survived the first two years, early operative treatment was associated with a better long-term survival. In those patients surviving, no difference in functional outcome was seen at final follow-up.

This study compared all-cause mortality rates of geriatric patients with FFPs over a period of more than 3 years. There are numerous factors that can have influence on the survival of such patients, in particular at this age and with the number of comorbidities known to be associated with fragility fractures [21]. There are few things, though, that have more impact on disability, morbidity and mortality of elderly patients as the ability to walk [22].

A therapy that could reduce pain after FFPs, accelerate mobilization and improve gait would therefore have a major beneficial effect on survival. Indeed, and in line with previous studies this study found a better survival in operatively treated patients in the long run [14]. However, the mortality in the *early operative group* remained high within the first two years and was even higher when compared to the *non-operative group.*

Previous studies on non-operative treatment of pelvis fractures report mortality rates of 13 % at 3 months [6] and 54 % at 5 years [7]. These numbers are consistent with the findings of our study. The higher mortality in the early operative group may be explained by perioperative risks associated with anesthesia and surgery in elderly people. In line with this, 52 % of the early-operative group had an ASA score greater than 3. Still, the 2-year mortality was higher than described by Höch et al. for their cohort of operatively treated patients with FFP (Höch et al. 2017). However, this study is the first one with a 100 % follow-up for mortality data as we had access to the complete national social insurance mortality database.

The limitations of this study are inherent with its retrospective study design. Hence, it mainly reports associations and not necessarily causations. It was sought to compensate for this by adjusting for potential confounders as age, gender and prevalent morbidity by conducting a propensity score matched analysis. The ASA classification may be an imprecise instrument to fully depict a patient's comorbidities. It is a very well validated instrument to predict perioperative mortality, however [19]. Hence, it was chosen as a surrogate parameter for matching. However, the crossing of survival curves indicating better survival of the early operative group after more than two years could be a result of other confounding factors that we did not account for. It, still, may be that the perioperative and delayed complications after operative treatment have a longer-lasting effect that is being overcome by the benefits of better mobility only after two years.

The effect of operative stabilization may be small but relevant in the long run. An increased risk for falling or even just a decreased gait speed due to sacral pain are known to be associated with a higher mortality [22]. This may have an impact on mortality even after two years.

As frequently seen in studies on geriatric populations, the follow-up rate of the functional outcome was low - in part due to the fact that 45.7 % of the patients had deceased at the time of final follow-up. This limits our conclusions on functional outcome. The primary outcome of this study, however, was not functional outcome but survival. For the mortality data we could provide a 100 % follow-up as we had access the national social insurance data. We also did not assess the effect of the two treatment concepts on early functional outcome and pain nor on quality of life. The quality of any treatment algorithm must be judged by parameters beyond mortality and complications only. The results of this study justify future prospective comparative trials in order to confirm the long-term effect of early operative fixation of FFPs.

Conclusion

Early operative fixation of patients who cannot be mobilized within three to five days was associated a higher mortality rate and complication rate at 1 year but with a better long-term survival after more than two years. Hence, patients with a life expectancy of less than 2 years may not benefit from surgery with regard to survival.

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Figure legends

Figure 1 Patient flow chart

Figure 2 Kaplan Meier plots of survival probabilities in patients with early operative and non-operative treatment regime.

Number at risk are given for both groups. Time is measured in years.

Figure 3 Time-varying treatment effect of non-operative treatment.

Black solid line represents the unadjusted treatment effect, dotted line indicates the propensity-score adjusted treatment effect, and the dashed line represents the time-varying effect estimated from the 82 pairs of matched patients with early operative and non-operative treatment. The hazard ratio of the non-linear effect was 2.86 (95% CI 1.38 to 5.94, p<0.001).

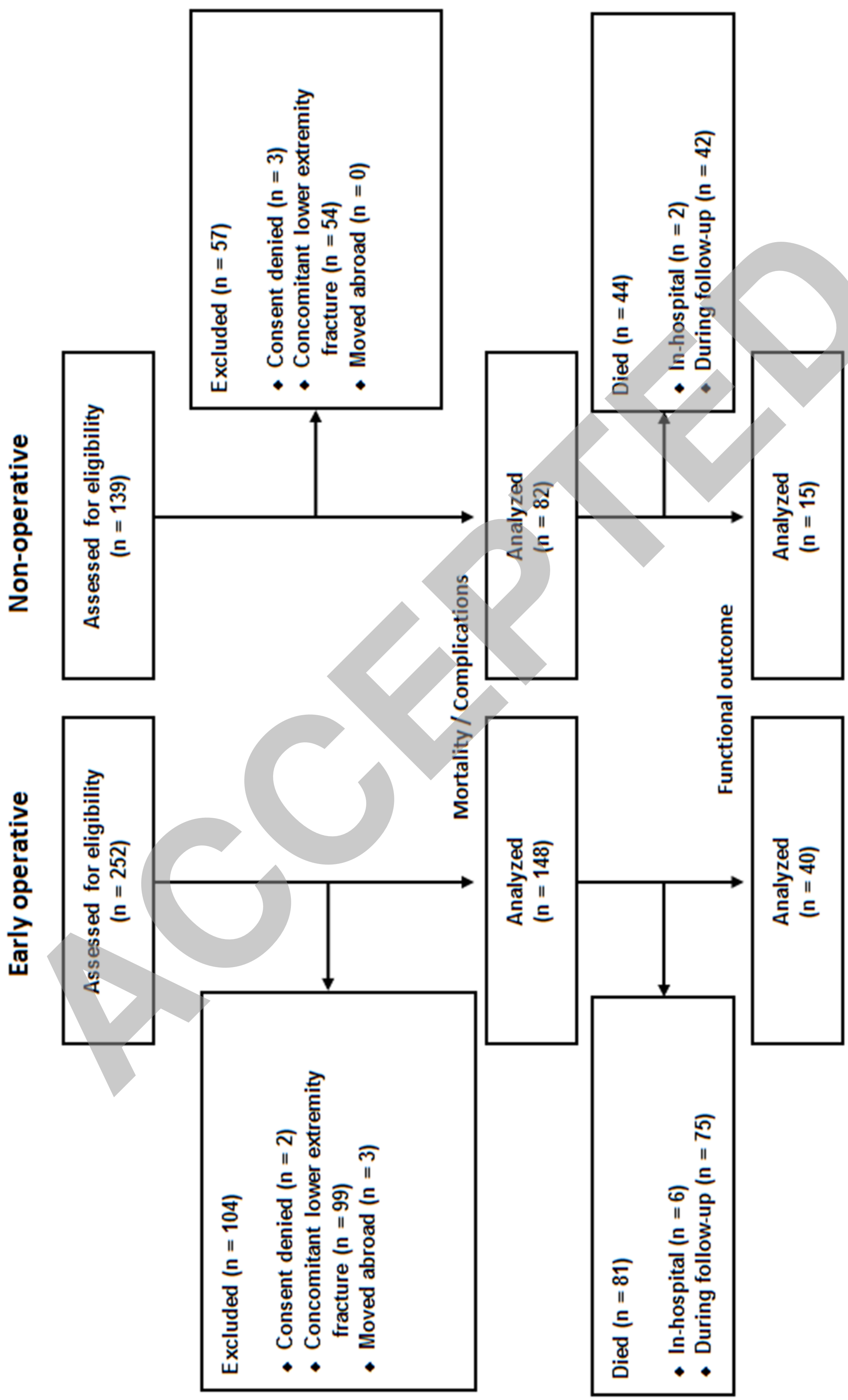
Table 1 Baseline characteristics

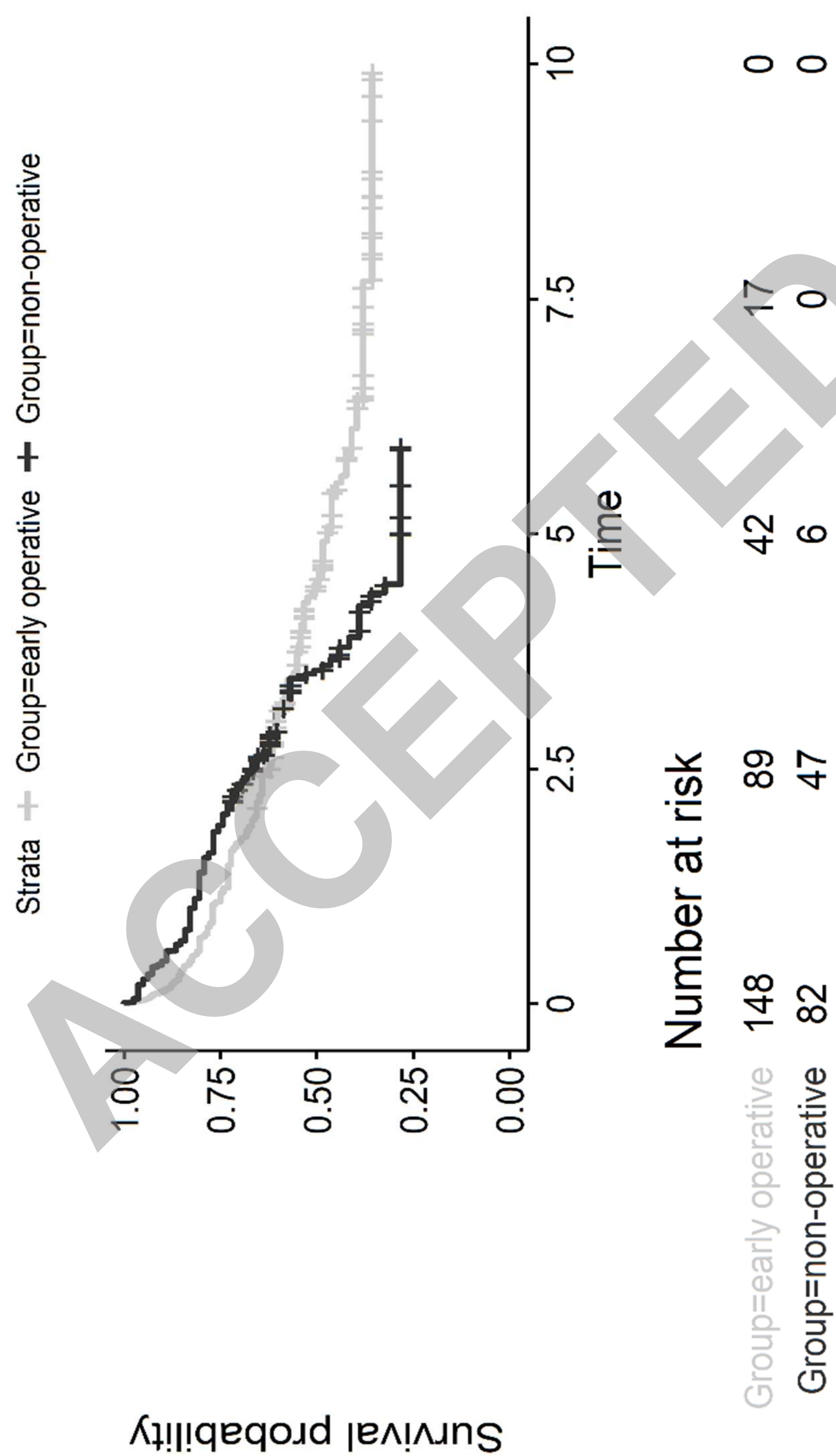
	Before matching			After matching[1)]		
	Early operative	Non-operative	p	Early operative	Non-operative	SMD[2)]
n	148	82		82	82	
Age (mean, SD)	79.66 (9.25)	84.43 (6.20)	<0.001	84.77 (5.93)	84.43 (6.20)	0.056
Gender female, n (%)	120 (81.1)	73 (89.0)	0.167	71 (86.6)	73 (89.0)	0.075
ASA (median, interquartile range)	3 [2, 3]	2 [2, 3]	0.165			
ASA ≥ 3, n (%)	77 (52.0)	36 (43.9)	0.297	40 (48.8)	36 (43.9)	0.098

1) Propensity score-matched for age, gender, ASA ≥ 3; 2) SMD = standardized mean difference, if < 0.1 variables are assumed balanced.

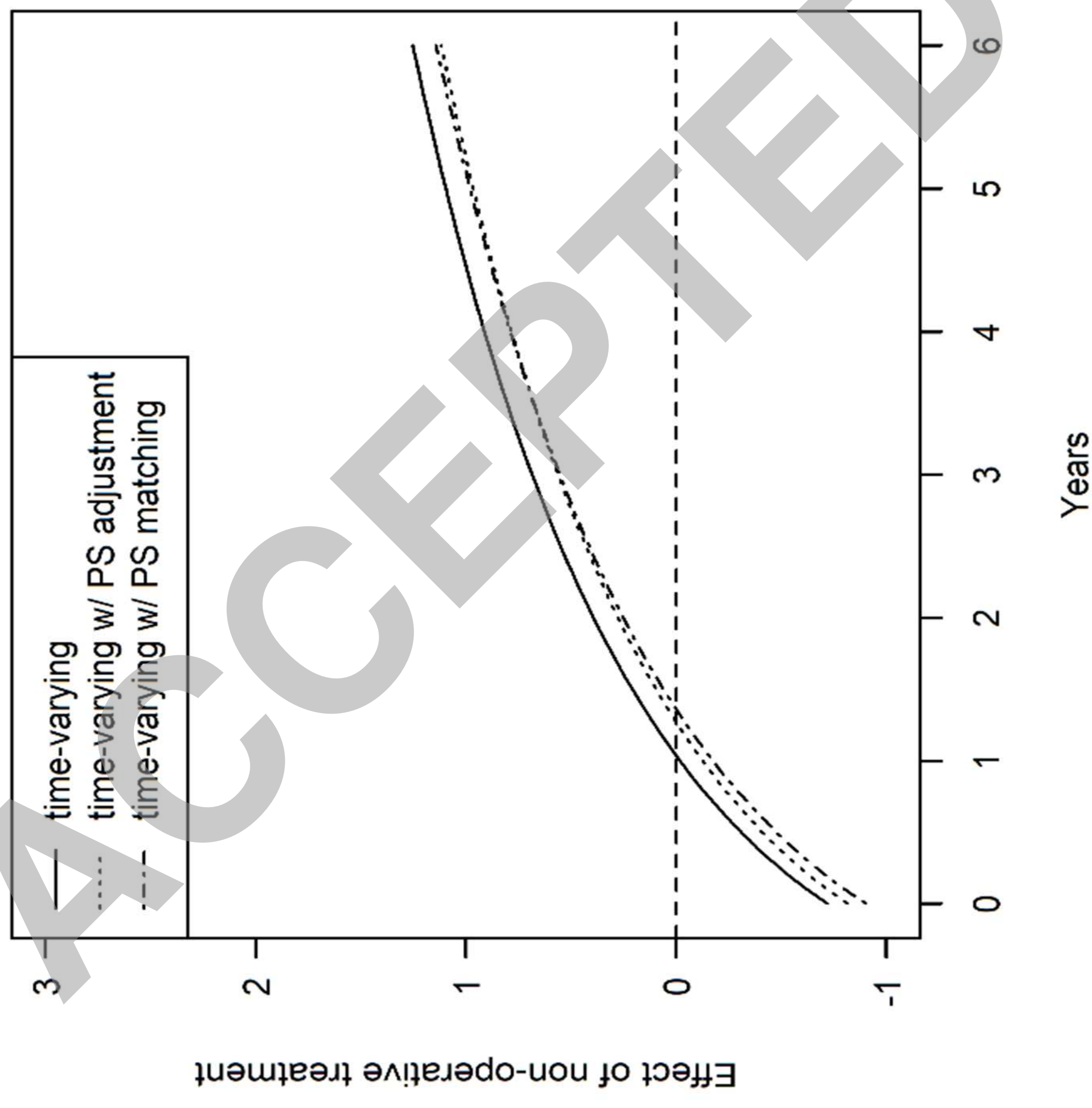
Table 2 Secondary outcomes

	Early operative	Non-operative	p
n	148	82	
Inhospital complications, n (%)	51 (34.5)	14 (17.1)	0.008
Infection, n (%)	37 (25.0)	11 (13.4)	0.057
Thromboembilic event, n (%)	3 (2.0)	0 (0.0)	0.49
Delirium, n (%)	14 (9.5)	1 (1.2)	0.032
Death, n (%)	6 (4.1)	2 (2.4)	0.791
Mod. Majeed score (mean, SD)	66.1 (12.6)	65.7 (12.5)	0.91


Early operative
Non-operative
Assessed for eligibility (n = 252)
Assessed for eligibility (n = 139)
Excluded (n = 104)
Consent denied (n = 2)
Concomitant lower extremity fracture (n = 99)
Moved abroad (n = 3)
Excluded (n = 57)
Consent denied (n = 3)
Concomitant lower extremity fracture (n = 54)
Moved abroad (n = 0)
Mortality / Complications
Analyzed (n = 148)
Analyzed (n = 82)
Died (n = 81)
In-hospital (n = 6)
During follow-up (n = 75)
Died (n = 44)
In-hospital (n = 2)
During follow-up (n = 42)
Functional outcome
Analyzed (n = 40)
Analyzed (n = 15)



Strata
Group=early operative
Group=non-operative
Survival probability
1.00
0.75
0.50
0.25
0.00
0
2.5
5
7.5
10
Time
Number at risk
Group=early operative 148 89 42 17 0
Group=non-operative 82 47 6 0 0
ACCEPTED


time-varying
time-varying w/ PS adjustment
time-varying w/ PS matching
Years
Effect of non-operative treatment
0
1
2
3
4
5
6
-1
0
1
2
3