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Development of Prediction Model for 1-year Mortality after Hip Fracture Surgery

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Purpose: Hip fractures are associated with increased mortality. The identification of risk factors of mortality could improve patient care. The aim of the study was to identify risk factors of mortality after surgery for a hip fracture and construct a mortality model.
Materials and Methods: A cohort study was conducted on patients with hip fractures at two institutions. Five hundred and ninety-seven patients with hip fractures that were treated in the tertiary hospital, and another 147 patients that were treated in a secondary hospital. The perioperative data were collected from medical charts and interviews. Functional Assessment Measure score, Short Form-12 and mortality were recorded at 12 months. Patients and surgery variables that were associated with increased mortality were used to develop a mortality model.
Results: Mortality for the whole cohort was 19.4% at one year. From the variables tested only age >80 years, American Society of Anesthesiologists category, time to surgery (>48 hours), Charlson comorbidity index, sex, use of anti-coagulants, and body mass index <25 kg/m^2 were associated with increased mortality and used to construct the mortality model. The area under the curve for the prediction model was 0.814. Functional outcome at one year was similar to preoperative status, even though their level of physical function dropped after the hip surgery and slowly recovered.
Conclusion: The mortality prediction model that was developed in this study calculates the risk of death at one year for patients with hip fractures, is simple, and could detect high risk patients that need special management.

Keywords: Hip fractures, Mortality, American Society of Anesthesiologists, Body mass index

INTRODUCTION

An association of hip fractures in older persons with a lower quality of life for the patient, as well as increased morbidity and mortality has been reported[1]. The annual estimated cost of treatment was 17 billion dollars in the USA with an even larger societal cost[2]. Patients with hip fractures typically present with multiple comorbidities, which, when combined with specific epidemiologic characteristics such as age, sex, and body mass index (BMI), can be a major factor influencing the final outcome after surgical treatment, increasing the risk of morbidity and mortality. The relative contribution of these risk factors can vary and has not been accurately assessed.

The Nottingham Hip Fracture Score (NHFS), which can predict mortality at one month, is the index used most often for estimating the probability of death after a hip fracture[3]. However, development of a similar score for estimating mortality in the longer term, preferably at one

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year, is needed. In the process of shared decision making and communication with the patient and/or his custodians, the ability to refer to a reliable predictive tool in regard to patients' long-term clinical outcome would be useful.

The primary objective of this study is to determine risk factors for mortality at 12 months after surgery for treatment of a hip fracture and to develop a prognostic model for use in preoperative decision making. Secondary outcomes include an evaluation of functional outcomes and quality of life one year after surgery for treatment of hip fractures.

MATERIALS AND METHODS

This study had a retrospective cohort design; data was collected prospectively in a tertiary care National Health System academic hospital (University General Hospital of Larissa) located in central continental Greece with a catchment population of approximately 900,000 inhabitants and in a remote secondary care public hospital (General Hospital of Kastoria) with a population of 70,000 people. The study was approved by the ethical committee of University General Hospital of Larissa (No. 5972) and was conducted according to Declaration of Helsinki principles. Informed consent was obtained from all participants included in the study. An analysis of patients admitted for treatment of hip fractures from August 2013 to August 2016 was performed. The flow chart for the study is shown in Fig. 1. Data from 597 patients from the tertiary hospital and 147 patients from the secondary hospital were available for analysis.

Patient's demographics, functional and cognitive prefracture status, along with quality-of-life assessment and perioperative data were retrieved from the hospitals' medical records for retrospective analysis. Inclusion criteria included patients older than 65 years of age, who were admitted to hospital with a hip fracture after a fall from a standing height or other similar low energy mechanism, defining a fragility or geriatric hip fracture. Pathological and high energy fractures were excluded. Most of the patients were females (67.3%), and older than 80 years (mean, 82.6±7.2 years). The patients' demographic data, medical history, fracture type, and surgical treatment are shown in Table 1. All surgeries were performed by or under the supervision of 14 trauma surgeons.

The epidemiologic data, medications (including anticoagulants and treatment for osteoporosis) were recorded. Use of anti-coagulants included direct oral anticoagulants, warfarin, or anti-platelets. Hemoglobin (Hgb) and albumin levels at admission, type of fracture,

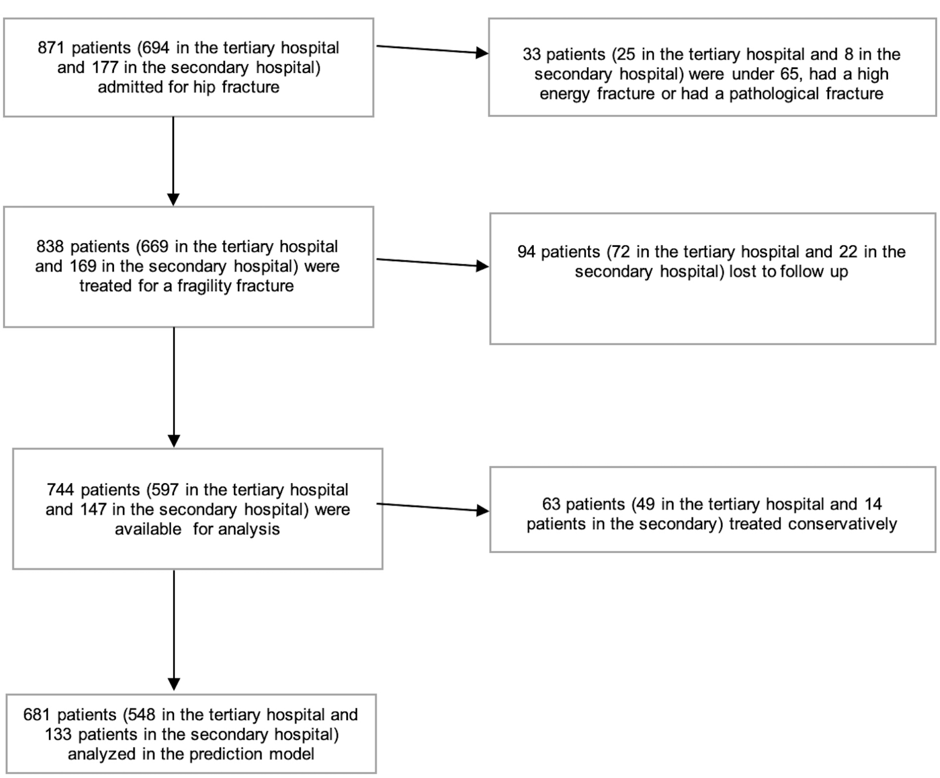

Fig. 1. Flow chart for the study.

Table 1. Epidemiologic, Injury, Surgery, and Functional Outcome Data of the Study Group

Variable	Value
Sex	
Female	501/744 (67.3)
Male	243/744 (32.7)
Age (yr)	82.6±7.2
BMI (kg/m^2)	26.8±3.0
Smoking	
Never	525/744 (70.6)
Ex-smoker	193/744 (25.9)
Smoker	26/744 (3.5)
Alcohol consumption	
Rarely	513/744 (69.0)
Once a week	213/744 (28.6)
Every day	18/744 (2.4)
Osteoporosis treatment	
Yes	257/744 (34.5)
No	487/744 (65.5)
Type of fracture	
Neck of femur	242/744 (32.5)
Per- or intertrochanteric	447/744 (60.1)
Per- or intertrochanteric with distal extension	55/744 (7.4)
Fracture management	
Surgery	681/744 (91.5)
Conservative treatment	63/744 (8.5)
Fracture treatment*	
Hemi-arthroplasty	197/681 (28.9)
Total hip replacement	31/681 (4.6)
Short nail	399/681 (58.6)
Long nail	54/681 (7.9)
Type of anesthesia*	
Spinal	672/681 (98.7)
General	9/681 (1.3)
ASA score	
I	34/744 (4.6)
II	268/744 (36.0)
III	394/744 (53.0)
IV	48/744 (6.5)
FIM+FAM score	
Before hip fracture	171.1±13.1
At one month	112.0±11.3
At four months	142.2±12.7
At one year	163.9±13.5
SF-12 PCS	
Before hip fracture	42.0±8.3
At one month	25.5±7.9
At four months	33.1±8.0
At one year	40.3±6.6
SF-12 MCS	
Before hip fracture	40.2±11.1
At one month	25.5±9.9
At four months	33.1±10.6
At one year	39.6±9.5

Values are presented as number (%) or mean±standard deviation.
BMI: body mass index, ASA: American Society of Anesthesiologists physical status score, FIM+FAM score: Functional Independence Measurement and Functional Assessment Measure score, SF-12 PCS: Short Form-12 physical component summary score, SF-12 MCS: Short Form-12 mental component summary score.
*Of the 744 patients, 681 patients were operated so these patients underwent some type of anesthesia or received some kind of implant.

type of surgery, anesthesia, Charlson comorbidity index (CCI)[4], American Society of Anesthesiologists (ASA)[5] physical status score, time to surgery, hospital stay, complications, re-admissions, and in-hospital mortality were also documented. Continuous variables were converted to categorical variables using rational cut-offs based on the literature. As a result, the final predictive model was easier to use and more end-user friendly. For example, 80 years was chosen as the age cut-off because increased mortality after this age has been reported[6]. The BMI cut-off for distinguishing normal from overweight or obese patients was 25 kg/m^2. Regarding alcohol consumption, patients were divided according to non-drinkers and patients with a low to hazardous intake level (drinking alcohol every day). An albumin level below 3.5 g/dL was considered abnormal and an Hgb level below 10 g/dL at admission was considered abnormal[7,8]. Late surgery was defined as time to surgery >48 hours[9]. Patients with ASA ≥3 and CCI >6 were considered high risk[10,11]. Patients who had received a transfusion of at least one unit of red cell consecrates were included in the transfusion group. Hospital of admission referred to the tertiary or the secondary hospital. Finally, the categories for type of hip fracture included neck of femur fractures managed with hemi- or total hip replacement and per-trochanteric or inter-trochanteric fractures with or without distal extension managed with a short or long nail.

Examination of patients was conducted in the outpatient clinic at one, four, and 12 months for assessment of the functional outcome and quality of life or patients were contacted and interviewed by telephone. For patients with dementia, the closest relatives living with the older person assisted with completion of the questionnaires. In case of death, the exact date was recorded.

The functional outcome was evaluated using the Functional Independence Measurement and Functional Assessment Measure score (FIM+FAM score) for physical function and independence (FIM+FAM motor) along with the cognitive function of the patient (FIM+FAM cognitive)[12]. The Short Form-12 (SF-12), a short version of SF-36, is used for evaluation of general health and health-related quality of life with a physical component summary score (PCS) and a mental component summary score (MCS) and its validity has been demonstrated in the Greek population[13,14].

For development of the mortality model, only variables that can be measured preoperatively were used, as we required a prognostic score at the time of admission. Therefore, even though variables such as complications or re-admission were noted, they were not utilized in the development of the model.

Descriptive statistics were used for reporting details regarding the study groups. Univariate analysis was performed to determine factors that had a significant effect on the mortality rate. The χ^2 test was used for categorical variables in univariate analysis.

Thirty subjects per variable were available, so that the sample size was considered large enough for an accurate analysis. Variables that showed statistical significance in the univariate analysis were entered into a multiple regression analysis model for determination of variables that independently predicted increased mortality. Next, the odd ratios [Exp(B)] for these variables were used in construction of a mortality model based on the relative value of the odds ratios. Finally, calculation of receiver operating characteristic (ROC) curve with area under the curve (AUC) was performed. A paired *t*-test was used for comparing qualitive variables at different time points (FIM+FAM score and SF-12 scores). Statistical analysis was performed using IBM SPSS Statistics (ver. 24; IBM Corp.) and P<0.05 was considered statistically significant.

RESULTS

In-hospital mortality was 2.4%. Mortality for the entire cohort was 19.4% at one year. Mortality was 18.3% in the tertiary hospital and 23.0% in the secondary hospital. The complication rate was 12.5% including both medical and surgery related complications. Medical complications included pneumonia (n=21), acute renal dysfunction (n=13), stroke (n=8), thrombosis (n=12), and pulmonary embolism (n=4). Surgery related complications included dislocation (n=10), mechanical failure of the nail or cutout (n=6), and fracture-related infections (n=11).

Among the variables tested, BMI <25 kg/m^2, age >80 years, CCI >6, time to surgery >48 hours, ASA ≥3, use of anti-coagulants, and male sex showed an association with increased mortality (Table 2). Complications and re-admission at first month also showed an association with increased mortality but were not entered into the regression model. When all other variables showing statistical significance were entered into the multivariate logistic regression model only age >80 years, ASA category, time to surgery (>48 hours), CCI, sex, use of anti-coagulants, and BMI <25 kg/m^2 showed statistical significance (Table 3). Regression coefficients were used for development of a hip fracture mortality score with a minimum value of 0 and a maximum value of 13. The higher points obtained using the mortality model were attributed to the ASA score and the CCI index (four and three, respectively) (Table 3). A patient with a value of 8 to 10 is considered average risk (20%-30% probability of death at one year). An ROC curve was constructed for the prediction model (Fig. 2). The calculated AUC was 0.814 (95% CI 0.769-0.859, P<0.001), which is considered excellent discrimination.

The final functional outcome and quality of life was assessed for patients who had survived at one year. The calculated preoperative FIM+FAM score was 171.1±13.1 for all patients. Decreased function of the patients was observed at one month and showed a gradual recovery at fourth months and one year but did not reach the pre-hip fracture level. The final FIM+FAM score was 163.9±13.5, indicating a statistically significant difference (paired *t*-test, P<0.001) but without clinical significance. The same pattern was observed for both components of the SF-12 (Table 1). The FIM+FAM motor score showed a significant decrease at one year follow-up from 94.1±14.1 to 90.0±13.6 (paired *t*-test, P<0.001). The FIM+FAM cognitive score also showed a significant decrease at one year follow-up from 77.0±13.8 to 73.9±13.1 (paired *t*-test, P=0.001). Evaluation of quality of life using the SF-12 showed a statistically significant reduction at one year follow-up. PCS and MCS changed from 42.0±8.3 to 40.3±6.6 (paired *t*-test, P<0.001) and from 40.2±11.1 to 39.6±9.5 (paired *t*-test, P<0.001), respectively. However, once again, these differences did not indicate clinical significance.

DISCUSSION

In this study, a prognostic model was developed for prediction of one-year mortality in patients with hip fractures. Age, sex, comorbidities, ASA, time to surgery, BMI, and use of anti-coagulants can affect the probability of death. However, patients who survive gradually reach a functional outcome that is similar to or lower than the preoperative status.

For development of the mortality score, only categorical variables were used in an effort to enhance the convenience of its use for clinicians. This mortality model was constructed from seven variables (Table 1,

Table 2. Univariate Analysis between Patient and Operation Variables, and Death at One Year

Variable	Mortality rate (%)	Pearson χ^2 test value	OR (95% CI)	*P*-value
Sex		3.584	1.3 (1.0-1.6)	0.045*
Male	19.2			
Female	13.4			
Age (yr)		9.704	2.1 (1.3-3.4)	0.002*
>80	18.9			
≤80	10.0			
BMI (kg/m^2)		9.695	3.5 (1.4-5.4)	0.002*
<25	23.6			
≥25	13.3			
Smoking		1.919	1.2 (0.8-1.6)	0.383
Smoker	18.0			
Non-smoker	15.2			
Alcohol consumption		0.442	1.1 (0.5-1.7)	0.802
Low to hazardous intake (every day)	20.0			
Non-drinker or rarely drinking	16.0			
Anti-coagulants use		8.832	1.9 (1.2-2.8)	0.003*
Yes	21.4			
No	12.7			
Osteoporosis treatment		0.018	1.0 (0.7-1.6)	0.892
Yes	15.9			
No	15.5			
Hemoglobin at admission (g/dL)		2.157	1.3 (0.6-1.9)	0.459
≤10	19.6			
>10	15.8			
Albumin at admission (g/dL)		0.372	1.1 (0.6-1.7)	0.542
≤3.5	22.1			
>3.5	17.5			
Hospital admission		2.765	1.3 (0.9-1.7)	0.096
Secondary	23.0			
Tertiary	18.3			
Type of fracture		2.639	1.3 (0.7-2.0)	0.267
Neck of femur	20.7			
Pertrochanteric or intertrochanteric[†]	19.7			
Anesthesia		3.254	1.3 (0.8-1.9)	0.197
General	21.2			
Spinal	16.3			
CCI		64.406	5.5 (3.5-8.5)	<0.001*
>6	31.3			
≤6	7.7			
ASA		61.338	4.9 (3.2-9.0)	<0.001*
≥3	25.1			
<3	3.1			
Time to surgery (hr)		9.993	2.0 (1.3-3.1)	0.002*
>48	18.6			
≤48	10.1			
Transfusion[‡]		2.994	1.3 (0.7-2.0)	0.293
Yes	21.3			
No	18.5			

Table 2. Continued

Variable	Mortality rate (%)	Pearson χ^2 test value	OR (95% CI)	*P*-value
Complications		36.798	3.8 (2.3-5.3)	0.001*
Yes	58.5			
No	17.6			
Re-admission within 30 days		11.439	2.1 (1.4-2.9)	0.001*
Yes	36.6			
No	15.1			
Place of discharge		0.029	1.0 (0.4-1.6)	0.864
Nursery home	15.9			
Home	15.4			

OR: odds ratio, CI: confidence interval, BMI: body mass index, CCI: Charlson comorbidity index, ASA: American Society of Anesthesiologists physical status score.
*$P<0.05$.
†Pertrochanteric or intertrochanteric with or without distal extension.
‡Transfusion with at least one unit of red cells concentrate.

Table 3. Multivariate Regression Analysis and Construction of the Mortality Model

	B	SE	Wald	Sig.	Exp(B)	95% CI for Exp(B)		Points in the mortality index
						Lower	Upper	
Age >80 yr	0.560	0.284	3.903	0.048	1.751	1.004	3.053	1
ASA score ≥3	1.615	0.388	17.372	0.000	5.030	2.353	10.751	4
Time to surgery >48 hr	0.585	0.289	4.099	0.043	1.795	1.019	3.163	1
CCI >6	1.476	0.268	30.296	<0.001	4.374	2.586	7.397	3
Male sex	0.261	0.247	1.119	0.049	1.298	1.002	3.504	1
Anti-coagulants	0.505	0.288	3.085	0.039	1.658	1.143	2.913	1
BMI <25 kg/m^2	0.753	0.261	8.332	0.004	2.123	1.273	3.539	2
Constant	−5.058	0.532	90.565	<0.001	0.006			13 (total)

SE: standard error, Sig.: significant, CI: confidence interval, ASA: American Society of Anesthesiologists physical status score, CCI: Charlson comorbidity index, BMI: body mass index.

Supplementary File). However, only one, the time to surgery, is modifiable. Another interesting observation is that mortality is extremely dependent on comorbidities, which is reflected in the CCI index and ASA score. CCI >6 and ASA score ≥3 adds three and four points to the mortality score, respectively. However, in fragile older patients with more comorbidities and a mortality score above 8, the addition of surgery delay increases the mortality by almost five actual percentage points. The predicted probability of death for a mortality score of 8, 9, and 10 is 17%-20%, 26%-28%, and 29%-31%, respectively. The positive effect of surgery without delay is more pronounced in fragile older patients. This fact contributes to the already established knowledge that surgeons should attempt to treat patients within 48 hours, particularly older patients with more comorbidities[15,16].

An unexpected relationship was observed between BMI and mortality. The risk of death is increased for normal patients with BMI <25 kg/m^2 compared to overweight patients. This has been described as the BMI or obesity paradox[17,18] and has also been observed in regard to mortality as well as complications for patients undergoing total joint replacement[19-21]. In contrast, no variables associated with the fracture like type of fracture are predictive of mortality.

In addition, the effect of anti-coagulant use on mortality was found to be independent from that of other factors including ASA, CCI index, or delayed surgery. It can be postulated that this relationship might not reflect severe comorbidities, such as coronary artery disease or cerebrovascular disease, but rather an increased rate of hematoma formation and transfusions. Hematoma formation and transfusion in turn may have a negative indirect effect on rehabilitation, infection rate, and mortality[22,23].

The mortality rate was higher for the lower volume

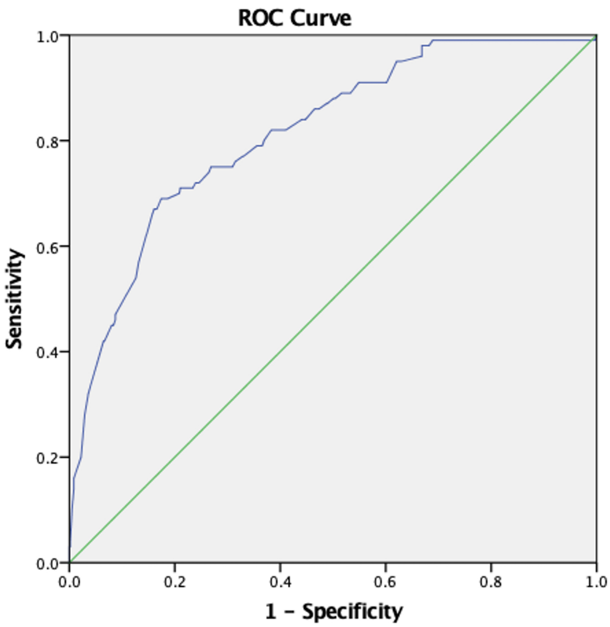

Fig. 2. Diagnostic ability of the prediction model. The receiver operator characteristic (ROC) curve and the area under the curve for the mortality model. The calculated area under the curve was 0.814.

secondary hospital compared with the tertiary high-volume center. However, this difference in mortality did not reach statistical significance. This finding is in accordance with a large study that found no difference in one year mortality after hip fracture surgery between low, medium, and high-volume centers[24]. The positive effect of hospital volume on elective orthopedic surgeries has not been replicated in hip fractures[25]. A recent systematic review reported worst outcomes and in hospital mortality after hip fractures in lower volume hospitals but no difference in one year mortality[26].

The NHFS can predict mortality at 30 days for patients with hip fractures. Its accuracy for prediction of one-year mortality has also been reported[3,27]. Better survival was observed for patients with NHFS ≤4 compared to patients with NHFS >5 (Kaplan–Meier analysis, 84.1% vs 54.5%, P<0.001)[3]. Other long-term models for prediction of mortality have also been developed[28-33]. These include similar variables such as age, sex, BMI, comorbidities, and ASA score, but also certain different variables including grip strength, vitamin D measurement, Barthel index[32], EQ-5D index, Mini-Mental State Examination[28], and activities of daily living[29]. A study by Bliemel et al.[28] included a small sample size compared to other studies. Although all of the models mentioned above have demonstrated acceptable discrimination, in our study the AUC was higher, reaching 0.814, which is considered excellent discrimination.

Assessment of functional outcome at one year, using FIM+FAM motor and cognitive scales showed a statistically significant decrease of 4.1 and 3.1 points, respectively. The smallest reported detectable difference for these subscales was 8.92 and 3.66 points[34]. This finding suggests that patients reached a similar final functional state, despite a decline in their level of physical function after hip surgery, which then showed a gradual recovery. The same pattern was noted for the quality-of-life assessment. SF-12 PCS decreased by 1.7 and SF-12 MCS decreased by 0.6. These changes fell below the minimal clinically important difference for SF-12 subscales ranging from 6.3 to 3 for SF-12 PCS[35,36] and from 7.0 to 0.6 for SF-12 MCS[36-38].

This mortality model is based on data obtained from patients treated within the period where our country suffered an unprecedented financial hardship with implementation of stringent austerity measures in all public and private domain services, and a negative impact on the health of the population. Therefore, the findings of this study should be interpreted within that context. We also acknowledge the following limitations. First, other variables that were measured and utilized by other researchers, such as grip strength, vitamin D, and cognitive function were not available. Second, the size of the study might be considered moderate. Third, although this new mortality model has not been validated, conduct of another study to validate the model is underway. Validation of other groups would also be helpful. However, this research was conducted as a dual center study with a low rate of patients who were lost to follow-up and an acceptable sample size, making the results more generalizable. However, conduct of future studies will be required for validation of the predictive model.

CONCLUSION

The mortality prediction model developed in this study can calculate the risk of death at one year for patients with hip fractures. It is simple to use and could be applied in every day clinical practice for informing patients and caregivers in the process of shared decision making. For example, an 86-year-old male patient with CCI >6, ASA equal to 3 who has undergone surgery after 48 hours from admission has a hip fracture mortality score of 10 and a mortality risk of 29% to 31% at one year. However, treatment management of hip fractures, which is based on early surgery, cannot be affected or modified by this model. Nonetheless, it can be regarded as a useful tool that may be helpful in detecting high risk patients, to ensure early initiation of appropriate management as well as during the perioperative period.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Supplementary Materials

Supplementary data is available at https://hipandpelvis.or.kr/.

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