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End-Stage Renal Failure Is an Independent Risk Factor for 1-Year Mortality After Hip Fracture Surgery

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Abstract

Introduction: End-stage renal failure (ESRF) with its associated comorbidities increase postoperative mortality in hip fracture patients. This study investigated the association of ESRF with various comorbidities in patients on dialysis and assessed rates ESRF as an independent risk factor for all-cause postoperative 1- year mortality rates. **Methods:** This was a retrospective cohort study on patients aged 55 years and older who underwent their first nonpathological, low-energy hip fracture surgery at an Asian tertiary hospital from June 2007 to 2012. Patients were identified as cases with ESRF on dialysis (study group) or non-ESRF patients (controls). Various comorbidity factors and postoperative 1-year mortality status were obtained from institutional electronic medical records. Univariate and multivariate logistic regression were used to identify significant risk factors for all-cause, 1-year mortality. **Results:** With no loss to follow-up, the 1-year postoperative mortality rate was 19.6% for the 46 patients with ESRF on dialysis and 8.4% for non-ESRF controls ($P = .028$). Fisher exact test showed that hypertension, ischemic heart disease (IHD), diabetes mellitus (DM), anemia, cerebrovascular disease, and vascular disease were significantly associated with ESRF ($P < .05$). Multivariable logistic regression analysis identified ESRF (adjusted odds ratio[AOR] = 2.85, $P = .021$), cancer (AOR = 3.04, $P = .003$), IHD (AOR = 2.07, $P = .020$), DM (AOR = 2.03, $P = .022$), and age (AOR = 1.08, $P < .0001$) as independent risk factors for 1-year mortality following hip fracture surgery. The area under the receiver–operating characteristic curve (95% confidence interval) for the multivariable predictor of 1-year mortality was 0.75 (0.60-0.82). **Conclusions:** Although associated with multiple comorbidities, ESRF was found to be independently predictive of 1-year mortality in patients undergoing hip fracture surgery, second to cancer in terms of magnitude of risk posed. As ESRF is a negative prognostic factor for 1-year mortality after hip fracture surgery, its importance should be recognized with implications on preoperative counseling to patients about the increased risk and implications on fracture prevention.

Keywords

hip fracture, end-stage renal failure, mortality, prediction model, logistic, regression, geriatrics

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Introduction

Hip fractures among the elderly individuals is a growing health concern in developed countries globally. In Singapore, a rapidly aging population[1] makes osteoporotic hip fractures a national health concern. The rate of hip fractures locally has risen 1.5 times among men and 5 times among women since the 1960s. It is predicted to rise from 1300 cases per year in 1998 to 9000 cases per year in 2050 owing to the aging population.[2]

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Patients with end-stage renal failure (ESRF), defined as a glomerular filtration rate (GFR) of <15 mL/min/1.73 m^2 and requiring dialysis or renal transplant are at higher risk of sustaining hip fractures.[3,4] Due to the high prevalence of metabolic bone disease in patients with ESRF, they are 17.4 times more susceptible to sustain a hip fracture than the general population.[5-7]

Comorbidities such as diabetes mellitus (DM), chronic heart disease, and cancer are significant risk factors for mortality in all patients undergoing hip fracture surgery. These comorbidities are common in patients with ESRF, thus potentially contributing to increased mortality among patients with ESRF.[8] The literature has shown that hip fracture patients with ESRF on dialysis have higher mortality rates than non-ESRF patients,[8] with 1-year postoperative mortality rates for patients on hemodialysis with hip fractures estimated at 37.2%.[8]

However, the causative impact of attendant comorbidities on mortality after hip fracture surgery in patients with ESRF remains presumptive. It remains uncertain whether ESRF, as a disease entity, predicts independently for postsurgical mortality as is established for cancer in patients with hip fracture.

We hypothesized that ESRF is independently prognostic of risk for 1-year postsurgery mortality in patients with hip fracture who undergo surgery. In this retrospective cohort study, we aimed to examine and quantify the risk of all-cause, 1-year mortality associated with hip fracture surgery in the ESRF population.

Materials and Methods

Patients undergoing surgery for a unilateral intertrochanteric (IT) hip fracture or neck of femur (NOF) hip fracture at the Singapore General Hospital (SGH) from June 2007 to June 2012 were divided into 2 groups: the study cohort comprising patients with ESRF on active hemodialysis and non-ESRF patients serving as the control group. Patients with known renal impairment but were not on dialysis and those who had undergone previous renal transplants were categorically excluded. Patients with a hip fracture resulting from a fall from standing height were study candidates, with the following exclusions: patients aged <55 years and patients with pathological fractures due to tumors, polytrauma, or previous hip fracture surgery. Forty-six patients with ESRF and 598 non-ESRF patients satisfied the inclusion criteria. Centralized Institutional review board approval was granted by our Centralized Institutional Review Board.

Data were captured and obtained from the SGH institutional database electronic medical records. Variables collected for each patient were age, gender, fracture type, and presence of the following comorbidities: hypertension (HTN), hyperlipidemia, ischemic heart disease (IHD), cerebrovascular accident, DM, cancer, anemia, arrhythmia, asthma, dementia, vascular, and thyroid disease. Study outcome of all-cause, 1-year mortality was determined via rigorous reviews of institutional and nationwide linked electronic health records.

Patient demographic variables, comorbidities, and the 1-year postoperative mortality outcome were compared between ESRF and non-ESRF groups using the 2-sample *t* test for patient age and Fisher exact test for the remaining variables, which were all categorical.

Univariate and multivariate logistic regression analysis was used to assess age, patient comorbidities, and ESRF as risk factors for 1-year postoperative mortality. Initially, univariate logistic regression was used to identify all variables significant at $P \leq .20$. Variables significant at $P \leq .20$ in univariate analysis were included in a multivariable stepwise logistic regression analysis with significance levels to enter and stay of 0.20.

The final multivariable prediction model consisted of variables selected in the stepwise regression. Odds ratios and 95% confidence intervals (CIs) were calculated. Predicted probabilities of 1-year mortality obtained from the model were used to construct a receiver–operating characteristic (ROC) curve and area under the ROC curve calculated as an overall measure of predictive utility.

An "optimal" dichotomizing cut point for prognosticating high-risk patients—those likely to die within 1 year—was obtained using Youden index that identifies the predicted probability for which sensitivity + specificity is maximized. Sensitivity, specificity, positive, and negative predictive values of the final multivariable model were assessed.

Results

Patient Demographics and Clinical Characteristics

Of 644 patients who underwent hip fracture surgery from June 2007 to June 2012, 46 (7.14%) were patients with ESRF on dialysis and 598 (92.9%) were non-ESRF patients. The mean age of patients with ESRF was 71.5 years versus 76.8 for non-ESRF ($P < .0001$). Gender did not differ significantly between the 2 groups with the percentage of males being 34.8% among patients with ESRF and 31.1% among non-ESRF patients ($P = .6224$). Fracture type did not differ significantly between study groups either. Among patients with ESRF, 76.1% sustained NOF fractures and 23.9% IT fractures, while among non-ESRF patients, 64.5% had NOF fractures and 35.5% IT fractures ($P = .1471$).

At a 100% follow-up rate, patients with ESRF were found to have a higher 1-year postoperative mortality when compared to non-ESRF patients, 19.6% versus 8.4%, respectively ($P = .028$).

Fisher exact test showed that demographic and comorbidity variables such as age ($P < .0001$), DM ($P = .0014$), HTN ($P = .0002$), IHD ($P = .0002$), anemia ($P = .0055$), cardiovascular accident ($P = .0067$), vascular disease ($P = .0212$), and anemia ($P = .0055$) were significantly associated with ESRF ($P < .05$;. Table 1).

Logistic Regression Analysis and Predictive Model

Demographic and comorbidity variables significantly associated with 1-year postsurgery mortality at $P \leq .20$ in univariate logistic regression analysis were age, cancer, IHD, ESRF, DM, arrhythmia, gender, HTN, vascular disease, and anemia (Table 2). Among these 10, multiple stepwise regression

Table 1. Comparison of Patient Demographic, Clinical Characteristic, and Outcome Variables by End-Stage Renal Failure Status.

Variable	Non-ESRF, n = 598	ESRF, n = 46	*P* Value[a]
Demographics			
Age, mean (SD), year	76.8 (8.4)	71.5 (8.4)	**<.0001**
Male gender (%)	31.1	34.8	.6224
Fracture type (%)			
NOF/IT	64.5/35.5	76.1/23.9	.1471
Comorbidities (%)			
Diabetes mellitus	28.6	52.2	**.0014**
Hypertension	62.5	89.1	**.0002**
Hyperlipidemia	35.8	39.1	.6370
Ischemic heart disease	18.7	43.5	**.0002**
Arrhythmia	6.2	6.5	.7586
Cardiovascular accident	12.7	28.3	**.0067**
Dementia	6.5	2.2	.3489
Asthma	2.5	2.2	1.0000
Vascular disease	1.0	6.5	**.0212**
Anemia	14.9	32.6	**.0055**
Cancer	8.5	15.2	.0952
Thyroid	5.0	8.7	.2938
Mortality outcome			
1-year mortality (%)	8.4	19.6	**.0280**

Abbreviations: ESRF, end-stage renal failure; IT, intertrochanteric; NOF, neck of femur; SD, standard deviation.

[a]Age, 2-sample *t* test; categorical variables, Fisher exact test. Boldface values are the factors significantly associated with ESRF ($P < 0.5$).

selected age ($P < .0001$), ESRF ($P = .021$), IHD ($P = .020$), cancer ($P = .003$), and DM ($P = .022$) as significant independent predictors of 1-year mortality following hip fracture surgery. Odds ratios with 95% CIs and successive contribution to the area under the ROC curve are found in Table 2.

The linear predictor obtained from the logistic regression was

$$y = -9.3108 + 0.0803 \times \text{Age} + 1.0465 \times \text{ESRF} + 0.7252 \times \text{IHD} + 1.1115 \times \text{Cancer} + 0.7078 \times \text{DM}$$

where age is in years and ESRF, IHD, cancer, and DM are categorical variables taking a value of "1" if present and "0" if absent. The predicted probability of 1-year postoperative mortality was obtained as $p = e^y/(1+ e^y)$.

The ROC curve derived from the predictive model is shown in Figure 1 where the plotted points are predicted probabilities. The area (95% CI) under the ROC curve was 0.75 (0.69-0.82). Applying Youden criterion (sensitivity + specificity − 1), the predicted probability cut point for prognosticating high-risk patients for 1-year postoperative mortality was 0.09. At the 0.09 cut point, sensitivity, specificity, positive predictive value, and negative predictive value was 70%, 70%, 17%, and 97%, respectively. The cumulative incidence of 1-year postoperative mortality was 7.91%.

Figure 2 shows predicted probabilities of 1-year postoperative mortality for ESRF and non-ESRF patients by comorbidity burden with age dichotomized at ≤75 and >75 years. Median age for all patients was 77 years.

Discussion

Increased mortality among patients with ESRF on dialysis under various clinical settings have been well established. According to statistics collated by the University of California among the general ESRF population in the United States, the 1-year mortality rate for patients with ESRF on dialysis was between 20% and 25%.[9] In a local study, the 1-year mortality rate in patients on dialysis was found to be 17.2%.[10] A study using Taiwan National Health Insurance Research Database reported 1-year mortality rates of 37.2% among patients with hip fracture on hemodialysis versus 16.6% in non-hemodialysis patients.[8] Beaubrun et al reported that the 1-year mortality rate among hemodialysis patients with hip fractures was 630 per 1000 patient-year (PY) PY.[11] Coco and Rush further reported that the 1-year mortality rate was 64% in 59 hip fractures of 1272 hemodialysis patients.[12] Mittalhenkle et al also observed that among 7636 hemodialysis patients who sustained a hip fracture, the 1-year mortality rate was approximately 50%.[13]

Consistent with the literature, the postoperative 1-year mortality rate of 19.6% for patients with ESRF on dialysis undergoing hip fracture surgery in this study was significantly higher than the 8.4% for non-ESRF patients. This was despite the patients with ESRF being younger (71.4 years), on average, than the non-ESRF patients (76.8 years). The lower mortality rates in this study compared to prior publications could be an indication of a higher threshold for surgery and patient selection, as a proportion of the frailer patients would be treated conservatively instead. It is difficult to tell if a subgroup of patients treated conservatively would have benefited medically and functionally from surgical intervention.

Comorbidities Associated With ESRF

The comorbidities attendant to ESRF in this study—HTN, IHD, DM, anemia, cerebrovascular disease, and vascular disease—were consistent with the literature. Gomez et al reported that of 771 patients with ESRF included in their study, 48% had diabetes, 31% had a history of previous myocardial infarction, and 22% had heart failure.[14] In the United States, it was reported that DM and HTN are the number 1 and 2 conditions, respectively, that lead to chronic kidney disease. Hence, most patients with ESRF also have DM and HTN.[15] This too is consistent with the findings of this article. In all, 52.2% of patients with ESRF in our study had DM versus 28.6% in non-ESRF patients, and 89.1% of patients with ESRF had HTN versus 62.5% in non-ESRF patients. Furthermore, it was reported by Go et al that patients with GFR between 15 and 29 mL/min/1.73m^2 and patients with ESRF, that is, GFR <15 mL/min/1.73 m^2 had a higher prevalence of coronary heart disease, stroke or transient ischemic attack, peripheral arterial disease, chronic heart failure, known proteinuria, DM, HTN, dyslipidemia, chronic lung disease, chronic liver disease, and cancer.[16]

Table 2. Summary of Univariate and Multivariate Logistic Regression on 1-Year Mortality.

	Univariate[a]			Multivariate[b]		
Variable	Raw OR[c] (95% CI)	*P* Value	AUC	Adjusted OR[c] (95% CI)	*P* Value	Cumulative ROC AUC
Cancer	3.833 (1.915-7.673)	**.0001**	0.5770	3.039 (1.448-6.379)	**.0033**	0.5770
Age	1.067 (1.031-1.105)	**.0002**	0.6489	1.084 (1.042-1.127)	**<.0001**	0.6879
IHD	2.568 (1.457-4.527)	**.0011**	0.5924	2.065 (1.120-3.807)	**.0202**	0.7166
ESRF	2.667 (1.218-5.840)	**.0142**	0.5446	2.848 (1.171-6.924)	**.0210**	0.7347
DM	1.939 (1.125-3.342)	**.0170**	0.5759	2.030 (1.108-3.716)	**.0218**	0.7515
Arrhythmia	3.217 (1.450-7.134)	**.0040**	0.5498			
Male gender	1.831 (1.063-3.153)	**.0292**	0.5699			
Hypertension	1.539 (0.846-2.799)	.1579	0.5465			
Vascular disease	2.900 (0.589-14.28)	.1907	0.5110			
Anemia	1.534 (0.797-2.953)	.2003	0.5324			

Abbreviations: AUC, area under the ROC curve; CI, confidence interval; DM, diabetes mellitus; ESRF, end-stage renal failure; IHD, ischemic heart disease; OR, odds ratio; ROC, receiver operating characteristic.

[a]Dementia, thyroid, asthma, hyperlipidemia, cardiovascular accident and fracture type were not significant at $P \leq .20$ in univariate analysis ($P > .45$).

[b]Multivariate prediction model: variables selected in stepwise regression significant at $P \leq .20$ from those significant at $P \leq .20$ in the univariate analysis.

[c]The reference group for all categorical variables is absence of disease; age is a continuous variable. Boldface values are the factors significantly associated with ESRF ($P < 0.5$).

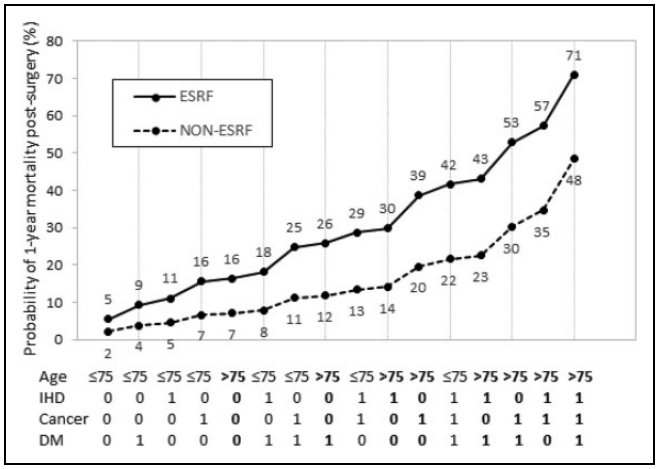

Figure 1. ROC curve obtained from logistic regression predictive model. ROC indicates receiver operating characteristic.

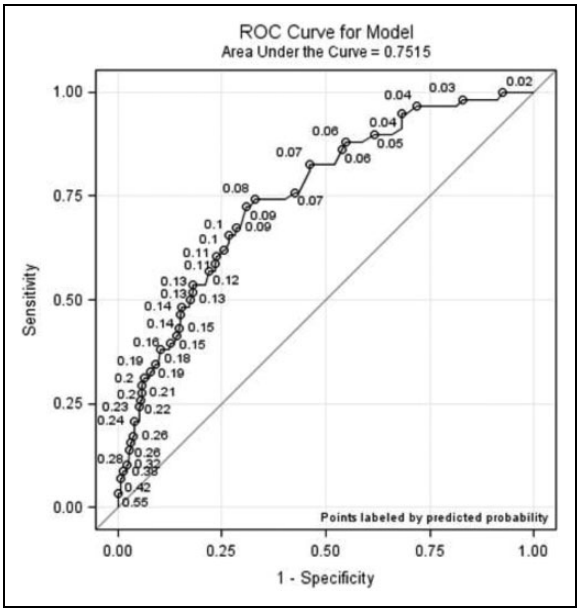

Figure 2. Predicted probability of 1-year postoperative mortality at ≤75 and >75 years of age by comorbidity and ESRF versus non-ESRF.

End-Stage Renal Failure as an Independent Predictor of 1-Year Mortality

Recognizing the attendant comorbidities associated with ESRF, the question of ESRF as an independent predictor of mortality arises. This study has confirmed ESRF to be a significant and independent risk factor for 1-year mortality in patients undergoing hip fracture surgery. Although commonly associated with ESRF, IHD and DM independently predict for 1-year mortality to a smaller degree than ESRF. This is not surprising, as ESRF represents an end-organ damage resultant from either one or the combination of these conditions. It is also noteworthy that the mortality after hip fracture surgery of 19.6% trended closer to the overall 1-year mortality of 17.2% in the local cohort of patients with ESRF than to the mortality rates of a general cohort of patients undergoing hip fracture surgery.

In a large cohort of surgical intensive care unit (ICU) patients, Apel et al found ESRF to be an independent predictor of inpatient mortality with higher disease severity and likelihood of organ failure during the surgical ICU admission.[17] Renal failure was 1 of 9 predictors of 30-day mortality after hip fractures in a recently developed mortality predictive model.[18] We have demonstrated that ESRF continues to independently predict for mortality up to 1-year after surgery for hip fractures. With no loss to follow-up, our odds ratio of 2.848 (1.171-6.924) for 1-year mortality is similar, and perhaps slightly higher, than an estimate of 2.32 from the

Taiwanese Registry data[8] for overall mortality up to 5 years. Furthermore, multivariate logistic regression analysis of multiple comorbidity risk factors for mortality showed the magnitude of risk as quantified by the odds ratio was second only to cancer and higher than that posed by IHD (adjusted odds ratio [AOR] = 2.07), DM (AOR = 2.03), and age (AOR = 1.08).

Preoperative workup in patients with hip fracture has often emphasized cardiovascular fitness, but less emphasis has been paid to ESRF as a clinical entity. The fact that ESRF is an independent predictor of mortality subsequent to a hip fracture should be carefully explained to patients and relatives during the perioperative counseling and consent taking process. A fall prevention program for this group of patients would be of paramount importance, in view of the poor prognostic factors after hip fractures in this cohort. It can also be extrapolated that this subgroup of patients are likely to consume high health-care resources, and ESRF as a comorbidity should be well accounted for in alternative payment models.

Strengths and Limitations

Strengths. The follow-up on mortality outcomes was 100% at 1 year, which leaves no question regarding reliability of the 1-year mortality rates. Studies with drop outs may over- or underestimate mortality. Because all-cause mortality may be more readily captured from institutional databases, there may be a potential to overestimate mortality in geriatric studies with dropouts. In addition, a comprehensive list of comorbidities were analyzed with a relatively large sample size of 598 non-ESRF patients and 46 patients with ESRF.

Limitations. Due to the inherent increased risks of undergoing surgery in the case of poorer health, as a matter of ethics and policy, very ill patients at our institution may not be given the option of surgery. This would introduce an element of selection bias into this study.

As case identification was based on surgical coding of patients under the care of the Orthopedic surgery department, the capability to capture characteristics and outcomes of conservatively treated patients admitted under the care of medical units was limited.

Conclusion

Notwithstanding the comorbidities associated with ESRF, our study has identified ESRF requiring dialysis as an independent risk factor for 1-year mortality after hip fracture surgery. The magnitude of the risk posed by ESRF was second only to cancer, which has long been recognized as an independent mortality risk and usually adjudicated for in cohort studies and database analysis.

Declaration of Conflicting Interests

The author(s) declared no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

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