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ORIGINAL ARTICLE

Comorbidity as the dominant predictor of mortality after hip fracture surgeries

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Abstract

Summary The aim of this study was to investigate the association of surgical delay and comorbidities with the risk of mortality after hip fracture surgeries. We found that CCI was the dominant factor in predicting both short- and long-term mortality, and its effect is vital in the prognostication of survivorship.

Introduction Hip fracture is a growing concern and a delay in surgery is often associated with a poorer outcome. We hypothesized that a higher Charlson Comorbidity Index (CCI) portends greater risk of mortality than a delay in surgery. Our aim was to investigate the associations of surgical delay and CCI with risk of mortality and to determine the dominant predictor.

Methods This retrospective study examines hip fracture data from a large tertiary hospital in Singapore over the period January 2013 through December 2015. Data collected included age, gender, CCI, delay of surgery, fracture patterns, and the American Society of Anaesthesiologist (ASA) score. Post-operative outcomes analyzed included mortality at inpatient, at 30 and 90 days, and at 2 years.

Results A total of 1004 patients with hip fractures were included in this study. Study mortality rates were 1.1% ($n = 11$) during in-hospital admission, 1.8% ($n = 18$) at 30 days, 2.7% ($n = 27$) at 90 days, and 13.3% ($n = 129$) at 2 years. Lost to follow-up rate at 2 years was 3.3%. We found that CCI was consistently the dominant factor in predicting both short- and long-term mortality. A CCI score of 5 was identified as the inflection point above which comorbidity at baseline presented a greater risk of mortality than a delay in surgery.

Conclusion Our analysis showed that CCI is the dominant predictor of both short- and long-term mortality compared with delay in surgery. The effect of CCI is vital in the prognostication of mortality in patients surgically treated for hip fractures.

Keywords CCI · Charlson Comorbidities Index · Hip fracture · Long-term mortality · Osteoporotic fracture · Short-term mortality · Surgical delay

Introduction

Osteoporotic fracture is a major health problem among the aging population, affecting close to 9 million patients worldwide [1]. Hip fractures in particular are a growing concern due to the projected increase in incidence with the associated high risk of mortality. It is estimated that by the year 2050, there will be close to 6.3 million hip fractures yearly [2]. As the most serious of all osteoporotic fractures, hip fractures are associated with the highest mortality rates. The 1-year mortality rate after sustaining a hip fracture can range from 10% to as high as 40% [3–6], and the risk of dying may persist for up to 5 years, making it a long-term public health concern [6].

Surgical delay has often been cited as one of the major contributing factors leading to a poorer outcome after surgical fixation of hip fractures. Early surgery has been associated with improved patient survival [7–9] and functional outcomes [10]. This, however, is still an ongoing debate as conflicting results have been reported regarding the association between early surgery and mortality [11–13]. Other risk factors, including patient demographics such as gender [5, 14] and age, systemic factors such as baseline comorbidities of the patient [15–19] and ASA score, and biochemical factors such as hypoalbuminemia [20] and hypovitaminosis D, have also been

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associated with increased risk of mortality following surgical fixation of hip fractures.

Patients with a higher comorbid load often experience a delay in surgery due to the need for pre-operative optimization. The cause of poorer outcomes in surgery may not be entirely attributable to timing of surgery but to multiple factors. The relationship between surgical delay and mortality may not be as clear as previously thought. We hypothesize that a higher Charlson Comorbidity Index (CCI) may impact mortality risk to a greater extent than surgical delay. The objectives of this paper are to (1) study risk predictors associated with both surgical delay and mortality and (2) investigate associations between baseline comorbidity and surgical delay and their effects on risk of mortality following hip fracture surgery. This paper aims to identify whether CCI or surgical delay is the predominant risk factor in prognosticating complications and mortality following hip fracture surgeries.

Methods and materials

This retrospective cohort study is based on data collected from January 2013 through December 2015 at a large tertiary hospital in Singapore. The studied cohort included all patients above 60 years of age who had undergone surgical fixation or hemiarthroplasty for traumatic hip fractures to either the neck of the femur or trochanteric fractures. We excluded patients with non-osteoporotic fractures, patients with periprosthetic fractures, patients with pathological fractures, patients with fractures treated conservatively, or those lost to follow-up. Variables of interest included age, gender, CCI, delay of surgery (defined as time to surgery greater than 48 h), fracture patterns, and the American Society of Anaesthesiologist (ASA) score.

All patients were assessed for comorbidities prior to surgery and graded using the age-adjusted Deyo-Charlson Comorbidity Index (CCI) [21, 22]. CCI scores were calculated based on 17 comorbid conditions, with each assigned a weight of 1 to 6 according to its impact on mortality. The age-adjusted CCI takes into account each decade after 40 years of age as one point (i.e., 1 point for age 41–50, 2 points for age 51–60, 3 points for age 61–70, and 4 points for age above 71). Time to surgery was calculated as the elapsed time from hospital admission to the actual start of surgery. In this study, the threshold for a delay to surgery was set at 48 h. The post-operative outcomes studied were short-term mortality during inpatient stay, mortality at 30 and 90 days following surgery, and long-term mortality at the 2-year follow-up.

Univariate and multivariate logistic regression analyses were used to assess the effect of variables recorded at baseline on risk of mortality at admission, at 30 and 90 days, and at 2 years post-surgery. Variables significant at $p \leq 0.20$ in univariate analysis were entered into a multivariable logistic regression incorporating a forward stepwise selection algorithm with significance levels to enter and stay of 0.05 and 0.10, respectively, the purpose being to identify a preferred predictor of mortality between the CCI and delayed surgery. Using the predictor selected by the stepwise selection, an ROC curve was constructed and significance of change in area under the curve was reported to determine the incremental effect of each additional prognostic factor identified. All analyses were performed using SAS v9.4 software (SAS Inc., Cary, NC, USA). The level of significance was taken as $p < 0.05$.

This study (CRIB Ref: 2015/2134) was approved by the SingHealth Centralised Institutional Review Board, Singapore.

Results

There were a total of 1087 hip fracture surgeries performed during the period from January 2013 to December 2015; 1004 patients met the inclusion criteria and were used in the analysis. The mean ± SD age was 77.9 ± 8.1 years, and 715 (71.2%) were females. There were 599 (59.7%) femoral neck fractures and 405 (40.3%) trochanteric fractures. The mean time to surgery was 96 ± 107 h, and 345 (34.4%) surgeries were performed within 48 h. Mortality rates were 1.1% ($n = 11$) in-hospital, 1.8% ($n = 18$) at 30 days, 2.7% ($n = 27$) at 90 days, and 13.3% ($n = 129$) at the 2-year follow-up. The demographics of the study is showed in Table 1.

Surgical delay

Univariate logistic regression identified CCI and ASA as predictors of surgical delay. The multivariate analysis stepwise selected CCI as the dominant risk predictor for surgical delay.

Inpatient mortality

The inpatient mortality rate was 1.1% ($n = 11$). Both the univariate and multivariate logistic regression identified ASA and CCI as significant risk factors for inpatient mortality (Table 2). Using the stepwise selection algorithm, CCI ($p < 0.05$) was identified as the predominant risk factor.

Short-term mortality at 30 and 90 days

The 30-day mortality was 1.8% ($n = 18$ patients). Univariate logistics regression identified ASA, CCI, and age as predictors of mortality. In multivariate logistics regression analysis, CCI and age were the main independent risk factors ($p < 0.05$) for short-term mortality at 30 days (Table 2). Using the stepwise algorithm, CCI remained as the dominant risk predictor of mortality and the area under the ROC curve did not change significantly after the addition of other predictive risk factors.

Table 1 Demographics of patients (total number $n = 1004$ patients)

	Parameters	Samples	Percent
1	Number of patients		
	Female	715	71.2
	Male	289	28.8
2	Fracture pattern		
	Femoral neck	599	59.7
	Trochanteric	405	40.3
3	Baseline CCI		
	0–2	75	7.5
	3–4	454	45.2
	5–6	325	32.4
	Above 7	150	14.7
4	Baseline ASA score		
	1–2	717	71.4
	3–4	287	28.6
5	Delay in surgery		
	No (less than 48 h)	345	34.4
	Yes (more than 48 h)	659	65.6
6	Mortality rates		
	Inpatient	11	1.1
	30 days	18	1.8
	90 days	27	2.7
	2 years	129	13.3

At 90-day follow-up, we reported a mortality rate of 2.7% ($n = 27$). Similar to inpatient mortality, ASA and CCI were identified as the risk factors for complications, but only CCI and ASA were shown in the multivariate logistics regression to be the predominant predictor (Table 2). Likewise in the stepwise algorithm, CCI was the dominant risk predictor of mortality and area under the ROC curve did not change significantly after taking into account the effect of other predictors.

Long-term mortality at the 2-year follow-up

The follow-up rate of this study at 2 years was 96.7% ($n = 971$ patients). A total of 129 patients (12.5%) died during this period and we lost 33 patients (3.3%) to follow-up. Univariate logistics regression showed that all the factors discussed were associated with an increased risk of long-term mortality. The effect of surgical delay was not significant under the multivariate logistics regression analysis and the stepwise selection algorithm study identified CCI as the most important factor associated with mortality at 2 years. Using CCI as the preeminent predictor, the addition of other factors to the model did not result in significant improvement to the area under the ROC curve (Fig. 1).

Identifying the optimal CCI "cut-point" for early surgery

In this study, more than 85% ($n = 48$) of the short-term mortality and 75% ($n = 96$) of the 2 years mortality had a CCI score of above 5 (Fig. 2). Using Youden's rule to identify the inflection point, we found that a CCI score of 5 to 7 was identified as the "optimal" cut-point, above which patient baseline comorbidity supersedes surgical delay as the greater risk of mortality.

Discussion

In this study, we observed mortality rates of 1.1% ($n = 11$) during in-hospital admission, 1.8% ($n = 18$) at 30 days, 2.7% ($n = 27$) at 90 days, and 13.3% ($n = 129$) at the 2-year follow-up. Compared with current literature which showed a mortality rate of 10–40% [3–6], we saw a much lower mortality rate likely attributed to improved treatment protocol, better understanding of octogenarians, and greater emphasis on perioperative management of hip fracture patients. Our high follow-up rate of close to 96.7% further authenticates the validity of our high survivorship.

Table 2 Multivariate logistics regression of factors affecting mortality

Factors	Inpatient mortality				30-day mortality				90-day mortality				2-year mortality			
	OR	95% CI		*p* value	OR	95% CI		*p* value	OR	95% CI		*p* value	OR	95% CI		*p* value
ASA score	4.64	1.13	19.00	*0.033*	2.02	0.74	5.48	0.169	2.34	1.02	5.35	*0.044*	1.59	1.05	2.40	*0.027*
Surgical delay	0.61	0.15	2.60	0.507	0.78	0.26	2.35	0.660	1.06	0.40	2.79	0.906	1.50	0.93	2.43	0.101
CCI	1.40	1.12	1.77	*0.004*	1.33	1.09	1.63	*0.005*	1.36	1.16	1.59	*< 0.001*	1.36	1.24	1.50	*< 0.001*
Gender (M vs F)	1.81	0.52	6.28	0.347	2.03	0.76	5.39	0.156	2.13	0.95	4.76	0.065	2.14	1.42	3.23	*< 0.001*
Age	1.03	0.95	1.11	0.470	1.07	1.01	1.14	*0.030*	1.03	0.98	1.08	0.203	1.03	1.00	1.05	*0.040*
Type of fractures	0.58	0.16	2.08	0.400	0.70	0.26	1.88	0.482	1.07	0.48	2.36	0.874	1.53	1.03	2.28	*0.037*

OR, odds ratio; *CI*, confidence interval

Italicized font indicates statistical significance ($p < 0.05$)

ROC Curves for comparison among predictive models at 2 years follow up

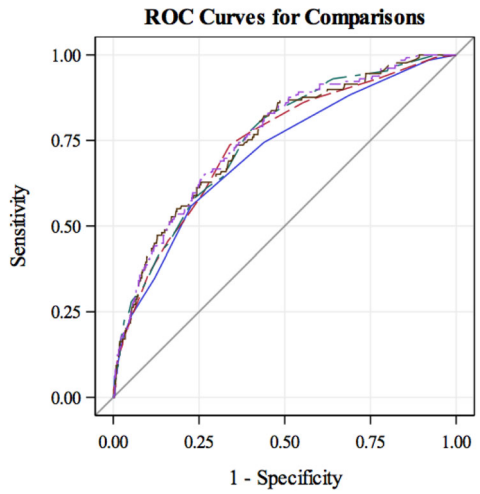
ROC Curve	Factors	ROC	95% CI		p-value
	CCI	0.71	0.664	0.761	-
	CCI vs CCI + Gender	0.74	0.694	0.785	0.078
	CCI + Gender vs CCI + Gender + ASA	0.75	0.706	0.793	0.256

Fig. 1 ROC curves for comparison among predictive models at 2-year follow-up

Compared with surgical delay and other risk predictors, CCI was found to be the best predictor of both short-term (inpatient, 30-day, and 90-day) and long-term (2-year) mortality. Using the stepwise selection algorithm to prioritize predictors, CCI was consistently found to be the superior factor. With CCI as the preeminent risk factor, the addition of other factors to the predictive model did not significantly improved the area under the ROC curve.

Youden's rule was used to identify an "optimal" cutoff point beyond which surgical intervention should not be delayed. We found that in patients with a CCI score below 5, early surgery greatly reduced the risk of both short- and long-

Effect of CCI on short and long term mortality after hip fracture surgery

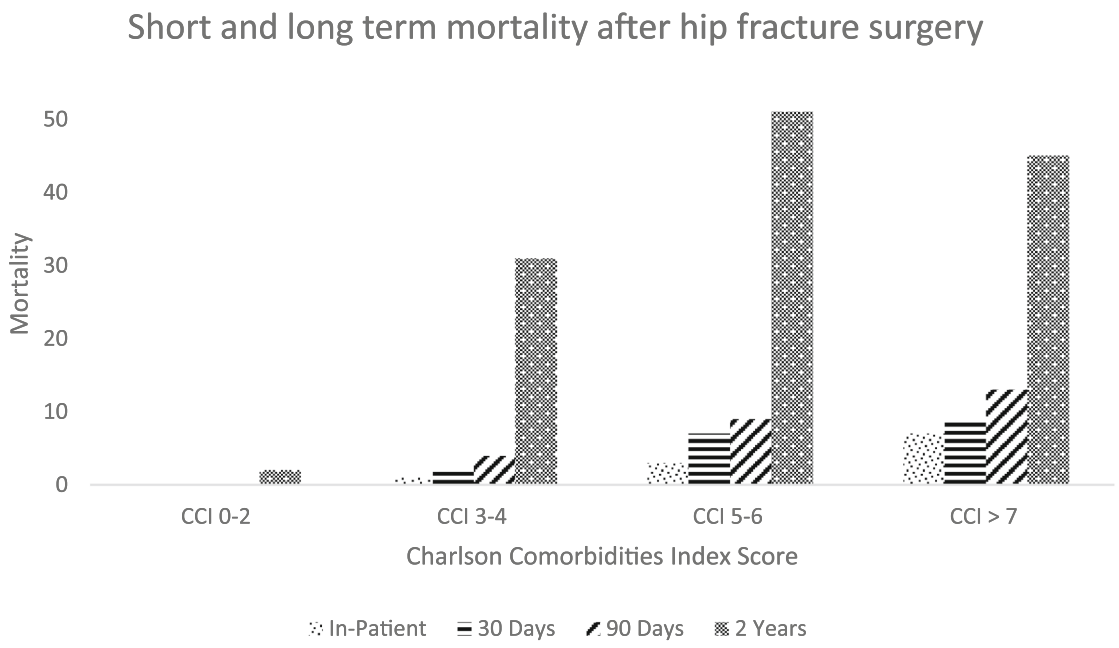


Fig. 2 Effect of CCI on short- and long-term mortality after hip fracture surgery

term mortality. On the contrary, in patients with a CCI score greater than 7, the increased risk of mortality was contributed primarily by poorer pre-morbid health status than by a delay in surgery.

We analyzed the risk factors categorized into patient's demographics (age and gender, fracture pattern, ASA score, CCI score) and systems factors (time to surgery). Using multivariable logistic regression, we analyzed the interplay between each of these factors on mortality after hip fracture surgery. More importantly, with the use of a stepwise selection algorithm as well as the ROC curve analysis, we were able to identify the most important predictive factors for prognosticating the risk of mortality.

The Deyo-Charlson Comorbidity Index is a validated clinical evaluation tool [21], derived from the original Charlson Comorbidity Index [23, 24] that was first published in 1987. It is a summative score, calculated based on a weighted scale of 17 comorbidities. In this study, we calculated the pre-operative age-adjusted CCI patient score to determine baseline comorbidity load and found it to be a significant risk predictor of both short- and long-term mortality. Similar results have also been shown in many other literature [17, 19, 25, 26]. Our analysis consistently showed that a higher CCI score was associated with increased risk of both short- and long-term mortality. Although CCI may be an unmodifiable risk predictor and pre-operative optimization may not be possible to significantly improve the pre-morbid load of a patient, findings from this study can help to more accurately prognosticate the risk of mortality following hip fracture surgery.

The effect of time to surgery after hip fracture has been a well-known subject of debate. A number of studies have been conducted to determine the importance of time to surgery as a predictor of both short- and long-term mortality. While some studies suggested that early surgeries were associated with better outcomes, including lower risk of mortality and shorter inpatient stay [27, 28], these data were constantly challenged by other outcome-based studies suggesting otherwise [29–31].

In the large population-based study conducted by Pincus et al., they found that a wait time of more than 24 h was associated with an increased risk of 30-day mortality [32]. In their study, they have also made use of CCI to grade the patient's baseline health, but only 54% of the population studied had a CCI score reported and analyzed. In order to more accurately study the effect of increasing comorbidities, we have further categorized our patient's health profile into 4 distinct groups based on their CCI and found that a score of more than 5 reflects the importance of baseline health more than timing to surgery. Although our results showed that a delay in surgery was not a risk predictor for mortality at 30 days, we do recognize that our low short-term mortality number may limit its accuracy.

In a recent nationwide cohort study published by Ozturk et al. in 2019, they found that surgical delay was seen in patients with slightly more comorbid and was associated with early mortality of up to 90 days in those with none to medium comorbidities rather than those with a higher comorbidity load [33]. These findings suggested that the effect of comorbidities may contribute to a delay in surgery and also play a major role in the prognostication of hip fracture survivorship. Similarly, in our study, we showed that a patient's baseline comorbidities affect their timing to surgery and may pose a greater impact on the survival after hip fracture surgery.

In another recent systematic review published in Nature by Klestil et al. in 2018, the group concluded that patients who are operated within 48 h had a reduced risk of mortality at 1 year but not on short-term mortality of within 1 month. Although the effect of patient's comorbidities was not conclusive in their study due to insufficient data, an observation was made suggesting a lack of correlations between timing to surgery and mortality in patients with acute medical conditions [34].

In our present study, we saw that surgical delay may not have an impact on short-term mortality of up to 90 days. However, we do observe that a delay of more than 48 h was an independent predictor of longer-term mortality at 2-year follow-up, but when adjusted for other factors, this effect was not evident in the prediction of mortality after surgery. The difference in our findings may be explained by our low early mortality rates which potentially limits the sensitivity of identifying a significant relationship between surgical delay and early mortality, as well as an increasing focus of pre-optimization in our current hip fracture treatment protocol. Furthermore, we showed that not only was CCI a significant risk predictor, it was the dominant factor affecting outcomes following hip fracture surgeries. The effect of other confounding factors including age and gender did not significantly increase the area under the ROC curve.

The relationship between CCI and surgical delay on mortality is not a simple one to define. With the use of Youden's rule, we have identified in our study a CCI inflection point where timing to surgery may play a part in the prognostication of both short- and long-term risks of mortality. This is a crucial piece of information because it provides greater clarity into the management of hip fracture patients based on their comorbid load rather than a wait time threshold. We propose that patients with a CCI score greater than 5 should not be hastily rushed into surgery, as the risk of post-surgical mortality is not entirely related to a delay in operation. Instead, they should be counselled appropriately during the decision-making progress and if possible, pre-operative optimization may be of greater importance in reducing their risks of death. At the same time, a 48-h threshold may be implemented in the sub-group of patients with a CCI score of less than 5, owing to the benefits associated with early surgery.

This paper has offered greater insight into the interrelationship between CCI and surgical delay on mortality. Findings from this study support the benefits for early surgeries in patients who are pre-morbidly healthier.

Strengths and limitations

The strength of the study lies in the large cohort study with a high follow-up rate of 96.7% at 2-year follow-up. We have also captured a more detailed range of baseline CCI scores and categorized them into 4 distinct groups to analyze the effect of increasing CCI on mortality after hip fracture surgery. This allows the use of Youden's rule to predict the inflection point of CCI and hence, we were able to identify the significant score of 5, above which mortality after hip fracture surgery may be more affected by CCI rather than the other factors studied. In addition, we made use of a stepwise selection algorithm to identify the most predictive factor affecting mortality.

This study however had several limitations. It is a retrospective observational study on the risk of mortality and no data was presented regarding patient functional outcomes, quality of life, or return to community. The low short-term mortality rates may limit the sensitivity of the study to accurately identify the effect of CCI.

Conclusion

In this study, we showed that among all factors studied, CCI is the dominant predictor of short- and long-term mortality following hip fracture surgery. While surgical delay was highly concomitant with CCI, delay in surgery was not a significant risk predictor of mortality. The inflection point of CCI score above 5 reflects an important threshold level where greater emphasis should be placed on pre-operative optimization rather than early surgery. On the other hand, delay in surgery should be avoided in patients with a lower CCI score so as to reap the benefits associated with early operation. The significance of baseline comorbidities should be given a greater emphasis in the prognostication of patients treated surgically for hip fractures.

Compliance with ethical standards

This study (CRIB Ref: 2015/2134) was approved by the SingHealth Centralised Institutional Review Board, Singapore.

Conflicts of interest None.

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