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PROGNOSTIC FACTORS FOR MORTALITY AFTER HIP FRACTURE: OPERATION WITHIN 48 HOURS IS MANDATORY

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Abstract

The aim of this study was to assess if surgery delay and other variables are associated to an increased mortality rate after surgical treatment of hip fractures in the elderly. Patients treated for a proximal femoral fracture between 2005 and 2012 at our Orthopaedic Department were included in this study. A logistic regression was performed to evaluate the relationship between mortality rate at different follow-up (30 days, six months and one year) and different patients' or treatment variables. 1558 consecutive patients were enrolled in this study (mean age 80.3 years, 75.8% female). The mortality rate was 4% at 30-day, 14.1% at six-month, and 18.8% at one year after surgery. The logistic regression revealed an increased mortality at all the end-points in patients affected by more than two co-morbidities (respectively $OR_{30\text{-}day}$=2.003, $OR_{6\text{-}month}$=1.8654 and $OR_{1\text{-}year}$=1.5965). Male gender was associated to an increased six-month (OR=1.7158) and one-year (OR=1.9362) mortality. Patients younger than 74 years old had a decreased mortality at all end-points ($OR_{30\text{-}day}$=0.0703, $OR_{6\text{-}month}$=0.2191 and $OR_{1\text{-}year=}$0.2486). In this study the surgery delay influenced mortality at one-year follow-up: operating within 48 hours was associated to a decreased mortality rate (OR=0.7341; p=0.0392). Additionally the patients that were operated within 72 hours were specifically analyzed in order to understand if the option of 'operating within day 3' was acceptable. In the logistic regression, operating between 48 and 72 hours was not reported as a risk factor for mortality, both compared to early surgery (within 48 hours) and to late surgery (after 72 hours).
This study showed that age, gender and number of co-morbidities influenced both early and late mortality in patients affected by proximal hip fractures. Early surgery influenced late mortality, with a decreased risk in patients operated within 48 hours. The option of operating within day 3 is not a valid alternative.

Introduction

The incidence of hip fractures in the elderly is high (over 120/100.000 inhabitants per year in the USA and in the EU), and it has been estimated an overall 29.8% increase between 2000 and 2009 [1]. The rate of hospitalization of these patients has been reported of about 93%, with women older than 75 years old accounting for 60% of all proximal femoral fractures [2]. In literature the mortality rate of hip fractures in elderly patients is reported as high as 20 to 40% within one year after surgery, despite the recent anesthesiologist and surgical advancements [3].

Given the severe limitations due to prolonged immobilization and poor return to deambulation in case of non-surgical treatment, for almost all patients, a surgical management is required to reduce the immobilization time and to improve the quality of life. Several study focused on the prognostic factors that could affect the mortality rate: age, gender, co-morbidity, post-operative complications, surgical treatment and delayed post-operative mobilization [4]. There is still a debate on literature about the potential effect of surgical delay on mortality rate after hip fractures. The paper published by Zuckerman et al in 1995, is a milestone on this topic: they reported the mortality rate of 367 hip fractures and concluded that an operative delay of more than 48 hours was a predictor of mortality within one year from surgery in elderly patients affected by hip fracture [5]. Other authors subsequently confirmed that a delay between two and four calendar days is associated with an increased mortality in patients affected by a hip fracture [3, 6-14]. Additionally, different studies underlined the importance on medical conditions, patient age and sex despite the surgery delay as predictors of mortality [4, 15-23]. Unfortunately it is often difficult to reduce the surgery delay, both because of patient's conditions and for lack of resources. Today however, there is still a lack of definitive data on the association between surgical delay and increased mortality rate.

Our primary aim in this study was to analyze the relationship between surgical delay and both early (30-days) and late (1 year) mortality, in order to assess if delayed surgery could be a negative prognostic factor in elderly affected by a proximal femoral fracture. The second goal of this study was to analyze the role of other prognostic factors, such as age, gender, medical co-morbidities and other surgery-related variables.

Materials and methods

We retrospectively reviewed our hospital database and electronic medical records of all the patients affected by proximal femoral fractures who were admitted to our center between January 2005 and December 2012. We collected patient's records (age, gender, co-morbidities and ongoing therapy) and data regarding the surgery (bilateral concomitant or subsequent fracture, fracture's morphology and treatment, surgery delay, post-operative protocol and failure of the implant). Patient's survivorship was assessed according to the National Population Registry that was checked in April 2014 for all patients. Exclusion criteria were pathological femoral fractures, peri-prosthetic fractures and distal femoral fracture. Furthermore, patients with incomplete information on the registries were excluded from the study. Patients were divided into younger or older than 74 years old, based on the widely used definition of elderly [24]. The surgery delay was grouped into three main groups: within 48 hours, within 72 hours and after 72 hours. Fracture morphology was divided into intra or extra-capsular fracture and we grouped the different treatments into synthesis (intramedullary nail, cannulated screws, sliding screw-plate devices) and replacement (total or partial hip replacement). Finally we grouped the post-operative protocols into patients with full weight-bearing protocol and those with no or partial weight bearing for the first postoperative month.

Statistical analyses

All the data were collected into an Excel ® (Microsoft, Redmond, WA) spreadsheet, and descriptive statistical analysis was used for averages and standard deviations (SD). The MedCalc®

(MedCalc Software, Ostend, Belgium) was used for statistical analysis investigating the cumulative survivorship that was calculated using the Kaplan-Meier method, and logistic regression of the single variables.

The variables were divided into three main groups: patient's variables (age, gender, co-morbidities and ongoing anti-coagulant therapy), treatment's variables (bilateral fracture, type of treatment, surgery delay) and post-operative's variables (failure and post-operative protocol).

T-test and Chi-squared test were used to analyze any differences both in parametric and non-parametric data. All the variables were tested with a simple regression to assess any correlation to the three main outcomes: thirty-day mortality, six-month mortality and one-year mortality. Only the variables with a $p<0.1$ at the simple regression test were retested into a logistic multiple regression, to exclude confounding variables. The relative odds ratios (OR) was considered statistical significant with $p<0.05$, and relative confidential intervals (CI) was reported.

Results

1734 proximal femoral fractures were admitted to our hospital for a hip fracture between 1st January 2005 and 31th December 2012. However, after exclusion of pathologic fractures, distal femoral fractures, peri-prosthetic fractures and patients with incomplete information on the registries, 1558 proximal femoral fractures in 1448 patients (55 bilateral) were included in the study (123 excluded from the study, 53 lost to follow-up because of incomplete information 3.1% of total). Of the 176 patients excluded from the study, 29 (1.7%) did no undergo surgery because of severe co-morbidities. Considering the small proportion of these patients, our results cannot be affected by their exclusion.

The mean age of included patients was 80.3 years (SD +/- 11.9, range 32-101), with 80.5% of patients older than 75 years old. There were 1098 women (75.8%) and 350 men (24.2%).

43.1% of patients have any co-morbidity, as reported in Tab.1, and 7.6% of patients were under anticoagulant therapy. Regarding the fracture morphology and its treatment, 52.8% had an intra-capsular (medial) fracture, while 47.2% had an extra-capsular (lateral) fracture. Table 2 reports the different surgical treatments and its grouping into two main subgroups: synthesis and replacement.

13.3% of patients underwent surgery within 24 hours, 33.2% within 48 hours and 36.1% after 96 hours. The most frequent reason for delaying (in 265 patients, 17.1%) was a medical co-morbidity that required treatment prior to surgery.

After surgery 55.1% of patients were allowed to walk with complete weight-bearing, while 30.7% were restricted to partial weight-bearing and 14.2% of patients were not allowed to walk for the first 30 post-operative days. The patients in whom a partial or total hip replacement was performed were allowed to weight-bearing from day 1, while some of the patients in which a synthesis was performed were under restricted or no weight-bearing because of fracture complexity. A revision of the implant was needed in thirty patients (1.9%), and it was mainly due to a peri-prosthetic fracture (8 patients, 26.7% of revision), or peri-prosthetic infection (5 patients, 16.7% of revision).

Statistical analysis of mortality rate and prognostic factors

The 30-day mortality rate was 4%, while the six-month mortality rate was 14.1% and it increased to 18.8% at one year after surgery. Fig 1 shows the different mortality rates occurring in relation to the surgery delays.

The cumulative survivorship, calculated with the Kaplan-Meier method, was 96% at 30 days after surgery (SD +/-0.005), and it decreased to 85.9% at six months (SD +/- 0.008) and 81.1% one year after surgery (SD +/- 0.009) (Fig. 2). Tab. 3 reports the mortality rate occurring at 30 days, six months and one year after surgery in correlation to different variables.

According to both simple and multiple logistic regression models, age, co-morbidities and type of surgical treatment had a significant impact on 30-days mortality. Specifically younger age and performing a synthesis were associated to a lower mortality risk (respectively $p= 0.0087$ and $p=0.002$) with respect to older age and hip replacement surgery. On the contrary, being affected by more than 2 co-morbidities was associated to an increased mortality risk mortality ($p=0.048$). Data were different both for six-month and one-year mortality, with gender, age and co-morbidities having a significant impact on mortality rate at both the end-points. Specifically male gender and having more than two co-morbidities were associated to a higher six-month mortality (respectively OR= 1.7158-$p=0.0011$ and OR= 1.8654-$p=0.028$), while younger age was associated to a lower mortality ($p<0.001$). Similarly male gender and having more than two co-morbidities were correlated to a higher one-year mortality (respectively OR= 1.9362-$p<0.001$ and OR= 1.5965-$p=0.0171$); on the contrary, younger age was correlated to a lower mortality ($p<0.001$). No statistically significant correlation was found between post-operative protocol (full, partial or no weight-bearing) and mortality rate.

The surgery delay had a significant impact on one-year mortality, with patients operated within 48 hours having a lower mortality risk ($p= 0.0392$). Analyses did not reveal any correlation between ongoing anticoagulant therapy or post-operative variables and mortality at all three end-points. Tab.4 summarizes the results of both simple and multiple regressions at the different end-points.

In order to find out the cutoff for acceptable surgery delay, the mortality of patients operated within 48 hours and 72 hours were compared, using again the linear and logistic regression. As shown in Tab. 5, the timing for surgery was evaluated twice; in a first analysis we included only patients operated within 72 hours, comparing those who underwent surgery within 48 hours to those who were operated in day 3 (between 48 and 72 hours). In the second part we evaluated only patients who underwent surgery after 48 hours, comparing those operated in day 3 with those patients who were admitted to surgery after 72 hours. As shown in the table, in both cases the surgery delay was not correlated to the mortality risk. With this result, in association to the one obtained from the first analysis, being operated within 48 hours resulted the only timing correlated to a lower mortality risk.

Discussion

This study has some limitations. Firstly it is an observational study, so it has not the accuracy that could be achieved with a randomized controlled trial. Besides there is no a priori protocol for determining the inclusion criteria for surgery, but they depended from clinicians. Finally we did not analyze the causes for surgery delay, so we actually are not able to determine if delays beyond 48 or 72 hours could be mainly associated to pre-existing medical co-morbidities that need to be assessed before surgery. However this bias is partially compensated by the logistic regression we performed, considering also the number of co-morbidities. Given these limitations, this study gathered some interesting findings.

1558 patients affected by hip fracture with an average age of 80.3 (SD +/- 11.9), and 77.6% of female patients were enrolled in this study. The co-morbidities were defined as described by Zuckerman et al [5] who included diabetes mellitus, cardiac disease, cerebro-vascular accident, renal disease, Parkinson disease and chronic obstructive pulmonary disease. Using this classification, 87.1% patients reported no or one co-morbidity, 10% two co-morbidities and only 2.9% three or more co-morbidities. These data are lower compared to those described by Zuckerman, and one explanation could be that we excluded ongoing anticoagulation therapy as co-morbidity itself, analyzing this factor as isolated. Besides, this data are a little bit different compared to those described by Dettoni et al in a similar population; this is probably due to a more detailed analysis of co-morbidities in our population, resulting in more groups and less patients for each of them [25]. In this study the average mortality rate was 4% within 30 days, 14.1% at six months and 18.8% at one year after surgery. These mortality rates were similar to values reported in literature, ranging between 14% and 22% [5, 26, 27]. The cumulative Kapan Meyer survivorship in this study was 96% at thirty days, 85.9% at six months and 81.1% one year after surgery, comparable to values reported in literature [28].

Different studies in literature reported on predictors of mortality after proximal femoral fractures, identifying advanced age, male gender, pre-existing medical conditions and higher American Society of Anesthesiologists (ASA) grade as main negative prognostic factors [4, 29-31]. In our study male gender was identified as an important risk factor for higher mortality, accounting for an OR of 1.9362 one year after surgery. On the contrary the influence of co-morbidities on mortality rate was significant thirty days after surgery, and the OR decreased from 2.0030 at 30 days to 1.5965 at one year after surgery. This data underlined the burden of having more than two co-morbidities on mortality, especially in the early postoperative period. As previously reported in literature we confirmed the association between younger age and lower mortality at all the end-points; however the lower mortality risk is seen thirty days after surgery, with an OR equal to 0.0703 [29].

At the analysis of the correlation between treatment and morality rate, we found an association between synthesis and a lower thirty-day mortality risk compared to hip replacement. This can be explained by the less invasiveness of the nailing compared to a partial or total hip replacement. Given this difference in mortality between treatment groups, a similar difference could be expected for the weight bearing status (as it is directly correlated to the treatment adopted: all replacement are allowed to full weight bearing, while partial or no weight-bearing is often advised in the synthesis group); nonetheless, no statistically significant correlation between post-operative protocol and mortality rate was found.

Finally, the use of anticoagulant therapy reported no correlation to an increased mortality, and it could be explained by the small percentage of patients under anticoagulant therapy (7.6%).

The core of this study was the association between surgery delay and mortality. Previous published studies analyzed singularly the early (30-day), intermediate (6-month) or late (1-year) mortality [4, 5, 29-31], with few exceptions analyzing both early and late mortality [3, 12, 17, 18]. In this study we did analyze all three endpoints, to better underline how the considered variables differently affected the mortality rate, finding a statistical significant increased late mortality in patients who underwent surgery after 48 hours from admission. These results confirm the data from Simunovic et al [6], who reported in their meta-analysis a decreased risk of late mortality in patients who underwent early surgery, while there was no statistical significant different at the short or medium term.

The association between surgery delay and increased mortality is still controversial in Literature. Several studies concluded that delaying surgery more than 48 hours increases mortality [3, 6-14]. On the contrary other studies demonstrated that medical conditions, patient age and sex are more important in influencing mortality compared to surgery delay [4, 15-23]. In this study the mortality rate was lower in patients who underwent surgery within 48 hours compared at all three end-points (ie: 30 days, six months and one year mortality) to patients operated after 48 hours, as shown in Tab 3. Specifically the thirty-day and one-year mortality rate was 2.6% and 15.4% in patients operated within 48 hours and 5.1% and 21% for those operated after 72 hours. When a cutoff of 72 hours was tested in the first regression analysis, no statistically significant differences were detected. When comparing the mortality rate in patients operated between 48 and 72 hours to patients operated within 48 hours and to patients operated after 72 hours, no statistically significant differences were detected.

These results confirmed that operating within 48 hours reduces mortality at one year follow-up. These data support the assumption of the Literature that the operation must be carried out within two calendar days from admission in order to reduce the mortality risk. Additionally, the data suggest that operating on day three is not an affordable alternative to the 48 hours delay. The 72 hours cutoff is not a valid option in femoral fracture treatment, since only the 48 hours cutoff significantly decreased the one year mortality rate.

Conclusion

This study did confirm the correlation between patient's variable, such as male gender, co-morbidities or age, and an increased or decreased mortality risk. Co-morbidities and gender were identified as associated to a higher mortality rate. Particularly, being affected by more than two co-morbidities was associated to a higher mortality rate at all the endpoints, underlying its overall importance on early mortality. On the contrary, male patients had an increased mortality risk at six months and one year after surgery. Age, treatment type and timing of surgery were associated to a lower mortality rate. Specifically patients younger than 74 years old were correlated to a lower mortality rate at all the endpoints, and osteosynthesis was associated to a reduced early (30 days) mortality.

Regarding surgery delay, the findings of this paper confirmed that the one year mortality rate was significantly lower in patients who underwent surgery within 48 hours, while no other cut-off (i.e. Being operated between 48 and 72 hours) was significantly associated to a higher or lower mortality risk.

This study confirmed that surgery must be performed within 48 hours to reduce the mortality risk, while the option of operating on day 3 (between 48 and 72 hours from admission) is not an acceptable alternative.

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Tables

Tab. 1 Co-morbidities affecting patients prior to hospital admission.

Tab. 2 Analysis of surgical treatments.

Tab.3 Mortality rates within 30 days, 6 months and one year in relation to different variable.

Tab.4 The relation of 30-day, 6-month and one-year mortality rate to particular prognostic factors in logistic regression models. (OR=Odds Ratio, CI= Confidence Interval, in brackets the significant variables. Significant results are underlined.).

Tab.5 The relation of 30-day, 6-month and one-year mortality rate to particular prognostic factors in logistic regression models in a selected population operated after 48 hours. (OR=Odds Ratio, CI= Confidence Interval, in brackets the significant variables, N/A= not applicable. Significant results are underlined.)

Figures

Fig 1 Mortality rates occurring in relation to the surgery delays.

Fig. 2 Survivorship represented using the Kaplan-Meier method. Time is expressed in months