Risk Factors for Prolonged Hospital Stay and In-Hospital Mortality in Hip Fracture Patients Aged Over 65 Years: A Composite Endpoint Analysis

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Abstract

Objectives: This study aimed to determine the risk factors that increase the risk of in-hospital mortality and/or prolonged hospital stay in hip fracture patients aged over 65 years.

Methods: We conducted a retrospective study of patients aged over 65 years who underwent hip fracture surgery in the period from January 2015 to December 2017. Our analysis included 54 variables related to medical, psychological, functional and laboratory comorbidities present at admission; treatment, complications and laboratory follow-up during the hospital stay; and functional status and destination on discharge. We performed a bivariate analysis and a multivariate analysis with a composite endpoint combining in-hospital mortality and hospital stay lasting more than 10 days.

Results: We included 360 patients with an average age of 84 years. Women accounted for 75% of the sample, and 53.5% of all patients had a pertrochanteric fracture. The mean number of comorbidities per patient was 2.72, and the most common comorbidities were high blood pressure, dementia and diabetes. The rate of in-hospital mortality was 3.6% (n=13) and the mean length of hospital stay was 8.48 days, with 16.4% of patients staying in hospital for more than 10 days. Medical complications, lower hemoglobin on admission, high blood pressure, obesity and Parkinson’s disease were significantly associated with our endpoint in the multivariate analysis.

Conclusions: Patients who suffer medical complications during hospitalization, and those with lower hemoglobin on admission, high blood pressure, obesity or Parkinson’s disease, have an increased risk of in-hospital mortality or prolonged hospital stay.

Highlights

A wide range of factors have been linked to in-hospital death and/or prolonged hospital stay in previous studies, but the literature is rather inconsistent on which factors are most significant. In our study we analyzed the association between 54 different variables and a composite endpoint.
combining these two outcome measures. Our results show that the patients at highest risk of these outcomes are those who suffer medical complications during their stay, and those with lower hemoglobin on admission, high blood pressure, obesity or Parkinson’s disease.

Introduction

Of all complications secondary to osteoporosis in the geriatric population, hip fracture is considered to be the most significant in terms of morbidity, mortality and economic burden\(^1\). The impact of this injury on health care systems worldwide is considerable, with 300,000 cases per year in the USA\(^2\) and around 36,000 cases per year in Spain\(^3\). The worldwide annual number of cases is expected to reach 6 million by 2050\(^4\).

Hip fracture patients are typically fragile and dependent with reduced functional and cognitive capacity. In addition, the injury predisposes these patients to significant complications during hospitalization, potentially lengthening their hospital stay and increasing their risk of mortality. Nikkel et al.\(^5\) associated increased length of hospital stay with mortality in the month after discharge, observing a 32% greater risk of death in patients who stayed in hospital for more than 10 days compared to patients whose stay lasted from 1 to 5 days. This risk was 103% greater in patients who spent more than 14 days in hospital. Consequently, we must consider prolonged hospital stay to be a very serious outcome for these patients. Laboratory factors such as postoperative hemoglobin level, demographic factors such as sex and day of admission, and psychosocial factors such as cognitive status may be predictive of length of hospital stay\(^6\) –\(^11\).

Regarding in-hospital mortality in hip fracture patients, the rate of occurrence ranges from 4.5–11.4%\(^6\)–\(^7\), and the associated variables are numerous and varied: age, sex, medical comorbidities, electrolyte concentrations, time to surgery, Charlson comorbidity index (CCI) score, etc.\(^12\) –\(^14\).
A wide range of risk factors would appear to influence prolonged hospital stay and in-hospital mortality, and the literature is rather inconsistent on which are the most significant. For this reason, studying the risk factors previously associated with either or both of these outcomes could help us to clearly identify the most at-risk patients. The purpose of our study was to measure the association between these factors and in-hospital mortality and/or hospital stay lasting more than 10 days in patients aged over 65 years who underwent hip fracture surgery.

Methods

Study design and sample

We conducted a retrospective study of hip fracture patients who were treated between January 2015 and December 2017 in a university hospital that serves a population of over 200,000 inhabitants. We included only patients aged over 65 years who underwent hip fracture surgery. Our exclusion criteria were conservative treatment, pathological fracture, polytrauma, bilateral hip fracture and history of hip fracture prior to the study period.

After admission, all patients were assessed by an anesthetist. Preoperative antibiotic prophylaxis comprised cefazolin, or vancomycin in case of allergies, and the antithrombotic prophylaxis protocol was the same for all patients. They type of surgical treatment was dependent on fracture type and on the criteria of the Traumatology Department.

Variables and outcome measures

The variables related to the patient’s status on admission were: age (84 years or younger, between 85 and 89 years, 90 years or older), sex (man or woman), type of hip fracture (intracapsular [subcapital] or extracapsular [pertrochanteric or subtrochanteric]), side
(left or right), patient’s place of residence (own home or retirement home), anticoagulant therapy (yes/no), antiplatelet therapy (yes/no; Adiro 100/other) prior treatment for osteoporosis (yes/no), presence (yes/no) of medical comorbidities (high blood pressure, atrial fibrillation, chronic obstructive pulmonary disease [COPD], cerebrovascular disease, coronary artery disease, kidney failure, history of cancer, hypothyroidism, obesity, Parkinson’s disease, dementia, heart failure, diabetes, rheumatic disease), or psychiatric comorbidities (history of anxiety, depression, obsessive-compulsive disorder, schizophrenia, bipolar disorder), total number of comorbidities, hemoglobin on admission (serum level in g/dL), serum creatinine (mg/dL), sodium (mmol/L), potassium (mmol/L), leukocytes (10e9/L), lymphocytes (%), platelets (10e9/L), albumin (g/dL), Charlson comorbidity index (CCI)\textsuperscript{15}, and American Society of Anesthesiologists Classification (ASA class)\textsuperscript{16}. We collected scores from the Katz Index of Independence in Activities of Daily Living (Katz ADL), Parker and Palmer’s new mobility scale (NMS), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC; pain and function), the Merle d’Aubigné scale, the 12-Item Short Form Health Survey (SF-12; physical and mental) and the Mini-Mental State Examination (MMSE; 0–10). These scores reflect patients’ functional and cognitive status prior to the fracture. The information was provided by the patients or their families\textsuperscript{17–21}.

We also included the following variables related to the patients’ hospital stay: day of admission (Monday to Sunday), time to surgery (days), surgical complications (infection, displacement of internal fixation or prosthetic material, peri-implant fracture), medical complications (infections not related to the surgical site, acute myocardial infarction, stroke), length of hospital stay (number of days, and whether this number was less than or equal to 10 or more than 10), postoperative hemoglobin level, presence of preoperative or
postoperative blood transfusion, and death in hospital. Patients’ discharge destination was also taken into account.

The comorbidities were coded as dichotomous variables (presence/absence). We established a composite endpoint including two outcomes: in-hospital mortality and hospital stay lasting longer than 10 days.

Data analysis
The quantitative variables were expressed as mean plus or minus standard deviation, and the qualitative variables as percentages.

We performed a bivariate analysis of the explanatory variables and composite endpoint occurrence. For the qualitative variables we used the chi-square test and for the quantitative variables the Student’s t-test or the nonparametric Mann-Whitney U test.

To estimate the magnitude of association between the endpoint and the explanatory variables, we applied a multivariate logistic model, estimating the odds ratios (OR) and corresponding 95% confidence intervals (CIs). The optimal model was obtained by backward elimination using the Akaike information criterion. All confounders were taken into account. We calculated goodness of fit indicators such as the Chi square value (Chi2) and predictive indicators such as the area under the ROC curve (AUC) with the corresponding 95% CI.

For the data analysis process we used the statistical software SPSS v.25 and R-3.5.1.

Results
Tables 1 and 2 show the characteristics of our sample. In total, 360 patients who were treated within the study period met our inclusion criteria. Most were women (75%), and over half of all patients had a pertrochanteric fracture (53.5%). The mean age was 84 years (65-104). The most common comorbidities were high blood pressure (70.6%),
dementia (29.7%) and diabetes (25.6%). The mean number of comorbidities on admission was 2.72. Thirteen patients died in hospital, meaning the rate of in-hospital mortality was 3.6%. The mean length of hospital stay was 8.48 days and 16.4% of patients were in hospital for more than 10 days.

Tables 3 and 4 show the associations between the endpoint and the qualitative and quantitative variables, respectively, after the bivariate analysis. The composite endpoint was significantly associated with: medical complications, antiplatelet therapy, coronary artery disease, COPD, heart failure, longer time to surgery, lower hemoglobin levels at admission and after surgery, preoperative and postoperative blood transfusion, larger number of comorbidities, lower sodium, lower creatinine, higher potassium, higher CCI, higher ASA class and lower NMS.

The multivariate analysis showed a statistically significant association between the endpoint and medical complications, lower hemoglobin level at admission, high blood pressure, obesity and Parkinson’s disease. Sex, age and hemoglobin level at admission act as adjustment variables (Table 5).

Conclusion

Medical complications during hospital stay, lower hemoglobin level at admission, high blood pressure, obesity and Parkinson’s disease are all factors that increase the risk of in-hospital mortality and/or hospital stay lasting more than 10 days in patients aged over 65 years who undergo hip fracture surgery. The rest of the variables analyzed showed no significant association in the multivariate analysis.

Discussion
In our study, the rate of in-hospital mortality was 3.6% and the mean length of hospital stay was 8.4 days. These results are similar to those published in previous studies\textsuperscript{22}, although length of hospital stay can vary according to geographical region: within some European countries the mean length of hospital stay ranges from 5 to 15 days\textsuperscript{23,24}, while in Spain this factor varies between the different autonomous regions, from 7.2 to 18.6 days\textsuperscript{3}.

Given the varied nature of the risk factors associated with the outcomes included in our endpoint, we analyzed clinical, surgical, laboratory, demographic, functional and psychosocial factors, giving a total of 54 variables. Different studies have shown that ASA class, sex of the patient, time to surgery and day of admission influence the length of hospital stay\textsuperscript{8-11}, but none of these factors was associated with our endpoint. As in the study conducted by Lott et al\textsuperscript{2}, we found no relationship between age as an isolated factor and prolonged hospital stay or in-hospital mortality. When analyzing hemoglobin levels, we found a statistically significant association between our endpoint and lower values at admission. Postoperative hemoglobin, on the other hand, was not a significant variable in our multivariate model. In this sense, our results are similar to those of Choi et al\textsuperscript{7}, who found that lower postoperative hemoglobin had no impact on length of hospital stay, but different from those of Willems et al\textsuperscript{6}, who did find an association between these two factors.

Our study suggests that the occurrence of medical complications is closely related to prolonged hospital stay and/or in-hospital mortality, which may be because patients with complications often require diagnostic tests and/or treatment to recover, as shown in
some studies\textsuperscript{10}.

Richards et al.\textsuperscript{11} showed that patients with low mental test scores and reduced mobility tend to stay longer in hospital. In view of this, we included factors such as cognitive, functional and psychiatric status, but found no statistically significant association with our endpoint in the multivariate analysis.

In previous studies, being older than 90 years, being a man, heart failure, cancer, kidney failure, lung disease, electrolyte imbalance, surgical delay, hemoglobin level $\leq 10$ g/dL, number of comorbidities $\geq 2$, CCI $\geq 2$ and rheumatic disease have been associated with increased risk of in-hospital mortality\textsuperscript{12-14}. In our study, only two of these variables were associated with the endpoint, namely lower hemoglobin levels at admission and occurrence of medical complications. The rest showed no clear relationship.

The factors associated with the endpoint in our study clearly show which patients have the highest risk of in-hospital mortality and/or prolonged hospital stay. As a result, these factors must be identified and acted upon. Lower hemoglobin levels at admission can be managed through early transfusion. Medical complications are preventable in many patients. High blood pressure, obesity and Parkinson’s disease cannot be modified at admission, but as with all the factors, knowing the risk associated with them can help to promote intensive multidisciplinary follow-up in patients with these characteristics.

Although one study found no significant reduction in in-hospital mortality after versus before implementation of a multidisciplinary care protocol\textsuperscript{23}, as we have described
previously there are encouraging results in the literature demonstrating, despite reduced sample size, the benefits of multidisciplinary care in terms of shortening hospital stay in hip fracture patients. Since prolonged hospital stay is associated with death shortly after discharge\textsuperscript{5}, we can conclude that this type of comprehensive care protocol provides considerable benefits in these cases. Our results show which risk factors should be taken into account for identifying the most at-risk patients.

**Declarations**

**Ethics approval and consent to participate.**

Research and ethics commission of the Sant Joan d’ Alacant University Hospital approved the use of patient data for research.

**Consent for publication**

Not applicable

**Availability of data and material**

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

**Competing interests**

The authors declare that they have not competing interest

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Authors' contributions

JSM: Study design, acquisition of data and subjects, interpretation of data, preparation of manuscript.

FJFM: Study design, acquisition of data and subjects, interpretation of data.

JMSR: Acquisition of data and subjects, preparation of manuscript.

JAQR: Statistic analysis.

DOB: Study design

MCCM: Interpretation of data, preparation of manuscript.

JFML: Study design

JCMC: Study design, interpretation of data, preparation of manuscript.

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Tables

Table 1. Characteristics of the sample – qualitative variables.

|                        | n   | %  |
|------------------------|-----|----|
| Sex                    |     |    |
| Man                    | 90  | 25.0|
| Woman                  | 270 | 75.0|
| Age (years)            |     |    |
| ≤ 84                   | 165 | 46.2|
| 85-89                  | 115 | 32.2|
| ≥ 90                   | 77  | 21.6|
| Type of fracture       |     |    |
| Pertrochanteric        | 191 | 53.5|
| Subcapital             | 145 | 40.6|
| Subtrochanteric        | 21  | 5.9|
|                        |                  |        |      |
|------------------------|------------------|--------|------|
| **Side**               | Right            | 174    | 48.3 |
|                        | Left             | 186    | 51.7 |
| **Discharge destination** | Own home         | 276    | 76.9 |
|                        | Retirement home  | 83     | 23.1 |
| **Day of the week admitted** | Monday         | 42     | 11.7 |
|                        | Tuesday          | 45     | 12.6 |
|                        | Wednesday        | 61     | 17.0 |
|                        | Thursday         | 50     | 14.0 |
|                        | Friday           | 54     | 15.1 |
|                        | Saturday         | 58     | 16.2 |
|                        | Sunday           | 48     | 13.4 |
| **Anticoagulant therapy** | No               | 304    | 84.4 |
|                        | Yes              | 56     | 15.6 |
| **Antiplatelet therapy** | No               | 267    | 74.2 |
|                        | Yes              | 93     | 25.8 |
| **Antiplatelet therapy type** | None            | 267    | 74.2 |
|                        | Adiro 100        | 50     | 13.9 |
|                        | Other antiplatelets | 43   | 11.9 |
| **Osteoporosis treatment** | No               | 315    | 87.5 |
|                        | Yes              | 45     | 12.5 |
| **High blood pressure** | No               | 106    | 29.4 |
|                        | Yes              | 254    | 70.6 |
| **Atrial fibrillation** | No               | 282    | 78.3 |
|                        | Yes              | 78     | 21.7 |
| Condition                  | No    | Yes   |      |
|----------------------------|-------|-------|------|
| COPD*                      | 310   | 50    | 86.1 |
| Cerebrovascular disease    | 302   | 58    | 83.9 |
| Coronary artery disease    | 304   | 56    | 84.4 |
| Kidney failure             | 298   | 62    | 82.8 |
| Cancer                     | 308   | 52    | 85.6 |
| Hypothyroidism             | 326   | 34    | 90.6 |
| Obesity                    | 287   | 73    | 79.7 |
| Parkinson's disease        | 344   | 16    | 95.6 |
| Dementia                   | 253   | 107   | 70.3 |
| Heart failure              | 286   | 74    | 79.4 |
| Diabetes                   | 268   | 92    | 74.4 |
| Rheumatic disease          | 332   | 28    | 92.2 |
| Characteristic                  | No  | (%)  | Yes  | (%)  |
|--------------------------------|-----|------|------|------|
| Mental disorder               | 229 | 63.6 | 131  | 36.4 |
| Surgical complications        | 338 | 96.0 | 14   | 4.0  |
| Medical complications         | 268 | 75.7 | 86   | 24.3 |
| Preoperative transfusion       | 297 | 94.0 | 19   | 6.0  |
| Postoperative transfusion      | 234 | 68.6 | 107  | 31.4 |
| Death in hospital              | 347 | 96.4 | 13   | 3.6  |
| Length of hospital stay        |     |      |      |      |
| ≤ 10 days                      | 301 | 83.6 | 59   | 16.4 |
| > 10 days                      |     |      |      |      |
| Endpoint reached               | 294 | 81.7 | 66   | 18.3 |

*COPD indicates chronic obstructive pulmonary disease

Table 2. Characteristics of the sample – quantitative variables.
|                                | n   | Minimum | Maximum | Mean  | SD*  |
|--------------------------------|-----|---------|---------|-------|------|
| Age (years)                    | 357 | 65.00   | 104.00  | 83.96 | 7.25 |
| Length of hospital stay (days) | 360 | 1.00    | 35.00   | 8.48  | 4.64 |
| Time to surgery (days)         | 343 | 0.00    | 18.00   | 3.03  | 1.73 |
| Total number of comorbidities  | 355 | 0.00    | 7.00    | 2.72  | 1.70 |
| Charlson Comorbidity Index     | 340 | 0.00    | 7.00    | 1.67  | 1.45 |
| Hemoglobin at admission (g/dL) | 350 | 6.90    | 17.60   | 12.05 | 1.86 |
| Postoperative hemoglobin (g/dL)| 359 | 6.00    | 16.00   | 10.36 | 1.83 |
| MMSE*                          | 360 | 0.00    | 10.00   | 7.87  | 3.50 |
| ASA class*                     | 356 | 1.00    | 4.00    | 2.52  | 0.59 |
| WOMAC* pain                    | 355 | 0.00    | 28.00   | 15.94 | 3.79 |
| WOMAC* function                | 359 | 0.00    | 150.00  | 20.34 | 9.60 |
| SF-12* physical                | 359 | 6.00    | 164.00  | 15.30 | 12.69 |
| SF-12* mental                  | 359 | 6.00    | 28.00   | 18.21 | 5.25 |
| NMS*                           | 359 | 0.00    | 9.00    | 5.88  | 2.70 |
| Katz ADL*                      | 359 | 0.00    | 6.00    | 4.56  | 1.95 |
| Albumin (g/dL)                 | 358 | 0.00    | 4.50    | 0.82  | 1.40 |
| Creatinine (mg/dL)             | 351 | 0.40    | 3.90    | 1.11  | 0.51 |
| Leukocytes (10e9/L)            | 359 | 2.20    | 32.40   | 10.92 | 4.05 |
| Lymphocytes (%)                | 359 | 0.10    | 87.60   | 16.11 | 13.74 |
| Platelets (10e9/L)             | 360 | 0.00    | 719.00  | 211.53| 88.56 |
| Sodium (mmol/L)                | 358 | 123.00  | 193.00  | 139.56| 5.58 |
| Potassium (mmol/L)             | 353 | 2.50    | 6.20    | 4.23  | 0.58 |

*ASA class indicates American Society of Anesthesiologists Classification; Katz ADL, Katz Index of Independence in Activities of Daily Living; MMSE, Mini-Mental State Examination;
|                          | Endpoint not reached | Endpoint reached | P value |
|--------------------------|----------------------|------------------|---------|
|                          | n        | %     | n        | %     |         |
| Sex                      |          |       |          |       |         |
| Man                      | 70       | 77.8  | 20       | 22.2  | 0.35    |
| Woman                    | 224      | 83.0  | 46       | 17.0  |         |
| Age                      |          |       |          |       |         |
| ≤ 84                     | 139      | 84.2  | 26       | 15.8  | 0.36    |
| 85-89                    | 94       | 81.7  | 21       | 18.3  |         |
| ≥ 90                     | 59       | 76.6  | 18       | 23.4  |         |
| Type of fracture         |          |       |          |       |         |
| Pertrochanteric          | 158      | 82.7  | 33       | 17.3  | 0.72    |
| Subcapital               | 117      | 80.7  | 28       | 19.3  |         |
| Subtrochanteric          | 16       | 76.2  | 5        | 23.8  |         |
| Side                     |          |       |          |       |         |
| Right                    | 139      | 79.9  | 35       | 20.1  | 0.48    |
| Left                     | 155      | 83.3  | 31       | 16.7  |         |
| Discharge destination    |          |       |          |       |         |
| Own home                 | 223      | 80.8  | 53       | 19.2  | 0.57    |
| Retirement home          | 70       | 84.3  | 13       | 15.7  |         |
| Surgical complications   |          |       |          |       |         |
| No                       | 279      | 82.5  | 59       | 17.5  | 0.15    |
| Yes                      | 9        | 64.3  | 5        | 35.7  |         |
| Medical complications    |          |       |          |       |         |
| No                       | 248      | 92.5  | 20       | 7.5   | <0.001  |
| Yes                      | 43       | 50.0  | 43       | 50.0  |         |
| Day of week admitted     |          |       |          |       |         |
| Monday                   | 33       | 78.6  | 9        | 21.4  | 0.56    |
| Tuesday                  | 39       | 86.7  | 6        | 13.3  |         |
| Wednesday                | 53       | 86.9  | 8        | 13.1  |         |
|               | Thursday | Friday | Saturday | Sunday |
|---------------|----------|--------|----------|--------|
|               | 37  | 74.0 | 13 | 26.0 |
|               | 43  | 79.6 | 11 | 20.4 |
|               | 46  | 79.3 | 12 | 20.7 |
|               | 41  | 85.4 | 7  | 14.6 |

| Condition               | No   | Yes  |   |   |
|-------------------------|------|------|---|---|
| Anticoagulant therapy   | 251  | 82.6 | 53 | 17.4 |
|                         | 43   | 76.8 | 13 | 23.2 |
| Antiplatelet therapy    | 225  | 84.3 | 42 | 15.7 |
|                         | 69   | 74.2 | 24 | 25.8 |
| Antiplatelet therapy type | None | 225  | 84.3 | 42 | 15.7 |
|                         | Adiro 100 | 38   | 76.0 | 12 | 24.0 |
|                         | Other antiplatelets | 31   | 72.1 | 12 | 27.9 |
| Osteoporosis treatment  | 256  | 81.3 | 59 | 18.7 |
|                         | 38   | 84.4 | 7  | 15.6 |
| High blood pressure     | 91   | 85.8 | 15 | 14.2 |
|                         | 203  | 79.9 | 51 | 20.1 |
| Atrial fibrillation     | 236  | 83.7 | 46 | 16.3 |
|                         | 58   | 74.4 | 20 | 25.6 |
| COPD*                   | 260  | 83.9 | 50 | 16.1 |
|                         | 34   | 68.0 | 16 | 32.0 |
| Cerebrovascular disease | 250  | 82.8 | 52 | 17.2 |
|                         | 44   | 75.9 | 14 | 24.1 |
| Coronary artery disease | 254  | 83.6 | 50 | 16.4 |
|                         | 40   | 71.4 | 16 | 28.6 |
| Kidney failure          | 247  | 82.9 | 51 | 17.1 |
|                         |      |      |   | 0.26 |
| Health Condition           | Yes | No   | Yes | No   |
|---------------------------|-----|------|-----|------|
| Cancer                    | 47  | 251  | 15  | 57   |
| Hypothyroidism            | 43  | 268  | 9   | 58   |
| Obesity                   | 55  | 239  | 18  | 48   |
| Parkinson’s disease       | 11  | 283  | 5   | 61   |
| Dementia                  | 87  | 207  | 20  | 46   |
| Heart failure             | 50  | 244  | 24  | 42   |
| Diabetes                  | 71  | 223  | 21  | 45   |
| Rheumatic disease         | 22  | 272  | 6   | 60   |
| Mental disorder           | 108 | 186  | 23  | 43   |
| Preoperative transfusion  | 11  | 248  | 8   | 49   |
| Postoperative transfusion | 77  | 204  | 30  | 30   |

| Conditions | Mean Age | Median Age | Min Age | Max Age |
|------------|----------|------------|---------|---------|
| Cancer     | 75.8     | 15         | 24.2    | 0.99    |
| Hypothyroidism | 82.7   | 9          | 17.3    |         |
| Obesity    | 75.3     | 18         | 24.7    |         |
| Parkinson’s disease | 68.8 | 5          | 31.2    |         |
| Dementia   | 81.3     | 20         | 18.7    | >0.99   |
| Heart failure | 67.6   | 24         | 32.4    | <0.001  |
| Diabetes   | 83.2     | 21         | 22.8    | 0.26    |
| Rheumatic disease | 78.6 | 6          | 21.4    | 0.85    |
| Mental disorder | 82.4 | 23        | 17.6    | 0.88    |
| Preoperative transfusion | 57.9 | 8          | 42.1    | 0.01    |
| Postoperative transfusion | 72.0 | 30        | 28.0    | 0.001   |
*COPD indicates chronic obstructive pulmonary disease

Table 4. Association with composite endpoint - quantitative variables.

| Endpoint reached                  | n   | Mean | SD* | P value |
|-----------------------------------|-----|------|-----|---------|
| **Age (years)**                   |     |      |     |         |
| No                                | 292 | 83.72| 7.11| 0.19    |
| Yes                               | 65  | 85.02| 7.85|         |
| **No. of comorbidities**          |     |      |     |         |
| No                                | 289 | 2.57 | 1.65| <0.001  |
| Yes                               | 66  | 3.38 | 1.77|         |
| **Time to surgery (days)**        |     |      |     |         |
| No                                | 281 | 2.86 | 1.40| 0.03    |
| Yes                               | 62  | 4.68 | 2.61|         |
| **Hemoglobin at admission (g/dL)**|     |      |     |         |
| No                                | 287 | 12.22| 1.85| <0.001  |
| Yes                               | 63  | 11.28| 1.71|         |
| **Postoperative hemoglobin (g/dL)**|    |      |     |         |
| No                                | 294 | 10.49| 1.87| 0.001   |
| Yes                               | 65  | 9.77 | 1.51|         |
| **CCI**                           |     |      |     |         |
| No                                | 280 | 1.54 | 1.41| <0.001  |
| Yes                               | 64  | 2.22 | 1.52|         |
| **MMSE**                          |     |      |     |         |
| No                                | 294 | 7.88 | 3.50| 0.93    |
| Yes                               | 66  | 7.83 | 3.52|         |
| **ASA class**                     |     |      |     |         |
| No                                | 290 | 2.46 | 0.56| <0.001  |
| Yes                               | 66  | 2.77 | 0.65|         |
| **WOMAC* pain**                   |     |      |     |         |
| No                                | 290 | 16.05| 3.72| 0.22    |
| Yes                               | 65  | 15.42| 4.07|         |
| **WOMAC* function**               |     |      |     |         |
| No                                | 293 | 20.51| 10.10| 0.38   |
|                                | Yes |     |     |
|--------------------------------|-----|-----|-----|
| SF-12* physical                | No  | 293 | 15.30 12.07 >0.99 |
|                                | Yes | 66  | 15.30 15.27   |
| SF-12* mental                  | No  | 293 | 18.39 5.29 0.19 |
|                                | Yes | 66  | 17.45 5.07   |
| NMS*                           | No  | 293 | 6.02 2.68 0.04 |
|                                | Yes | 66  | 5.26 2.74   |
| Katz ADL*                      | No  | 293 | 4.63 1.92 0.18 |
|                                | Yes | 66  | 4.27 2.04   |
| Albumin (g/dL)                 | No  | 292 | 0.85 1.44 0.37 |
|                                | Yes | 66  | 0.68 1.23   |
| Creatinine (mg/dL)             | No  | 286 | 1.08 0.51 0.008 |
|                                | Yes | 65  | 1.27 0.48   |
| Leukocytes (10e9/L)            | No  | 293 | 10.88 4.09 0.66 |
|                                | Yes | 66  | 11.12 3.89   |
| Lymphocytes (%)                | No  | 294 | 16.39 13.90 0.42 |
|                                | Yes | 65  | 14.86 13.01 |
| Platelets (10e9/L)             | No  | 294 | 210.17 88.47 0.54 |
|                                | Yes | 66  | 217.59 89.36 |
| Sodium (mmol/L)                | No  | 292 | 139.82 5.77 0.03 |
|                                | Yes | 66  | 138.42 4.50   |
| Potassium (mmol/L)             | No  | 289 | 4.18 0.53 0.02 |
|                                | Yes | 64  | 4.42 0.74   |

*ASA class indicates American Society of Anesthesiologists Classification; CCI, Charlson
Comorbidity Index; Katz ADL, Katz Index of Independence in Activities of Daily Living; MMSE, Mini-Mental State Examination; NMS, Parker and Palmer’s New Mobility Score; SD, standard deviation; SF-12, 12-Item Short Form Health Survey

Table 5. Multivariate logistic model and quality indicators

|                          | OR*     | 95% CI*          | P value |
|--------------------------|---------|------------------|---------|
| **Sex**                  |         |                  |         |
| Man                      | 1       |                  |         |
| Woman                    | 0.607   | (0.279-1.323)    | 0.21    |
| **Age (years)**          |         |                  |         |
| ≤ 84                     | 1       |                  |         |
| 85-89                    | 1.041   | (0.465-2.329)    | 0.92    |
| ≥ 90                     | 1.316   | (0.520-3.328)    | 0.56    |
| **Medical complications**|         |                  |         |
| Yes                      | 22.799  | (10.423-49.872)  | <0.001  |
| **High blood pressure**  |         |                  |         |
| Yes                      | 2.999   | (1.271-7.078)    | 0.01    |
| **Obesity**              |         |                  |         |
| Yes                      | 2.717   | (1.184-6.237)    | 0.02    |
| **Parkinson’s disease**  |         |                  |         |
| Yes                      | 5.105   | (1.135-22.952)   | 0.03    |
| **Hemoglobin at admission (g/dL)** | 0.669   | (0.544-0.824)    | <0.001  |

*OR indicates odds ratio; CI, confidence interval.

Indicators

| n   | Endpoint no. | Chi2  | P value | AUC*     | 95% CI*          |
|-----|--------------|-------|---------|----------|------------------|
| 342 | 60           | 103.9 | <0.001  | 0.8602   | (0.805-0.9139)   |

*AUC indicates area under the ROC curve; CI, confidence interval

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