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Severe aortic stenosis is associated with perioperative mortality in proximal femur fracture patients

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Abstract

Objectives: Evaluate the correlation between aortic stenosis and perioperative mortality in patients following surgical fixation of proximal femur fractures.

Design: Retrospectively reviewed case series.

Setting: Two Academic, Level 1 Trauma Centers.

Patients/Participants: One hundred fifty-eight patients, definitively diagnosed with aortic stenosis by means of echocardiogram, who underwent surgical fixation for an isolated proximal femur fracture (OTA/AO 31-A, 31-B, 32-A, 32-B, and 32-C fractures) between January 2000 and June 2015. The severity of the aortic stenosis was based upon accepted echocardiographic hemodynamic parameters designated by the 2014 American Heart Association guidelines.

Main Outcome Measures: Post Injury mortality, 30-day mortality, and 1-year mortality.

Secondary Outcome Measures: Postoperative mortality stratified by severity of aortic stenosis based on aortic valve area (AVA) and ejection fracture (EF) as determined by preoperative echocardiography.

Results: One hundred fifty-eight patients were available for final analysis. Kaplan–Meier survival analysis revealed a significantly longer time to mortality among *Non-severe aortic stenosis* patients compared to *Severe aortic stenosis* patients, *P* value .006. Twenty-three percent of patients with *Severe aortic stenosis and 10% of patients with Non-severe aortic stenosis* died within 30 days of surgery. No significant difference was observed in mean survival among AS patients who underwent surgery within 48 hours of injury (34.5 months) and those delayed more than 48 hours after injury (25.0 months), *P* value .116. Among the commonly measured hemodynamic parameters of aortic stenosis, only AVA and EF were significantly associated with mortality, *P* value .015, and *P* value < .001, respectively. There were no significant effects for Aortic Vmax, Peak ΔP, and Mean ΔP. An AVA of $0.8\,cm^2$ or less is associated with a significantly shorter (22 months) postinjury mortality than patients with an AVA > $0.8\,cm^{2.}$ (37 months), *P* value .009.

Conclusions: Severe aortic stenosis is associated with a shorter postoperative time to mortality after surgical fixation of hip fractures compared to patients with Non-severe stenosis. Aortic valve area and Ejection Fraction are the only hemodynamic parameters significantly associated with postoperative mortality.

Level of Evidence: Prognostic Level III

Keywords: aortic stenosis, decision support techniques, hip fracture, mortality, proximal femur fracture

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1. Introduction

Aortic Stenosis (AS) is the most common valvular heart disease, and is frequently cited as a risk factor for perioperative mortality during noncardiac surgery.[1,2] AS occurs in 2% to 9% of elderly patients and increases with increasing age.[2] Every year, more than 300,000 patients over the age of 65 years are hospitalized for proximal femur fractures.[3] Given the overlap in these demographics, it is no surprise that many proximal femur fracture patients have comorbid AS.

The American Heart Association (AHA) classifies AS into stages based upon hemodynamic and anatomic parameters.[4] These parameters are measured by echocardiogram and include Left Ventricular Ejection Fraction (LVEF), Average Pressure Gradient Across the Aortic Valve (mean ΔP), Peak Pressure Gradient Across the Aortic Valve (Peak ΔP), Maximum Aortic Velocity (V_{max}), and Aortic Valve Area (AVA).[4] While there are many ways of defining AS, patients are most commonly stratified

based on the presence or absence of *Severe AS*, defined as an AVA of 1 cm or less.[5,6]

The Anesthesia literature has described AS in noncardiac surgical patients and found moderate-to-severe aortic stenosis to be a significant predictor of perioperative complication.[2,5,7] However, many published studies have not specifically assessed the impact of AS on hip fracture patients; instead, they have tended to either group these patients among other orthopaedic procedures (such as elective hip and knee replacement) or neglect them altogether.[2,6,7] The studies that have specifically addressed this issue are contradictory in their findings. Keswani et al[8] found a significant increase of 30-day and 1-year mortality among 65 patients. Adunsky et al[9] found no increase in 1-year mortality, but a 3% increase to in-hospital mortality among AS patients. Conversely, Leibowitz et al and McBrien et al found no increase in mortality associated with this comorbidity among hip fracture patients.[10,11] The influence of AS as a possible risk factor for perioperative mortality is important given that nearly 39% of hip fracture patients have AS and disproportionately higher mortality than those without AS.[12,13]

The primary purpose of this study is to determine if severe aortic stenosis is associated with mortality following the surgical management of hip fractures. The secondary purpose was to evaluate the role of commonly recorded hemodynamic measures in AS including AVA, LVEF, mean ΔP, Peak ΔP, V_{max} on the assessment of perioperative mortality following hip fracture surgery.

2. Materials and methods

2.1. Patient group

This project was approved by the Partners Human Research Committee under Protocol #: 2018P000377, Principle Investigator Michael J. Weaver, MD. A retrospective review was performed of cases at 2 ACS level 1 trauma centers between January 1, 2000 and June 30, 2015. Inclusion criteria were patients aged 55 years or greater; with a diagnosis of AS, who underwent surgical treatment for a proximal femur fracture. Fracture types included femoral neck (FNF), intertrochanteric femur fractures (IT), and subtrochanteric femur fractures; OTA/AO 31-A, 31-B, 32-A, 32-B, and 32-C fractures. Exclusion criteria included patients for whom an echocardiogram was not available within 30 days prior to surgery, inability to confirm vital status for at least 12 months after initial presentation, polytrauma, patients with Hypertrophic cardiomyopathy or Pulmonary Hypertension, and patients who underwent preoperative aortic valvuloplasty or replacement.

2.2. Aortic stenosis classification

Patients were categorized into stage of AS based upon an echocardiogram done prior to surgery. Echocardiographic variables collected included AVA (calculated according to the continuity equation), mean ΔP, peak ΔP, V_{max}, and LVEF.

Patients were categorized into AHA stage based upon published guidelines regarding echocardiographic data (Table 1).[4] These stages were further classified as Non-severe AS (stages A and B) and Severe AS (stages C and D).

2.3. Proximal femur fracture classification

Proximal femur fractures were classified at the time of operation by the treating surgeon as either femoral neck, intertrochanteric, or subtrochanteric.

2.4. Statistical analysis

All statistical calculations were performed using IBM SPSS Statistical Subscription software (IBM Corp, Armonk, NY). Statistical significance was defined as an alpha error of less than 5% ($P < .05$). Heteroscendastic Student t test was utilized to compare the means of unequal variance. Kaplan–Meier survival analysis validated via the log rank test was used to depict graphic relationships of survival. Multivariable cox proportional hazards analysis was used to assess survival impact of age at presentation, hip fracture type, New York Heart Association (NYHA) classification, Charlson Comorbidity Index (CCI), time to surgery (TTS), and the echocardiographic parameters of AS.

3. Results

One hundred fifty-eight patients were available for final analysis (Fig. 1). Of these 158, there were 119 females and 39 males. Demographic information for the included patients is provided in Table 2.
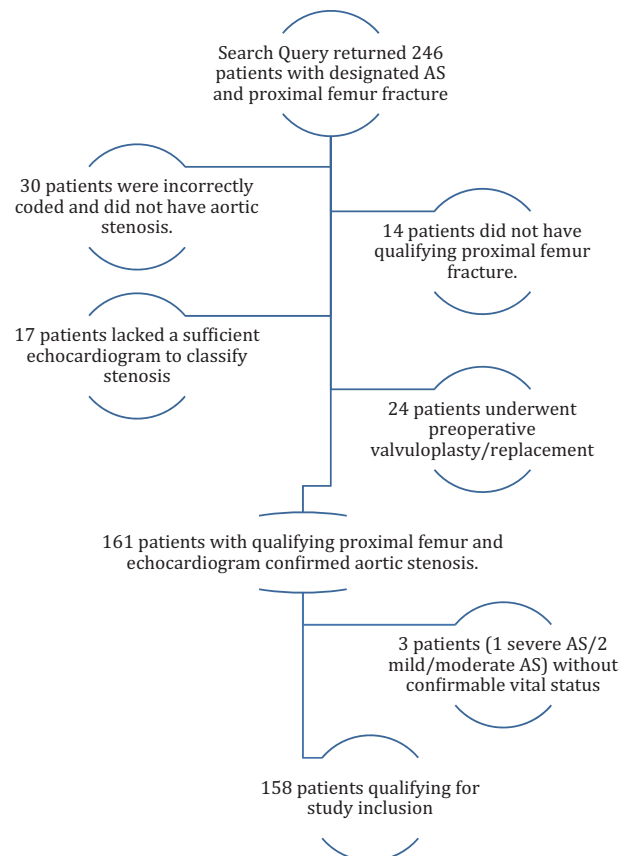

Figure 1. Search query with exclusion characteristic descriptions.

Table 1

Aortic Stenosis stage with associated valve hemodynamic parameters[4]

Stage		Valve hemodynamics
A	Aortic Sclerosis	$V_{max} < 2$ m/s
B	Progressive AS	V_{max} 2.0–3.9 m/s with mean $\Delta P \leq 39$
C, D	Severe AS	$V_{max} \geq 4$ m/s; AVA ≤ 1 cm^2; mean $\Delta P \geq 40$ mm Hg

Table 2

Demographic Data—Femoral Neck Fracture (FN), Intertrochanteric Femur Fracture (IT), Subtrochanteric Femur Fracture (ST), New York Heart Association (NYHA) Classification, Charlson Comorbidity Index (CCI)

Male sex—no./total no. (%)	39/158 (25%)
Age at presentation—median yr (range)	87 (55–100)
Time to surgery—median days (range)	2 (0–14)
Hip fracture type—no./total no. (%)	
FN	61/158 (39%)
IT	81/158 (51%)
ST	16/158 (10%)
Ethnicity—no./total no. (%)	
Caucasian	142/158 (90%)
East Asian	1/158 (1%)
African American	3/158 (2%)
Not Reported	8/158 (5%)
Hispanic	4/158 (3%)
Smoking—no./total no. (%)	
current	22/158 (14%)
previous	31/158 (20%)
NYHA Classification—no./total no. (%)	
No heart failure	96/158 (61%)
II	11/158 (7%)
III/IV	51/158 (32%)
CCI mean (range)	7 (2–15)
10-year projected survival according to CCI—mean (range)	14.46%(0%-93%)

Table 3

Multivariable cox proportional hazards analysis assessing Charlson Comorbidity Index (CCI), severity of AS, time to surgery, age at presentation, hip fracture type, smoking status, and New York Heart Association (NYHA) classification

	Hazard ratio	*P* value	95% CI
Severity of AS	1.257	.032	1.020–1.550
CCI	1.137	.002	1.050–1.231
Time to surgery	1.199	.405	0.783–1.835
Age at presentation	1.024	.138	0.992–1.056
Hip fracture type	1.116	.391	0.868–1.435
Smoking status	1.058	.708	0.788–1.419
NYHA class	1.137	.124	0.965–1.338

Kaplan–Meier survival analysis, depicted in Figure 2, illustrates decreased postoperative survival in patients with *severe AS* as compared with patients with nonsevere AS who underwent surgery for hip fracture; this difference was significant, χ^2 7.43 with *P* .006. (20/86) 23% of patients with severe AS and (7/72) 10% of patients with Non-severe AS died within 30 days of surgery. One-year mortality in these groups was (37/86) 43% and (20/72) 28% in *Severe* and *Non-severe AS*, respectively.

Table 3 depicts the results from the multivariable cox proportional hazards analysis which show that among the
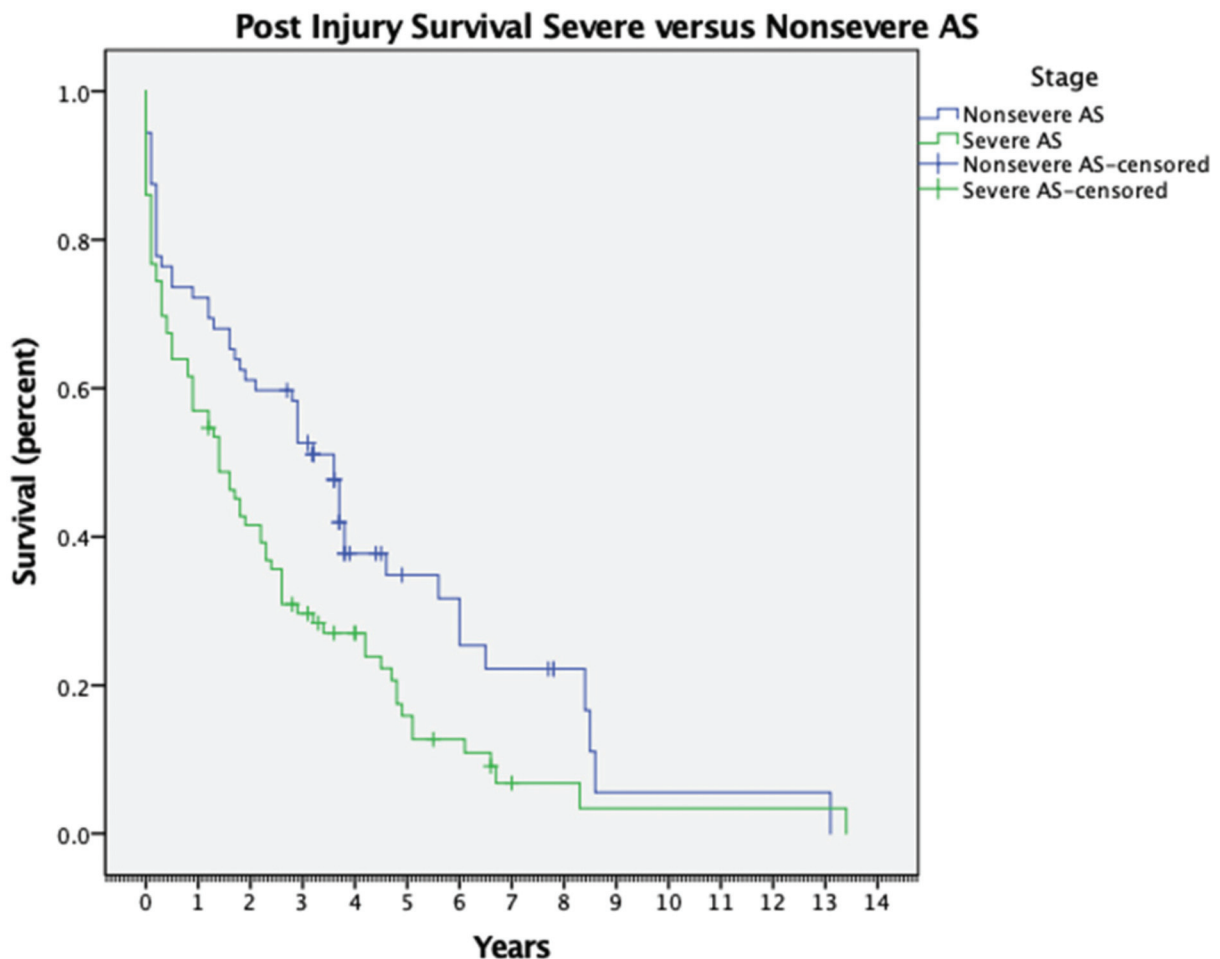

Figure 2. Kaplan–Meier survival curve comparing survival in non-severe AS patients (blue line) with severe AS patients (green line); *P* value .006.
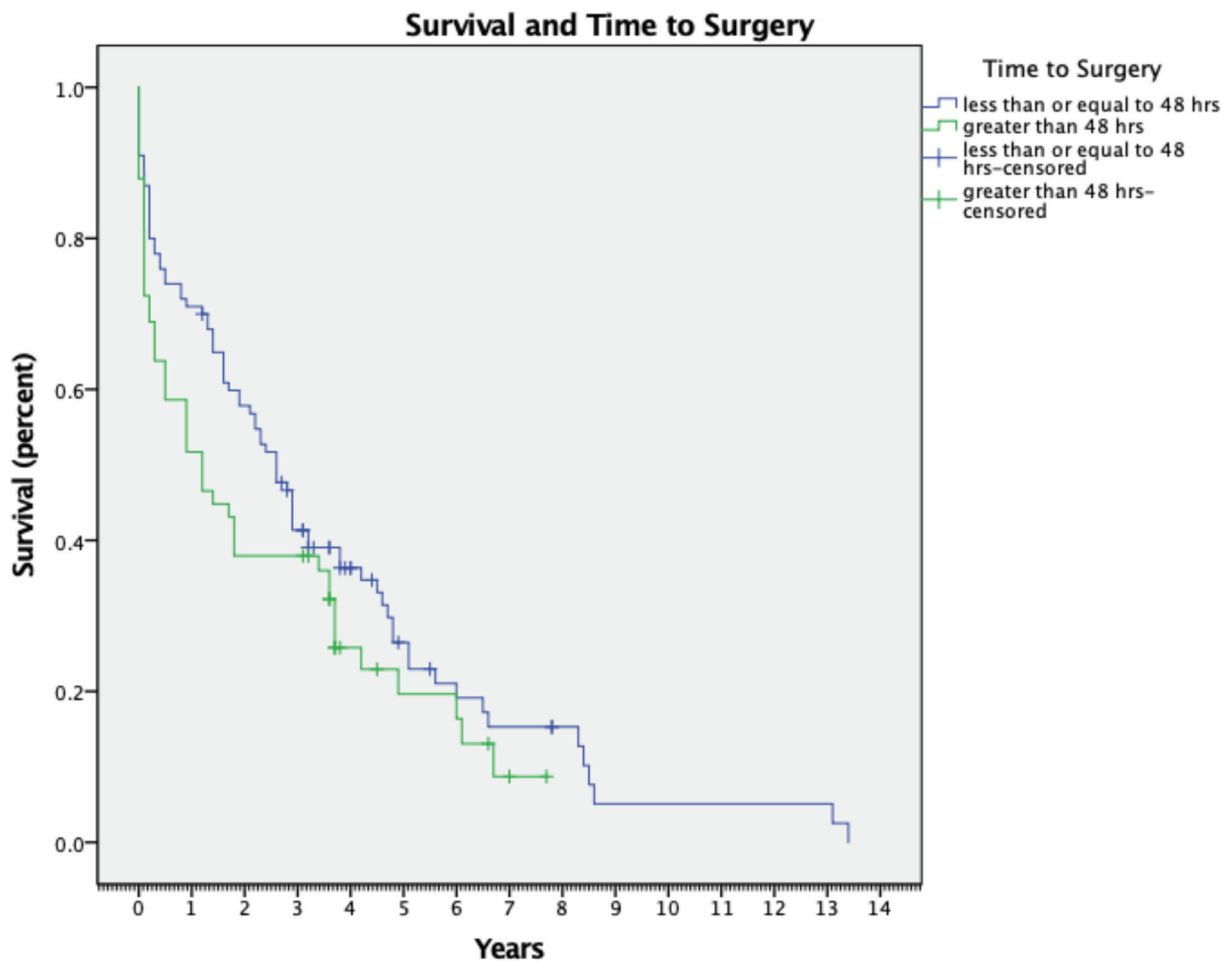
Survival and Time to Surgery

Figure 3. Kaplan–Meier survival curve comparing survival in aortic stenosis patients who underwent surgery within 48 hours of injury (blue line) and more than 48 hours after injury (green line); *P* value .116.

variables assessed only Charlson comorbidity index (*P* value .002) and stage of aortic stenosis (*P* value .032) were significantly associated with increased mortality.

Figure 3 illustrates the time to mortality among aortic stenosis patients who underwent surgery within 48 hours of injury (average survival 34.5 months) and those patients who underwent surgery more than 48 hours after injury (average survival 25.0 months), this comparison did not reach statistical significance, χ^2 2.466 with *P* value .116.

Among echocardiographic hemodynamic parameters only AVA (HR 0.433; *P* .015, 0.95% CI, 0.22–0.85) and EF (HR 0.974; *P* < .001, 0.95% CI, 0.961–0.988) reached significance. These relationships are depicted in Figures 4 and 5. Patients with an AVA of 0.8 cm^2 or less had an average survival (22 months) over a year shorter (15 months) than patients with an AVA of 0.8 cm^2 or more (37 months), *P* value .009. Patients with a lower EF had significantly earlier average postinjury mortality; EF of 40% or below 10 months, 41% to 49% 23 months, and EF 50% or more 33 months, *P* < .05. There was no significant effect present for Aortic Vmax, Peak ΔP, and Mean ΔP.

4. Discussion

Perioperative mortality following hip fracture repair remains high. Moderate to severe aortic stenosis has been identified as an independent risk factor for cardiac complications and mortality following elective noncardiac surgery.[2,5,6] In the hip fracture population, current studies offer mixed results and conclusions; some report no associations with mortality while others demonstrate increased 30-day and 1-year mortality.[8–11] Our study of 158 hip fracture patients is one of the largest performed to date and identifies severe stenosis to be an independent risk factor for reduced postoperative survival following fracture surgery.

The timing of hip fracture surgery remains controversial. Some studies have shown a delay in surgery is related to an increase in perioperative mortality.[12,14,15] However, it is important to ensure that all modifiable risk factors have been addressed and patients are optimized for surgery.[16] Our data show that in the setting of known or suspected AS, an echocardiogram is useful in helping to understand perioperative risk, specifically due to the ability to assess AVA and EF. However, obtaining a preoperative echocardiogram may delay surgery. Patients who have received a preoperative echocardiogram wait an average of 1.8 days longer prior to surgery compared to those who do not receive preoperative echocardiograms.[16,17] If an updated echocardiogram is required for perioperative assessment of a patient with aortic stenosis, the study should be obtained in an expeditious manner; however, our results do not indicate a significant difference in survival associated with surgical delay over 48 hours in patients with aortic stenosis (Fig. 3).
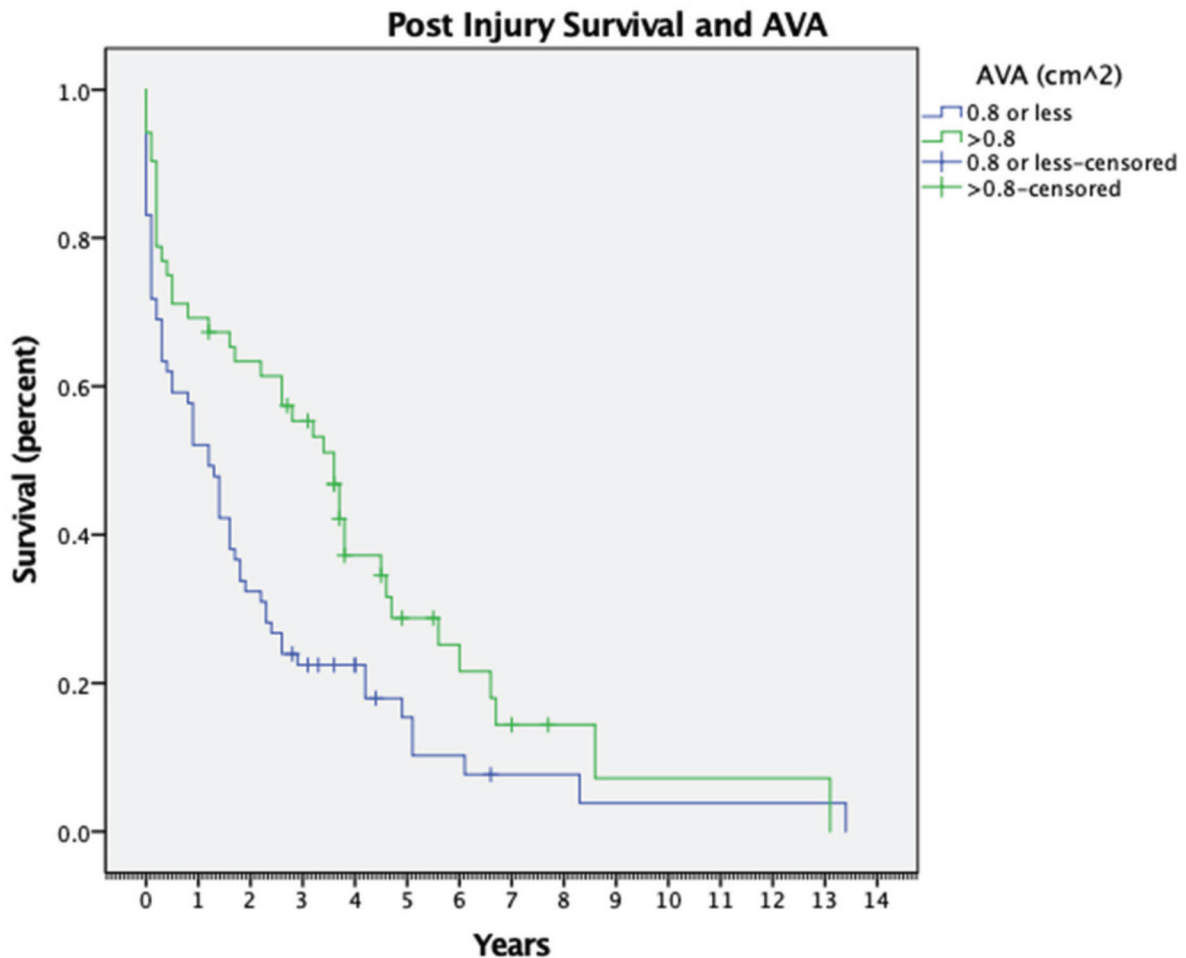
Post Injury Survival and AVA

Figure 4. Aortic valve area (AVA) versus median survival.

Today, the diagnosis and classification of AS is nearly entirely dependent upon echocardiogram. According to the AHA, the hemodynamic parameters that define severity of AS are LVEF, mean ΔP, Peak ΔP, V_{max}, and AVA.[4] A patient meeting any one of these parameters for Severe AS (Table 1) is subsequently classified to a grading of Severe.[4] However, there is dissent within the anesthesia literature regarding the validity of this method. Minners et al[16] discuss this after review of 3483 echocardiograms with remarkably discordant severity classifications depending on which hemodynamic parameter is applied. Our data indicate that among the measurements advocated by the AHA for classification, AVA and EF are the only parameters significantly correlated with higher early postoperative mortality in hip fracture patients ≥55 years.

A second area of dissent within the anesthesia literature is the AVA cutoff at which the definition of severe stenosis is determined. While the most up-to-date AHA guidelines define severe stenosis by AVA $\leq 1.0\,cm^2$,[4] recent publications by the AHA and European Society of Cardiology have suggested that a smaller value may more accurately represent the risk associated with the designation *Severe* ($0.6\,cm^2$ or $0.8\,cm^2$).[18,19] In keeping with the most recent literature, we compared time to mortality using an AVA threshold value of $0.8\,cm^2$, below which represents severe stenosis. As shown in Figure 4, AVA values of $0.8\,cm^2$ or below had a shorter time to mortality than AVA values above

that threshold. Further investigation is needed to determine if a more stringent classification of severity may more accurately describe perioperative risk among hip fracture patients with AS. A valve area threshold for severe stenosis defined by an AVA$\leq 0.8\,cm^2$ rather than $\leq 1.0\,cm^2$ may more accurately determine perioperative risk and better inform decision-making.

This investigation has a number of limitations. The retrospective nature of this study introduces selection bias. By excluding patient who did not have an echocardiogram within 30 days prior to surgery, these data could be biased toward more severe cases. For example, a point of care provider could defer a repeat echo in a patient who had an echo just outside our inclusion date range in the event that the known level of stenosis was minor. It is also likely that patients with subclinical stenosis could undergo surgery for a hip fracture without being identified; given a provider is more likely to overlook Mild or Moderate AS, these data could be skewed toward more severe cases.

Patients were identified as having both a hip fracture and aortic stenosis through a medical record review. It is possible that some patients with both aortic stenosis and a hip fracture were not accurately coded and therefore would have erroneously escaped capture in this cohort.

Three patients whose final vital status could not be confirmed also introduce the possibility for selection bias. While these 3 patients were balanced regarding AS severity, CCI, and gender, it
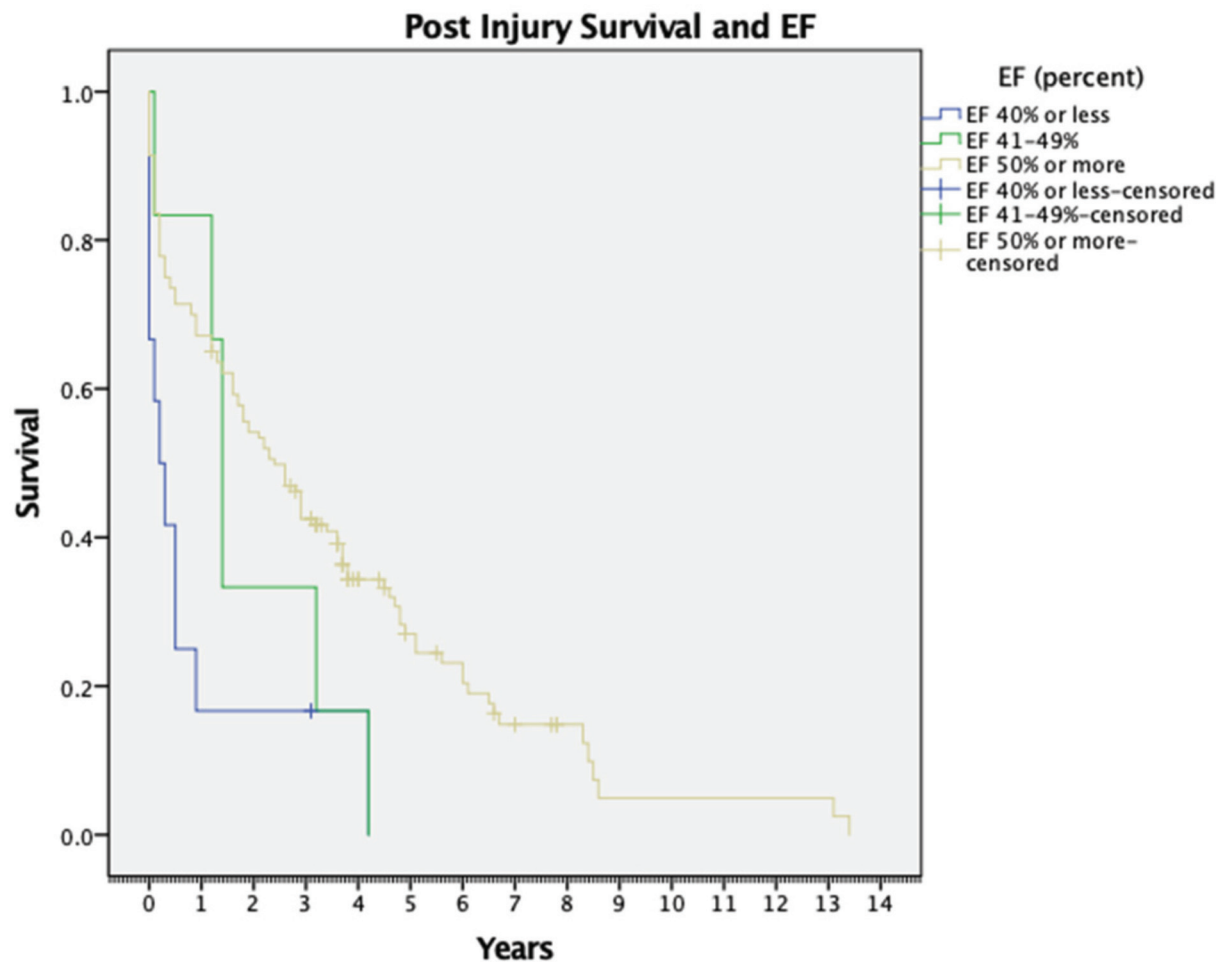
Figure 5. Post injury survival and left ventricular ejection fraction (EF).

is possible that this missing data could significantly affect findings in an unpredictable way.

AS was graded by review of the records and based upon the echocardiogram reports. Echocardiography is user-dependent, and differences between sonographers may influence our results.[18] There has been some evidence that the AVA measured sonographically underestimates true aortic valve size when compared to valve areas measured at autopsy.[19]

5. Conclusions

Patients with aortic stenosis, particularly those with severe aortic stenosis (AVA < or = 8 cm^2) are at increased risk for perioperative mortality following hip fracture repair. Of the hemodynamic parameters routinely monitored with echocardiogram only AVA and LVEF are associated with increased mortality. Hemodynamic parameters such as mean DP, Peak DP, and V_{max} are not associated with increased mortality following surgical hip fracture repair.

References

1. Maganti K, Rigolin V, Sarano M, et al. Valvular heart disease: diagnosis and management. Mayo Clin Proc. 2010;85: 483–500.
2. Kertai MD, Bountioukos M, Boersma E, et al. Aortic stenosis: an underestimated risk factor for perioperative complications in patients undergoing noncardiac surgery. Am J Med. 2004;116: 8–13.
3. Hip fractures among older adults. Home and recreational safety. Available at: https://www.cdc.gov/homeandrecreationalsafety/falls/adulthipfx.html. Accessed June 27, 2018.
4. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease; 2014.
5. Agarwal S, Rajamanickam A, Bajaj NS, et al. Impact of aortic stenosis on postoperative outcomes after noncardiac surgeries. Circ Cardiovasc Qual Outcomes. 2013.
6. Calleja AM, Dommaraju S, Gaddam R, et al. Cardiac risk in patients aged > 75 years with asymptomatic, severe aortic stenosis undergoing noncardiac surgery. AJC. 2010.
7. Tashiro T, Pislaru SV, Blustin JM, et al. Perioperative risk of major noncardiac surgery in patients with severe aortic stenosis: a reappraisal in contemporary practice. Eur Heart J. 2014;35: 2372–81.
8. Keswani A, Lovy A, Khalid M, et al. The effect of aortic stenosis on elderly hip fracture outcomes: a case control study. Injury. 2016.
9. Adunsky A, Kaplan A, Arad M, et al. Aortic stenosis in elderly hip fractured patients. Arch Gerontol Geriatr. 2008;46: 401–8.
10. McBrien ME, Heyburn G, Stevenson M, et al. Previously undiagnosed aortic stenosis revealed by auscultation in the hip fracture population: echocardiographic findings, management and outcome. Anaesthesia. 2009.
11. Leibowitz D, Rivkin G, Schiffman J, et al. Effect of severe aortic stenosis on the outcome in elderly patients undergoing repair of hip fracture. Gerontology. 2009;55: 303–6.
12. Endo A, Baer HJ, Nagao M, et al. Prediction model of in-hospital mortality after hip fracture surgery. J Orthop Trauma. 2018;32: 34–38.
13. Loxdale SJ, Sneyd JR, Donovan A, et al. The role of routine pre-operative bedside echocardiography in detecting aortic stenosis in patients with a hip fracture. Anaesthesia. 2012;67:51–54.

14. Zuckerman JD, Skovron ML, Koval KJ, et al. Postoperative complications and mortality associated with operative delay in older patients who have a fracture of the hip. J Bone Joint Surg Am. 1995;77:1551–1556.

15. Carretta E, Bochicchio V, Rucci P, et al. Hip fracture: effectiveness of early surgery to prevent 30-day mortality. Int Orthop. 2011;35:419–424.

16. Charalambous CP, Yarwood S, Paschalides C, et al. Factors delaying surgical treatment of hip fractures in elderly patients. Ann R Coll Surg Engl. 2003;85:117–119.

17. Ryan DJ, Yoshihara H, Yoneoka D, et al. Delay in hip fracture surgery: an analysis of patient-specific and hospital-specific risk factors. J Orthop Trauma. 2015;29:343–348.

18. Maréchaux S, Ringle A, Rusinaru D, et al. Prognostic value of aortic valve area by doppler echocardiography in patients with severe asymptomatic aortic stenosis. J Am Heart Assoc. 2016.

19. Minners J, Allgeier M, Gohlke-Baerwolf C, et al. Inconsistencies of echocardiographic criteria for the grading of aortic valve stenosis. Eur Heart J. 2008;29:1043–1048.