Biomarkers as predictors of inpatient mortality in fractured neck of femur patients

Ryan Geleit[a], Matthew Bence[a], Phillip Samouel[b], Johnathan Craik[a].

a. Department of Trauma and Orthopaedic Surgery, Epsom and St Helier Hospital NHS Trust, UK
b. Kingston University, UK

Corresponding author at:
Mr. Ryan Geleit
Department of Trauma and Orthopaedic Surgery
Epsom and St Helier Hospital NHS Trust
St Helier Hospital
Wrythe Ln
Carshalton
SM5 1AA
UK
Email address: rgeleit@nhs.net (R.Geleit)

Keywords:
Hip fracture
Femur
Biomarkers
Mortality
Survival

Declarations of interest: none

Abstract

Introduction
Hip fractures are common and it is estimated to cost the National Health Service (NHS) around £2 billion/year. The majority of these patients are elderly and they require careful perioperative management as morbidity and mortality are high. This study aims to look at routinely gathered biomarker data and baseline demographics to evaluate if they may be used to predict inpatient mortality.

Patients and Methods
The study included 2158 patients from a single Centre over a 5-year period. Inclusion criteria: age>60, confirmed fractured neck of femur on radiological imaging. Exclusion criteria: pathological fractures, patients treated non-operatively, missing data. Univariate followed by multivariate analysis was conducted to identify the independent predictors of inpatient mortality.

Results
The variables found to be independent predictors of inpatient mortality were: age > 85, sex (male), albumin < 35, lymphocytes < 1, American Society of Anesthesiologist (ASA) grade > 3. For the final derived multivariate logistic regression model, a receiver operator characteristic (ROC) curve was constructed to assess the ability of the included variables to predict inpatient mortality. The area under the curve was 0.794 which together with sensitivity of 63.2% and a specificity of 79.1% at a cut value of 0.1.

Conclusion
This paper supports research previously conducted in this field, showing the prognostic value of both biomarker (albumin and lymphocytes), and non-biomarker data (ASA grade, age and gender) in predicting mortality in patients who have sustained a hip fracture.

Introduction

Hip fractures are common and are increasing in number. Hip fracture care in the National Health Service (NHS) costs approximately £2 billion annually. In the United Kingdom (UK) around 75,000 people are admitted to hospital and treated for a fractured neck of femur every year (1).

Due to the fact that hip fractures are both very common and are associated with a high level of inpatient mortality(1), it is important to try an identify those patients who are at greatest risk as early as possible. This is in order to counsel patients and relatives about the injury, the procedure and the prognosis. It also highlights, to clinicians, those who are vulnerable and who may need a higher level of inpatient care. It may also help with discussions surrounding resuscitation at an earlier stage(2).

A number of previous studies have highlighted various biomarkers as independent predictors of mortality after hospital admission for a traumatic fractured neck of femur. These have included albumin (3-12), lymphocytes (7, 8, 13-16), neutrophils (13, 17), creatinine (18-21), haemoglobin (Hb) (17-19, 22, 23), sodium (Na) (6, 24, 25) and potassium (K) (20, 26). In addition, many of these papers have highlighted baseline demographic data as additional predictors of mortality and have included abbreviated mental test score (AMTS), pre-injury residence, number of co-morbidities and previous malignancy.

Other markers that may have a bearing on inpatient/post-operative mortality in hip fracture patients included: parathyroid hormone (PTH) (27, 28), troponin (29) and vitamin D (30, 31). However, these biomarkers are not routinely taken for hip fracture patients on admission to UK hospitals and therefore are outside the scope of this study. Urea was found to be a predictor of mortality in some studies (32) but has been discounted in others (33).

It appears there may be some agreement that low albumin may be an indicator of increased post-operative mortality for hip fractures but there is clearly no consensus regarding the other markers. The aim of the study was to investigate associations between in-patient mortality for fractured neck of femur patients and routine blood tests taken at admission in conjunction with other baseline demographic data.

Materials and Methods

We prospectively collected data on all patients admitted to the unit between April 2014 and August 2019. The data collected for analysis included: age, type of fracture, pre-injury residence, AMTS, ASA, operation performed, discharge destination and admission biomarker values (Hb, Na, K, creatinine, neutrophils, lymphocytes, albumin). Any missing biomarker data was manually cross checked by the authors. Those patients who were treated non-operatively were excluded from the data as it was deemed these patients would have a higher risk of inpatient death and are a small but distinct subset of hip fracture patients.

Inclusion criteria: Any patient with a confirmed hip fracture admitted to the unit between April 2014 and August 2019 were considered for inclusion. All types of fractured neck of femur where data is supplied to the National Hip Fracture Database were included (intracapsular, extracapsular and subtrochanteric fractures). Inclusion criteria: patients over 60 years of age, confirmed fractured neck of femur on imaging (x-ray, computerised tomography (CT) or magnetic resonance imaging (MRI)).
Exclusion criteria: pathological fracture, patients treated non-operatively, absent bloodwork data.

Statistical Product and Service Solutions (SPSS) version 27 was used to analyse the data. This included examination of the summary diagnostics followed by a univariate and a multivariate analysis through binary logistic regression to ascertain the significant predictors to death. Independent variables, both continuous and categoric were transformed to dummy variables where required. The data analysis followed a three-stage procedure. First, a descriptive analysis focused on identifying the key factors that differentiate the patients that lived and those that died. The second concentrated on the derivation and validation, using binary logistic regression to identify significant factors and the predictive power between the two components. The third section executed forward stepwise logistic regression to obtain the final prediction model.

Results

Of the 2267 patients admitted to the unit during the study period, 2158 patients met the criteria for inclusion in the study. The breakdown of those excluded can be seen in table 1. 1574 (73%) of patients were female with the average age being 88. Inpatient mortality of these subjects in the analysis was 117 (5.4%). Of note, 21 patients (34%) treated non-operatively died in hospital which was by far the most likely ‘discharge destination’ for these patients. In addition, only 11 patients treated non-operatively had complete biomarker and baseline demographic data available.

Table 1: Breakdown of excluded patients

Exclusion criteria	Number of patients
Pathological fracture	24
Non operatively treated	61
Absent dataset	24

Descriptive Analysis

Prior to executing logistic regression, examination of the summary statistics for those who died and those who survived was considered. Specifically, an assessment was made comparing the differences in means in the key variables identified in previous studies between those that lived and those that died (33, 34). The results are given in Table 2. The descriptives show a significant difference at 0.01 level for: age, creatinine, haemoglobin, albumin, AMTS and ASA. Lymphocytes were significant at 0.05 and sodium at 0.10 level. Our expectation is that where significant differences are identified those factors will feature in the multivariate modelling both in the derivation and validation models.

Table 2: Summary Statistics

	Normal Range	Survivors Average	Non-survivors Average	Mean Difference	Std. Error Difference	t-value	P-value
Age		87.39	90.50	-3.11	0.80	-3.88	<0.001
Sodium (mEq/L)	133 -146	137.09	137.76	-0.67	0.41	-1.64	0.100
Potassium (mmol/L)	3.5 - 5.3	4.21	4.28	-0.07	0.05	-1.48	0.139
Creatinine (μmol/L)#	20 - 103	91.20	116.59	-25.39	8.48	-3.00	0.003
Haemoglobin (g/L)	115 - 145	123.02	115.96	7.06	1.61	4.40	<0.001
Neutrophils (10^9/L)	1.7 - 7.5	9.28	9.01	0.26	0.38	0.69	0.489
Lymphocytes (10^9/L)	1.0 -3.5	1.20	1.00	0.20	0.09	2.15	0.032
Albumin(g/L)#	35 - 50	34.42	30.95	3.48	0.54	6.40	<0.001
AMTS#		7.09	5.53	1.56	0.36	4.38	<0.001
ASA#		3.15	3.79	-0.65	0.05	-14.14	<0.001

Variances unequal

Multivariate Analysis: derivation and validation

To predict the likelihood of death binary logistic multiple regression was applied to the following full model: Y = f(age, gender, sodium, potassium, creatinine, haemoglobin, neutrophils, lymphocytes, albumin, AMTS, ASA, pre-injury residence). A comparison between the derivation and the validation samples is presented in Table 3. There is consistency in the multivariate results (estimates and significance) between the derivation and the validation samples except for AMTS. Furthermore, the similarity is also reflected by the areas captured under the receiver operator characteristics (ROC) curve for the two models shown in Figures 1 and 2. A perfect fit would produce a right angle with an area under the curve (AUC) of 1. The ROC curve for the derivation sample, shown in figure 1, demonstrates an area under the curve of 0.803 (95% CI 0.76, 0.85) with a sensitivity of 58.7% and a specificity of 83.1% at a cut value of 0.1. The ROC curve for the validation sample, shown in figure 2, demonstrates an area under the curve of 0.806 (95% CI 0.77, 0.84) with a sensitivity of 59.6% and a specificity of 82.7% at a cut value of 0.1.

Table 3. Multivariate analysis for derivation and validation samples.

	Derivation Sample[1]		Validation Sample[2]	
	B	P-value	B	P-value
Age>85	**0.536**	**0.067**	**0.523**	**0.043**
Sex (Male)	**0.403**	**0.025**	**0.447**	**0.037**
Sodium	0.012	0.707	0.026	0.272
Potassium	-0.017	0.457	-0.013	0.946
Creatinine	0.000	0.753	0.001	0.365
Haemoglobin	0.007	0.392	-0.009	0.119
Neutrophils	-0.026	0.486	-0.004	0.891
Lymphocytes <1x10^9/L	**0.479**	**0.071**	**0.536**	**0.008**
Albumin<35g/L	**0.860**	**0.004**	**0.552**	**0.014**
AMTS	-0.085	0.083	-0.025	0.422
ASA>3	**1.436**	**0.000**	**1.678**	**<0.001**
Pre-injury Residence	-0.061	0.855	-0.112	0.664
Constant	-5.348	0.024	-7.223	0.044

Note: 1 denotes a random sample of 50%; 2 denotes the whole sample

Figure 1: ROC for Derivation Sample

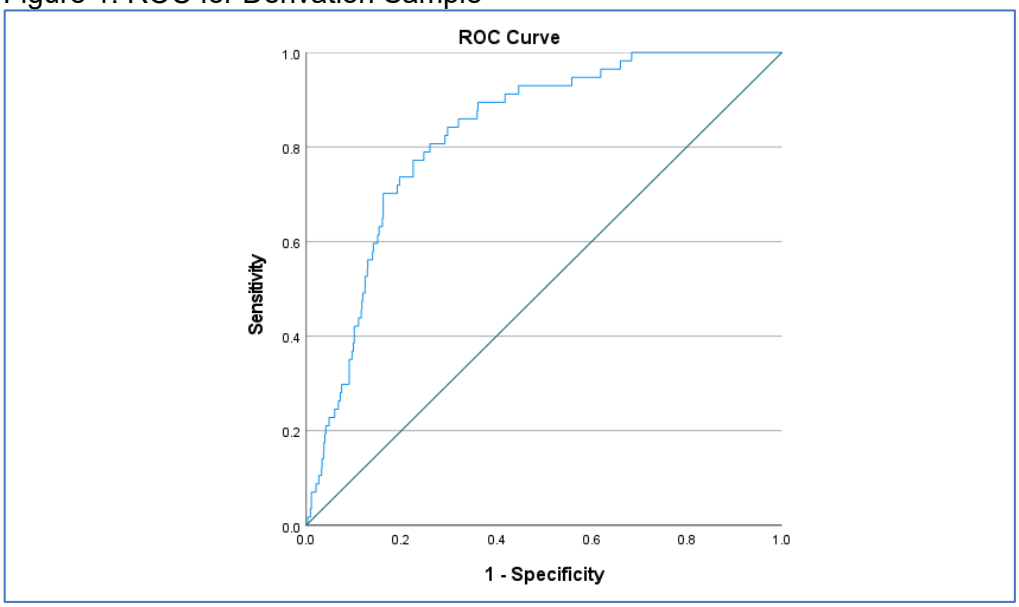
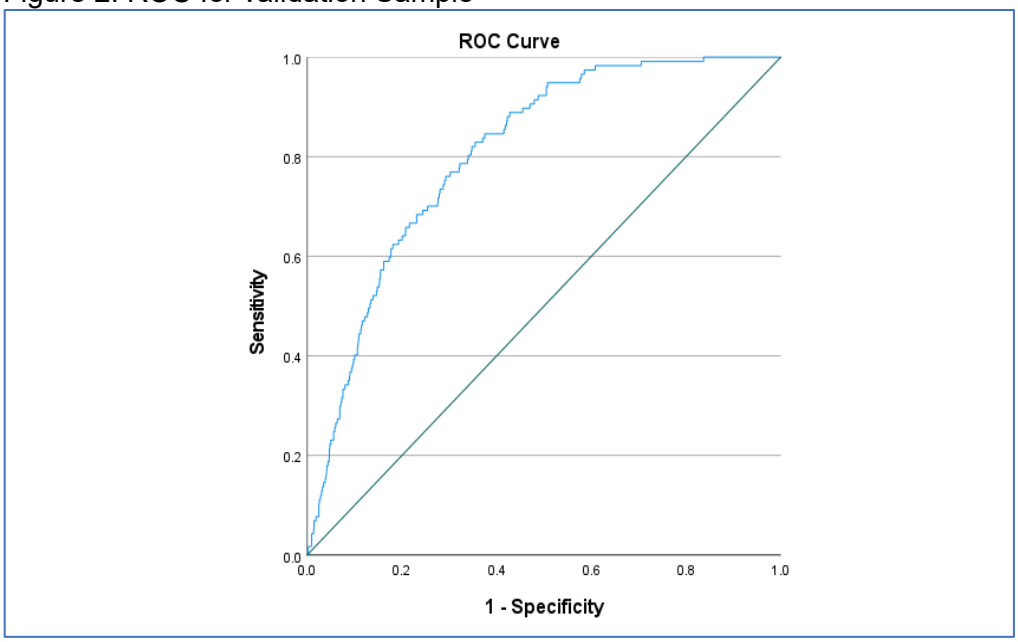


Figure 2: ROC for validation Sample



The validation model, containing all predictors, was statistically significant, χ^2 (df = 12, n = 2,158) = 132.816, p < 0.001, indicating that the model was able to distinguish between respondents who lived and those who died. The model as a whole explains 17.40% (Nagelkerke R^2) in survivors/non survivors state and overall, correctly classified 94.6% of cases. Proceeding with forward stepwise logistics regression, a reduced model of only five predictor variables made a unique statistically significant contribution (age, male gender, lymphocytopenia, hypoalbuminemia, and ASA >3). This can be seen in table 4. The strongest predictor of dying is ASA with an odds ratio of 5.981. This indicates that patients who had ASA larger than 3 had a 5.981 fold higher mortality rate compared to those who had ASA of 3 or below.

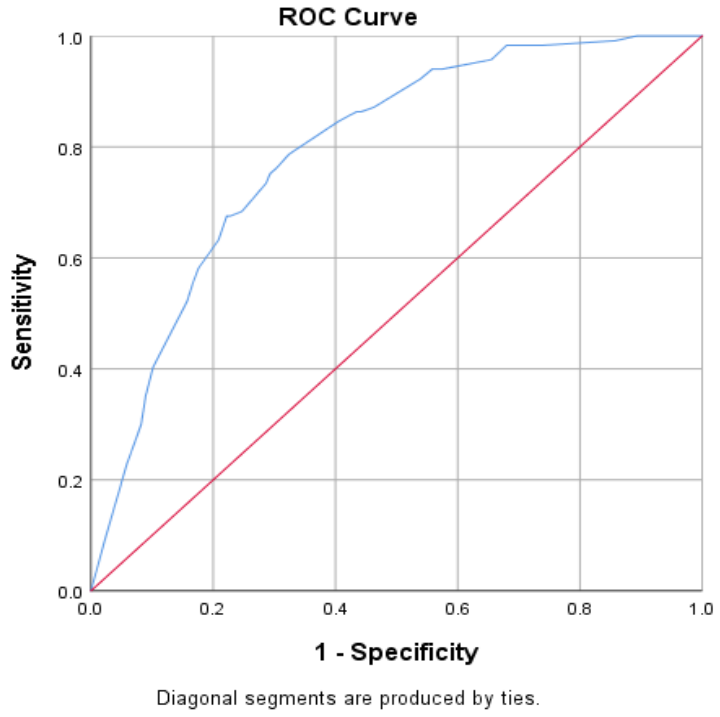
Table 4: Multivariate analysis for reduced model

	B	P-value	Exp(B)	95% confidence interval for Exp(B)	
				Lower	Upper
Age > 85	0.562	0.027	1.754	1.067	2.885
Male	0.492	0.016	1.636	1.098	2.437
Lymphocytes < 1	0.547	0.006	1.728	1.171	2.549
Albumin < 35	0.671	0.002	1.957	1.288	2.974
ASA > 3	1.789	<0.001	5.981	3.824	9.354
Constant	-5.090	<0.001	0.006		

ROC curve for the reduced model

The ROC curve for the reduced model was plotted to assess the ability of the variables to predict inpatient mortality. The area under the ROC curve ranges from 0.5 and 1.0 with larger values indicative of better predictive fit. The area under the curve (AUC) is 0.794 (95% CI 0.757, 0.830). The area under the curve is significantly different from 0.5 with a p-value of <0.001 denoting that the logistic regression classifies the group significantly better than by chance. Using a cut value of 0.1 the model returns a sensitivity of 63.2% and a specificity of 79.1%.

Figure 3: ROC curve depicting the ability of the identified risk factors to predict inpatient mortality with hip fracture patients.



Discussion

Our results for biomarkers are comparable to previous studies in the literature. There is good evidence that low albumin is associated with higher inpatient mortality. Albumin can be thought of as a surrogate marker of nutritional status, with lower albumin indicating poorer levels of nutrition. It therefore would imply that patients with a worse peri-operative nutritional state would likely have a poorer post-operative course. The analysis also indicates that lymphocytes are also an independent predictor of inpatient mortality which is not universally evident in previously published work. A number of previous studies have shown correlation between lymphocytes and mortality following hip fracture in elderly patients.(8, 15, 17) whilst other have not found these to be independent predictors(33). Total lymphocyte count has been used as a marker of nutritional status in patients but is less widely in this guise and has largely been superseded by other evaluations including albumin levels. With both hypoalbuminemia and lymphocytopenia being independent predictors of inpatient mortality it does shine a light on pre-operative nutrition as an important predictor of outcome for these elderly patients.

In addition to the work on biomarkers we also found that male sex, age >85 and ASA>3 are also independent predictors on inpatient mortality. Male sex has been shown to be an independent risk factor in other large-scale studies although the exact reason for this has yet to be identified (35). A number of theories have been proposed including immunogenic theories and the fact that men are at increased risk of peri-operative infections (36). These theories have yet to be conclusively proved in the literature. Increasing age has shown to be a predictor of inpatient mortality (19, 33) and our analysis shows that those patients over 85 years of age are at a significantly higher risk of death even with the cohort of 'young' hip fracture patients (<60 years) excluded as part of the methodology. This may be due to a general increasing age of the hip fracture population.

The American society of Anaesthesiologists have a widely accepted and validated system to assess and communicate a patient's pre-anaesthesia medical comorbidities. It grades a patient from 1 to 6 which can be seen in table 5(37).It is used to identify those patients at higher risk of morbidity and mortality when undergoing a surgical procedure. The system has been in place for over 60 years and forms an essential part of the NHS adaptation of the World Health Organisation's (WHO) surgical safety checklist(38). There are of course limitations to the grading system including, but not limited to inter-observer reliability and its subjective nature. We must, however, point to a 2015 study by Hacket et al on 2.2 million surgical cases that demonstrates that ASA has a strong independent association with post-operative medical complications and mortality across all procedures (39).

Table 5. ASA grading system

ASA grade	Definition
I	A normal healthy patient
II	A patient with mild systemic disease
III	A patient with severe systemic disease
IV	A patient with severe systemic disease that is a constant threat to life
V	A moribund patient who is not expected to survive without the operation
VI	A declared brain-dead patient whose organs are being removed for donor purposes

The largest meta-analysis on this subject by Hu (40) included 75 papers that looked at peri-operative hip fracture mortality. The paper found strong evidence for: advanced age, male gender, nursing home or facility residence, poor preoperative walking capacity, poor activities of daily living, higher ASA grading, poor mental state, multiple comorbidities, dementia or cognitive impairment, diabetes, cancer and cardiac disease. Some of these parameters were not captured in our dataset and we found no association between pre-injury residence or AMTS (poor mental state/dementia) and mortality. The paper by Hu also showed moderate evidence for: low albumin, low haemoglobin, high creatinine as independent predictors of death. There were inconclusive or limited evidence for: total lymphocyte count, neutrophil to lymphocyte ratio, high potassium, high & low sodium and altered PTH. A meta-analysis by Li (14) only identified one biomarker (albumin) as a predictor of mortality following hip fracture. This analysis included 19 studies of variable size and quality and did not include a number of other important studies published on the subject. Another meta-analysis by Lauland (41) suggested low albumin, low lymphocytes, high creatinine and high PTH as

predictors of mortality after hip fracture. However, this metanalysis only included 15 studies with variable follow up and quality. A meta-analysis by Smith et al(42) identifies abnormal ECG, cognitive impairment, age >85 and reduced pre-fracture mobility as indicators of increased likelihood of death up to 12 months post hip fracture surgery. This study did not include routine biomarkers in its data collection.

There is currently debate regarding haemoglobin's ability to predict post mortality following hip fracture. Although some studies (33, 40) have shown an association of a low haemoglobin on admission and increased post-operative mortality, some studies have not replicated this. Mosfeldt et al (20) conducted a prospective study of 792 patients and found that haemoglobin does not predict mortality at 90 days. Fisher et al(31) looked retrospectively at 1820 patients admitted to a Canberra hospital for fractured neck of femur. Haemoglobin was not an independent predictor of death in this study. Bhaskar et al(17) suggested that low haemoglobin may be an indicator of inpatient death but this 2011 study did not use regression analysis or hazard models to account for confounders or to look at the true effect of these counts on the mortality. One study by Gruson(22) found variability in haemoglobin's ability to predict mortality. It was not a statistically significant predictor for mortality during inpatient stay or at 3 months but was significant at 6 and 12 months. Our analysis demonstrates that haemoglobin was not an independent predictor of inpatient mortality.

Previous studies have aimed to identify markers that can predict inpatient or post-operative mortality. Some studies have aimed to produce a tool to predict those patients at increased risk of post-operative death (33, 43). Pugely at al created a tool that aimed to stratify inpatient death based on five variables found to be independent predictors of mortality (age, male, functional status, malignancy and ASA grade). It must be noted that routine biomarkers were not included in their analysis, despite a number of previous studies supporting their use as predictors of mortality (7, 10, 41).

A 2008 paper by Maxwell et al identified haemoglobin as an independent predictor of mortality (33). The study only looked at urea and Hb as possible biochemical predictors of 30-day mortality. However, the inclusion of urea was based on one study of 111 patients where creatinine (not urea) was used as a marker of renal insufficiency(44). This paper suggested there was an association with increased creatinine and increased risk of post-operative mortality within the first 24 months post operatively. Despite this, Maxwell et al. did not find urea to be predictive in their multivariate analysis.

The assessment of our model shows a sensitivity of 63.2% and a specificity of 79.1%. This compares favourably with the model by Maxwell which demonstrated sensitivity of 44.2% and a specificity of 80.8%(33). Some caution must be applied due to the possibility of excluding those who died with 'normal' biomarker/non-biomarker parameters (false negatives). The development of an accurate and clinically applicable model based on this data should be the focus for further research.

One limitation of the study is the fact that data was only gathered from one institution. We were also unable to look at other potential biomarkers as predictors of mortality that aren't routinely collected on admission bloodwork. In addition, a more in-depth analysis of each patients' co-morbidities and their cause of death were not captured.

Conclusion

Our study has shown that biomarkers have important prognostic value in determining mortality following the treatment of patients who have suffered a fractured neck of femur. We have highlighted the association between albumin and lymphocytes and inpatient mortality. It is therefore very likely that pre-injury nutrition plays a key role in determining a patient's outcome following surgery for fractured neck of femur. In addition, the study also found ASA grade, male sex and age to be independent variables predictive of inpatient mortality which support a number of previous studies in this area.

Acknowledgements

Injury
International Orthopaedics
Int J Surg
Arch Gerontol Geriatr
Journal of Orthopaedic Trauma
European Journal of Orthopaedic Surgery & Traumatology
Acta Orthopaedia

References:

1. Physicians RCo. National Hip Fracture Database (NHFD) Annual Report 2022 2022 [Available from: https://www.rcplondon.ac.uk/projects/outputs/nhfd-annual-report-2022.
2. (UK) RC. ReSPECT for healthcare professionals 2023 [Available from: https://www.resus.org.uk/respect/respect-healthcare-professionals.
3. Aldebeyan S, Nooh A, Aoude A, Weber MH, Harvey EJ. Hypoalbuminaemia-a marker of malnutrition and predictor of postoperative complications and mortality after hip fractures. Injury. 2017;48(2):436-40.
4. Bohl DD, Shen MR, Hannon CP, Fillingham YA, Darrith B, Della Valle CJ. Serum Albumin Predicts Survival and Postoperative Course Following Surgery for Geriatric Hip Fracture. J Bone Joint Surg Am. 2017;99(24):2110-8.
5. Harrison SJ, Messner J, Leeder DJ, Stephenson J, Sidhom SA. Are Albumin Levels a Good Predictor of Mortality in Elderly Patients with Neck of Femur Fractures? J Nutr Health Aging. 2017;21(6):699-703.
6. Lizaur-Utrilla A, Gonzalez-Navarro B, Vizcaya-Moreno MF, Lopez-Prats FA. Altered seric levels of albumin, sodium and parathyroid hormone may predict early mortality following hip fracture surgery in elderly. Int Orthop. 2019.
7. O'Daly BJ, Walsh JC, Quinlan JF, Falk GA, Stapleton R, Quinlan WR, et al. Serum albumin and total lymphocyte count as predictors of outcome in hip fractures. Clin Nutr. 2010;29(1):89-93.
8. Ozturk A, Ozkan Y, Akgoz S, Yalcin N, Aykut S, Ozdemir MR. The effect of blood albumin and total lymphocyte count on short-term results in elderly patients with hip fractures. Ulus Travma Acil Cerrahi Derg. 2009;15(6):546-52.
9. Pimlott BJ, Jones CA, Beaupre LA, Johnston DW, Majumdar SR. Prognostic impact of pre-operative albumin on short-term mortality and complications in patients with hip fracture. Arch Gerontol Geriatr. 2011;53(1):90-4.
10. Pioli G, Barone A, Giusti A, Oliveri M, Pizzonia M, Razzano M, et al. Predictors of mortality after hip fracture: results from 1-year follow-up. Aging Clin Exp Res. 2006;18(5):381-7.
11. Hershkovitz A, Polatov I, Beloosesky Y, Brill S. Factors affecting mortality of frail hip-fractured elderly patients. Arch Gerontol Geriatr. 2010;51(2):113-6.
12. Wilson JM, Lunati MP, Grabel ZJ, Staley CA, Schwartz AM, Schenker ML. Hypoalbuminemia Is an Independent Risk Factor for 30-Day Mortality, Postoperative Complications, Readmission, and Reoperation in the Operative Lower Extremity Orthopaedic Trauma Patient. J Orthop Trauma. 2019;33(6):284-91.
13. Fisher A, Srikusalanukul W, Fisher L, Smith P. The Neutrophil to Lymphocyte Ratio on Admission and Short-Term Outcomes in Orthogeriatric Patients. Int J Med Sci. 2016;13(8):588-602.
14. Li S, Zhang J, Zheng H, Wang X, Liu Z, Sun T. Prognostic Role of Serum Albumin, Total Lymphocyte Count, and Mini Nutritional Assessment on Outcomes After Geriatric Hip Fracture Surgery: A Meta-Analysis and Systematic Review. J Arthroplasty. 2019;34(6):1287-96.
15. Koval KJ, Maurer SG, Su ET, Aharonoff GB, Zuckerman JD. The effects of nutritional status on outcome after hip fracture. J Orthop Trauma. 1999;13(3):164-9.
16. Symeonidis PD, Clark D. Assessment of malnutrition in hip fracture patients: effects on surgical delay, hospital stay and mortality. Acta Orthop Belg. 2006;72(4):420-7.
17. Bhaskar D, Parker MJ. Haematological indices as surrogate markers of factors affecting mortality after hip fracture. Injury. 2011;42(2):178-82.
18. Bjorkelund KB, Hommel A, Thorngren KG, Lundberg D, Larsson S. Factors at admission associated with 4 months outcome in elderly patients with hip fracture. Aana j. 2009;77(1):49-58.
19. Ho CA, Li CY, Hsieh KS, Chen HF. Factors determining the 1-year survival after operated hip fracture: a hospital-based analysis. J Orthop Sci. 2010;15(1):30-7.
20. Mosfeldt M, Pedersen OB, Riis T, Worm HO, Mark S, Jorgensen HL, et al. Value of routine blood tests for prediction of mortality risk in hip fracture patients. Acta Orthop. 2012;83(1):31-5.
21. Singh Mangat K, Mehra A, Yunas I, Nightingale P, Porter K. Is estimated peri-operative glomerular filtration rate associated with post-operative mortality in fractured neck of femur patients? Injury. 2008;39(10):1141-6.
22. Gruson KI, Aharonoff GB, Egol KA, Zuckerman JD, Koval KJ. The relationship between admission hemoglobin level and outcome after hip fracture. J Orthop Trauma. 2002;16(1):39-44.
23. Halm EA, Wang JJ, Boockvar K, Penrod J, Silberzweig SB, Magaziner J, et al. The effect of perioperative anemia on clinical and functional outcomes in patients with hip fracture. J Orthop Trauma. 2004;18(6):369-74.

24. Madsen CM, Jantzen C, Lauritzen JB, Abrahamsen B, Jorgensen HL. Hyponatremia and hypernatremia are associated with increased 30-day mortality in hip fracture patients. Osteoporos Int. 2016;27(1):397-404.
25. Tinning CG, Cochrane LA, Singer BR. Analysis of hyponatraemia associated post-operative mortality in 3897 hip fracture patients. Injury. 2015;46(7):1328-32.
26. Norring-Agerskov D, Madsen CM, Abrahamsen B, Riis T, Pedersen OB, Jorgensen NR, et al. Hyperkalemia is Associated with Increased 30-Day Mortality in Hip Fracture Patients. Calcif Tissue Int. 2017;101(1):9-16.
27. Di Monaco M, Vallero F, Di Monaco R, Tappero R, Cavanna A. 25-hydroxyvitamin D, parathyroid hormone, and functional recovery after hip fracture in elderly patients. J Bone Miner Metab. 2006;24(1):42-7.
28. Fisher A, Goh S, Srikusalanukul W, Davis M. Elevated serum PTH is independently associated with poor outcomes in older patients with hip fracture and vitamin D inadequacy. Calcif Tissue Int. 2009;85(4):301-9.
29. Talsnes O, Hjelmstedt F, Dahl OE, Pripp AH, Reikeras O. Clinical and biochemical prediction of early fatal outcome following hip fracture in the elderly. Int Orthop. 2011;35(6):903-7.
30. Fakler JK, Grafe A, Dinger J, Josten C, Aust G. Perioperative risk factors in patients with a femoral neck fracture - influence of 25-hydroxyvitamin D and C-reactive protein on postoperative medical complications and 1-year mortality. BMC Musculoskelet Disord. 2016;17:51.
31. Fisher A, Fisher L, Srikusalanukul W, Smith PN. Usefulness of simple biomarkers at admission as independent indicators and predictors of in-hospital mortality in older hip fracture patients. Injury. 2018;49(4):829-40.
32. Lewis JR, Hassan SK, Wenn RT, Moran CG. Mortality and serum urea and electrolytes on admission for hip fracture patients. Injury. 2006;37(8):698-704.
33. Maxwell MJ, Moran CG, Moppett IK. Development and validation of a preoperative scoring system to predict 30 day mortality in patients undergoing hip fracture surgery. Br J Anaesth. 2008;101(4):511-7.
34. Hadique S, Culp S, Sangani RG, Chapman KD, Khan S, Parker JE, et al. Derivation and Validation of a Prognostic Model to Predict 6-Month Mortality in an Intensive Care Unit Population. Ann Am Thorac Soc. 2017;14(10):1556-61.
35. Kannegaard PN, van der Mark S, Eiken P, Abrahamsen B. Excess mortality in men compared with women following a hip fracture. National analysis of comedications, comorbidity and survival. Age Ageing. 2010;39(2):203-9.
36. Wehren LE, Hawkes WG, Orwig DL, Hebel JR, Zimmerman SI, Magaziner J. Gender differences in mortality after hip fracture: the role of infection. J Bone Miner Res. 2003;18(12):2231-7.
37. Anesthesiologists ASo. ASA Physical Status Classification System 2014 [updated December 13th 2020. Available from: https://www.asahq.org/standards-and-guidelines/asa-physical-status-classification-system.
38. Kannan T. ASA grading: a step forward. J Perioper Pract. 2017;27(3):54-8.
39. Hackett NJ, De Oliveira GS, Jain UK, Kim JY. ASA class is a reliable independent predictor of medical complications and mortality following surgery. Int J Surg. 2015;18:184-90.
40. Hu F, Jiang C, Shen J, Tang P, Wang Y. Preoperative predictors for mortality following hip fracture surgery: a systematic review and meta-analysis. Injury. 2012;43(6):676-85.
41. Laulund AS, Lauritzen JB, Duus BR, Mosfeldt M, Jorgensen HL. Routine blood tests as predictors of mortality in hip fracture patients. Injury. 2012;43(7):1014-20.
42. Smith T, Pelpola K, Ball M, Ong A, Myint PK. Pre-operative indicators for mortality following hip fracture surgery: a systematic review and meta-analysis. Age Ageing. 2014;43(4):464-71.
43. Pugely AJ, Martin CT, Gao Y, Klocke NF, Callaghan JJ, Marsh JL. A risk calculator for short-term morbidity and mortality after hip fracture surgery. J Orthop Trauma. 2014;28(2):63-9.
44. Kuokkanen HO, Korkala OL. Factors affecting survival of patients with hip fractures. Acta Orthop Belg. 1992;58(4):425-8.