Prediction of Early Postoperative Major Cardiac Events and In-Hospital Mortality in Elderly Hip Fracture Patients: The Role of Different Types of Preoperative Cardiac Abnormalities on Echocardiography

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Introduction: Transthoracic echocardiography (TTE) is a common cardiac screening test before hip fracture surgery. However, the general TTE test delays surgery, so it would be meaningful if we could simplify the TTE by only assessing cardiac abnormality specifically. Therefore, we aimed to establish the most clinically relevant abnormality by comparing the predictive value of each major cardiac abnormality in postoperative cardiac complications and mortality in elderly hip fracture patients.

Patients and Methods: From January 2014 to January 2019, the medical records of all surgically treated elderly patients (>65 years) with hip fracture were analyzed. The major TTE abnormalities were defined as left ventricular hypertrophy, systolic pulmonary arterial pressure >25 mm Hg, moderate-severe valve abnormality, left ventricular ejection fraction (LVEF) <50%, and pericardial effusion. The outcomes were postoperative cardiac complications and in-hospital mortality.

Results: There were 354 patients involved finally. Postoperative cardiac complications were encountered in 7.6% (n=27) of patients. The mortality rate was 2.8% (n=10). History of coronary artery disease (CAD) (OR: 3.281, 95% CI: 1.332–8.079, p=0.010) and presence of aortic stenosis (AS) (OR: 5.656, 95% CI: 1.869–17.117, p=0.002) were independent predictors of postoperative cardiac complications. In addition, age (OR: 1.264, 95% CI: 1.047–1.527, p=0.015), history of CAD (OR: 19.290, 95% CI: 2.002–185.885, p=0.010), presence of AS (OR: 7.164, 95% CI: 1.988–51.413, p=0.040) and LVEF <50% (OR: 8.803, 95% CI: 1.115–69.472, p=0.039) were independent predictors of mortality. However, the rest of preoperative TTE abnormalities were not associated with postoperative cardiac complications or mortality.

Conclusion: Among the TTE abnormalities presented by elderly patients with hip fracture, moderate-severe AS was the predictor of postoperative cardiac complications. Moreover, moderate-severe AS and LVEF <50% were the predictors of in-hospital mortality. Therefore, we could simplify the TTE process by assessing aortic valve and LVEF specifically on focused echocardiography, which could avoid surgery delay.

Keywords: aging, hip fracture surgery, mortality, postoperative cardiac complications, echocardiographic abnormality
Introduction

Hip fracture is the major reason for hospital admission in elderly patients and is becoming the most important public health issue. With constantly increasing incidence, it is estimated to increase to 6.3 million worldwide by the year 2050.1 Despite advances in surgical technique, the surgery is still associated with high mortality rate and frequent postoperative cardiac complications in elderly patients with hip fracture.2 The mortality rate was reported as high as 4–12% during hospitalization and 10–40% within the first postoperative year.3–5 Moreover, the postoperative cardiac complications were the most fearsome perioperative complications that account for morbidity and mortality in elderly hip fracture.6,7 Therefore, early identification of patients at risk for postoperative cardiac complications is crucial, which promotes early preventive medical intervention. To date, several studies have discovered the predictors of postoperative cardiac complications in elderly hip fracture, including cardiac biomarkers,6,8 Cardiac Risk Index,9 and C-reactive protein.10 However, to the best of our knowledge, the association between different types of preoperative echocardiographic abnormalities and postoperative cardiac complications in elderly patients following hip fracture surgery has not been studied yet.

Preoperative transthoracic echocardiography (TTE) is frequently considered in elderly patients with hip fracture, because it is a reliable tool to assess cardiac structural and functional abnormality.11 So far, only few studies have shown preoperative TTE abnormality as the predictor of postoperative complications and mortality after hip fracture, including mild pericardial effusion,12 aortic stenosis (AS).13,14 However, available studies mainly focused on the association between the preoperative TTE abnormality and postoperative complications rather than cardiac complications specifically.12 In addition, the conclusion of the previous study was still controversial.13,14 Furthermore, previous studies mainly focused on one type of preoperative TTE abnormality rather than comprehensively evaluating multiple TTE abnormalities at the same time.12–14

Therefore, we conducted this study to evaluate the predictive value of different types of cardiac abnormalities, evaluated with preoperative TTE, in cardiac complications and in-hospital mortality in elderly patients after hip fracture surgery.

Patients and Methods

Study Design

The study was based on data collected from January 2014 to January 2019 in a large tertiary hospital. The medical records of elderly patients aged over 65 years with hip fracture (femoral neck, intertrochanteric or subtrochanteric) undergoing surgery were retrospectively analyzed. Only patients with a preoperative TTE examination were included in this study. We excluded patients with poly-trauma, patients with pathological fractures, patients with periprosthetic fractures, patients with history of malignant tumor, and patients without complete medical records. The current study’s protocol was approved by the Ethics Committee of Guangdong Provincial People’s Hospital, Guangdong Academy of Medical Sciences. (No. GDREC2018522H(R1)). In the process of the study, researchers covered all data confidentiality and compliance with the Declaration of Helsinki. We retrospectively extracted the patients’ impact data without any intervention measures. Thus, patient consent to review their medical records was not required in this retrospective study.

Data Collection

Hospital records were reviewed for age, sex, fracture type, preoperative medical comorbidities, surgery type, American Society of Anesthesiologists (ASA) class, anesthesiologic type, preoperative TTE report, in-hospital postoperative cardiac complications, and in-hospital mortality. The primary study endpoint was in-hospital postoperative cardiac complications. The secondary outcome of interest was in-hospital mortality.

Definition of Postoperative Cardiac Complications

Postoperative cardiac complications were defined as acute myocardial infarction, congestive heart failure, major arrhythmia, or primary cardiac death. Postoperative acute myocardial infarction (AMI) was defined as elevation of myocardial necrosis markers two times above the upper limits of the normal range in patients presenting with specific features (clinical or electrocardiogram signs). Congestive heart failure was diagnosed by means of clinical examination, specific features of chest radiography and elevation of related biomarkers. Cardiac arrhythmia was defined as new onset arrhythmia detected by electrocardiogram, mainly including ventricular tachycardia or
atrial fibrillation. Cardiac death was defined as sudden death that could not be explained by any other non-cardiovascular postoperative complications.

Preoperative TTE and Major Abnormality
After the patient was sent to the orthopedic department, a flowchart including medical history, physical examination, electrocardiography, and standard blood tests was done. Usually, patients with the following were recommended to undergo TTE in our clinic according to ACC/AHA guidelines, including dyspnea of unknown origin, worsening of known signs or symptoms of cardiac disease, known history of valvular dysfunction or heart failure without TTE in the last year or worsened symptoms, and suspicion of moderate or greater valvular stenosis or regurgitation. But the final decision whether to undergo TTE or not was not fully based on the recommendations but influenced by other factors, including preoperative consultation with anesthesiologist, cardiologist and orthopedic surgeons’ clinical experience. Preoperative TTE was performed using Cardiovascular Ultrasounds System (General Electrics TM, Milwaukee, WI, USA). Standard parasternal and apical two- and four-chamber views were assessed with the patient in the left lateral decubitus position, calculating the diameter of chamber, wall thickness. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson’s method. Transvalvular flow was assessed by early peak (E) and late peak (A) velocities, E/A ratio and deceleration time of E velocity (DTE). Standard echocardiographic evaluation of mitral or aortic valvular disease was assessed similar to previous method. The systolic pulmonary artery pressure (PAPs) was estimated using Bernoulli, s formula. Space between the visceral and parietal pericardium was assessed through the cardiac cycle.

Major TTE abnormalities were defined as: 1) left ventricular hypertrophy, defined by ratio of posterior wall/septal thickness <1.1; 2) moderate-severe aortic valve stenosis, defined by a mean pressure gradient >40 mmHg and/or an indexed aortic valvular area < 1 cm²/m²; 3) severe mitral valve stenosis, defined by a mean pressure gradient >10 mmHg and/or an indexed mitral valvular area < 1 cm²/m²; 4) Grade III–IV mitral or aortic valvular regurgitation; 5) left ventricle ejection fraction (LVEF) <50%; 6) systolic pulmonary artery pressure (PAPs) >25 mmHg; 7) pericardial effusion.

Statistical Analysis
The Kolmogorov–Smirnov test was carried out to assess the normality of the continuous variables. Continuous variables are expressed as mean ± standard deviation (SD) and compared using Student’s t-test. Categorical variables are expressed as percentages and compared using the Chi-squared test or Fisher’s exact test as appropriate. To identify relationship between preoperative TTE abnormality and post-operative cardiac complications, in-hospital mortality after hip fracture surgery, only variables with P-values <0.05 in the t-test, Chi-squared test or Fisher’s exact test were subjected to multivariate logistic regression model. Variables with statistical significance (p<0.05) retained in the final model were considered as independent risk factors. Odds ratio (OR) and 95% confidence interval (95% CI) were calculated. The calibration of each model was assessed by the Hosmer–Lemeshow goodness-of-fit test, with p>0.05 indicating an acceptable result. Statistical analyses were performed using SPSS 20.0 statistics software (SPSS Inc. Chicago, IL, USA).

Results
Clinical Characteristics
The clinical characteristics of the study population were shown in Table 1. A total of 1052 elderly patients underwent hip fracture surgery in our clinic during the study period. Among them, 399 elderly patients underwent preoperative TTE, of whom 354 (88.7%) were included in the study. Among the excluded patients (n=45), 9 patients presented with polytrauma other than the hip fracture.

Table 1 Clinical Characteristics of the Patients

| Patient Characteristics | Value (%) |
|-------------------------|-----------|
| Patients included       | 354       |
| Gender (female/male)    | 270/84    |
| Age (years)             | 81.97±6.52|
| Fracture type           |           |
| Femoral neck            | 200 (56.5%)|
| Intertrochanteric       | 143 (40.4%)|
| Subtrochanteric         | 11 (3.1%)  |
| Surgery type            |           |
| Total hip arthroplasty  | 50 (14.1%) |
| Hemiarthroplasty        | 150 (42.4%)|
| Proximal femoral nail anti-rotation | 154 (43.5%) |
| American Society of Anesthesiologists (ASA) class | |
| ASA I                   | 57 (16.1%) |
| ASA II                  | 122 (34.5%)|
| ASA III                 | 128 (36.2%)|
| ASA IV                  | 47 (13.3%) |
| Postoperative adverse cardiac events | 27 (7.6%) |
| In-hospital mortality   | 10 (2.8%)  |
15 patients presented with periprosthetic or pathological fractures, 16 patients with malignant tumor history, and 5 patients were without complete medical records. Of the 354 patients included, 270 (76.3%) were female and 84 (23.7%) were male. The mean age of patients was 81.97±6.52 years. Patients with femoral neck fracture accounted for 56.5% of the study population. Proximal femoral nail anti-rotation (PFNA) was the most common type of treatment accounting for 43.5%. Postoperative cardiac complications occurred in 27 (7.6%) cases, 13 cases of acute non-fatal myocardial infarction; 7 cases of new-onset atrial fibrillation (2 atrial fibrillation, 1 ventricular fibrillation, 4 atrioventricular block), 6 cases of heart failure, 1 case of sudden cardiac death. The in-hospital mortality rate of the included patients was 2.8% (n=10).

As for distribution of preoperative TTE abnormality in elderly patients, 67 cases (18.9%) showed left ventricular hypertrophy, 20 cases (5.6%) had severe AS, 11 cases (3.1%) presented with severe mitral valve stenosis, 12 cases (3.4%) presented with moderate-severe aortic or mitral valve regurgitation, 10 cases (2.8%) demonstrated LVEF <50%, 77 cases (21.8%) presented with PAPs >25mmHg, 15 cases (4.2%) showed pericardial effusion.

### Postoperative Cardiac Complications

Patients were divided into 2 groups based on whether there were postoperative cardiac complications or not. The differences between 2 groups were shown in Table 2. There were no statistically significant differences in age, sex, fracture type, treatment type, distribution of ASA class, anesthesiology type. Patients who presented with postoperative cardiac complications had significantly higher prevalence of coronary artery disease (44.4% vs 17.1%), higher presence of moderate-severe AS (22.2% vs 4.3%) and LVEF <50% (11.1% vs 2.1%) compared with uncomplicated patients. As shown in the multivariate analysis (Table 3), history of CAD (OR: 3.281, 95% CI: 1.332–8.079, p=0.010), presence of moderate-severe AS (OR:5.656, 95% CI: 1.869–17.117, p=0.002) were the dominant predictors of postoperative cardiac complications. The Hosmer–Lemeshow test showed the good fit (x²=0.376, p=0.540).

### In-Hospital Mortality

Comparing characteristics in relation to in-hospital mortality, the group of patients who died and those who survived were homogeneous in terms of the sex, fracture type, treatment type, anesthesiology type. However, those patients who died were significantly older than the survivors (86.42 vs 80.99, p=0.005). The prevalence of CAD, arrhythmia, chronic obstructive pulmonary disease (COPD), ASA IV were

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**Table 2 Comparison of Patients with and Without In-Hospital Postoperative Cardiac Complications**

| Parameters                          | With Cardiac Events (n=27) | Without Cardiac Events (n=327) | P-value |
|-------------------------------------|---------------------------|-------------------------------|---------|
| Age                                 | 82.22±4.99                | 81.88±6.63                   | 0.195   |
| Female, n (%)                       | 22 (81.5%)                | 248 (75.8%)                  | 0.508   |
| Fracture type                       |                           |                               |         |
| Femoral neck                        | 15(55.6%)                 | 185(56.5%)                   | 0.934   |
| Intertrochanteric                   | 11(40.7%)                 | 132(40.4%)                   | 0.918   |
| Subtrochanteric                     | 1(3.7%)                   | 10(3.1%)                     | 0.588   |
| Surgery type                        |                           |                               |         |
| Total hip arthroplasty              | 7(25.9%)                  | 43(13.2%)                    | 0.165   |
| Hemiarthroplasty                    | 8(29.7%)                  | 142(43.4%)                   | 0.163   |
| Proximal femoral nail anti-rotation | 12(44.4%)                 | 142(43.4%)                   | 0.918   |
| Comorbidities on admission          |                           |                               |         |
| Hypertension                        | 19(70.4%)                 | 218(66.7%)                   | 0.694   |
| Coronary artery disease             | 12(44.4%)                 | 56(17.1%)                    | 0.001*  |
| Arrhythmia                          | 15(55.6%)                 | 130(39.8%)                   | 0.109   |
| COPD                                | 5(18.5%)                  | 35(10.7%)                    | 0.359   |
| Cerebrovascular disease             | 7(25.9%)                  | 55(16.8%)                    | 0.351   |
| Diabetes                            | 6(22.2%)                  | 72(22.0%)                    | 0.980   |
| Previous fragility fracture         | 0(0%)                     | 37(11.3%)                    | 0.129   |
| Chronic kidney disease              | 2(7.4%)                   | 16(4.9%)                     | 0.908   |
| ASA class                           |                           |                               |         |
| ASA I                               | 2(7.5%)                   | 55(16.8%)                    | 0.314   |
| ASA II                              | 8(29.6%)                  | 114(34.9%)                   | 0.582   |
| ASA III                             | 10(37.0%)                 | 118(36.1%)                   | 0.921   |
| ASA IV                              | 7(25.9%)                  | 40(12.2%)                    | 0.085   |
| Anesthesiology type                 |                           |                               |         |
| General anesthesia                  | 1(3.7%)                   | 35 (10.7%)                   | 0.409   |
| Regional anesthesia                 | 26 (96.3%)                | 292 (89.3%)                  |         |
| Echocardiographic abnormality       |                           |                               |         |
| Left ventricular hypertrophy        | 5(18.5%)                  | 62(19.0%)                    | 0.955   |
| Moderate-severe aortic valve stenosis | 6(22.2%)               | 14(4.3%)                     | 0.001*  |
| Severe mitral valve stenosis        | 1(3.7%)                   | 7(2.1%)                      | 0.473   |
| Moderate-severe aortic or mitral valve regurgitation | 1(3.7%) | 11(3.4%) | 0.925 |
| LVEF <50%                           | 3(11.1%)                  | 7(2.1%)                      | 0.036*  |
| PAPs >25mm Hg                       | 6(22.2%)                  | 71(21.7%)                    | 0.951   |
| Pericardial effusion                | 1(3.7%)                   | 14(4.3%)                     | 0.886   |

**Note:** *Statistical significance.
Abbreviations: COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; LVEF, left ventricle ejection fraction; PAPs, systolic pulmonary artery pressure.*
significantly higher in those patients who died. In particular, the presence of LVEF <50% and moderate-severe AS were more prominent in those who died (Table 4). As the multivariate analysis showed (Table 5), age (OR: 1.264, 95% CI: 1.047–1.527, p=0.015), history of CAD (OR: 19.290, 95% CI: 2.002–185.885, p=0.010), presence of AS (OR: 7.164, 95% CI: 1.988–51.413, p=0.040), and LVEF <50% (OR: 8.803, 95% CI: 1.115–69.472, p=0.039) were the dominant predictors of in-hospital mortality. The Hosmer–Lemeshow test showed the good fit (χ²=0.902, p=0.999).

### Discussion

Postoperative cardiac complications are one of the most common and life-threatening adverse events in elderly patients following hip fracture and TTE is the most common tool used to assess cardiac risk preoperatively. However, the prognostic value of preoperative TTE abnormalities and postoperative outcome is still controversial. To the best of our knowledge, this was the first study comprehensively investigating the association between different types of preoperative TTE abnormalities and postoperative cardiac complications or mortality in elderly patients following hip fracture surgery. Our results showed that moderate-severe AS was an independent predictor of postoperative cardiac complications and in-hospital mortality. In addition, LVEF <50% was also an independent predictor of in-hospital mortality. However, no significant relationship was found in the rest of listed preoperative TTE abnormalities.

The postoperative cardiac complications rate was 7.6% in our study, which was similar to previous studies. The presence of significant valvular disease has been identified as an important predictor for cardiac events in patients undergoing noncardiac surgery in a previous study, which was similar to ours. To date, only a few studies have investigated the prognostic value of AS in postoperative outcome in elderly patients following hip fracture surgery. Rostagno et al conducted a study involving 428 elderly patients with hip fracture (145 with AS and 283 controls) and in agreement with our result, they showed there was a higher rate of postoperative myocardial
Table 5 Multivariate Analysis for the Prediction of In-Hospital Mortality

| Parameters              | Odds Ratio | Confidence Interval (CI) | P-value |
|-------------------------|------------|--------------------------|---------|
| Age                     | 1.264      | 1.047–1.527              | 0.015   |
| Coronary artery disease | 19.290     | 2.002–185.885            | 0.010   |
| COPD                    | 1.991      | 0.313–12.683             | 0.466   |
| Arrhythmia              | 5.186      | 0.482–55.799             | 0.174   |
| ASA 4                   | 1.552      | 0.260–9.275              | 0.629   |
| Moderate-severe aortic stenosis | 7.164 | 1.988–51.413 | 0.040   |
| LVEF <50%               | 8.803      | 1.115–69.472             | 0.039   |

Abbreviations: COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; LVEF, left ventricle ejection fraction.

infarction in patients with AS (8.3% vs 1.1%, p<0.001). However, a study from Keswani et al, involving a total of 153 elderly patients (46 with moderate or severe AS and 107 controls) showed there was no difference in the perioperative cardiac complication rate (17% vs 8.4%), which contradicts our study (30% vs 6.3%, p=0.001). One possible explanation was that their study regarded vascular accidents (deep vein thrombosis) as part of postoperative cardiac complications, which we thought were due to surgical complications rather than underlying cardiac abnormality. Besides, history of CAD was also identified as independent risk factor for postoperative cardiac complications, in agreement with a previous study.

The in-hospital mortality rate was 2.8% in our study, which is in agreement with a previous study result. Both AS and LVEF <50% were independent predictors of in-hospital mortality. AS was established as an important factor that was associated with higher mortality in previous studies. In agreement with the results from our study, in-hospital mortality (6.2% vs 3.3%) reported by Adunsky et al and 30-day mortality (14.7% vs 4.2%, p < 0.001) reported by Leibowitz et al were significantly higher for AS patients as compared to controls.

The presence of LVEF <50% was shown to be associated with mortality in patients undergoing vascular surgery. However, to our knowledge, only few studies have reported the association between LVEF and postoperative outcome in elderly hip fracture. A recent study based on national database involving 2,020,712 patients, demonstrated that LVEF <50% increased the rate of postoperative adverse events such as in-hospital all-cause death, in-hospital cardiac arrest or acute ischemic stroke. However, another study involving 181 patients diagnosed with intertrochanteric fracture (only 65 had preoperative TTE) did not show the association between low LVEF and mortality. One explanation for this was that their study only included patients with intertrochanteric fracture, which had different baseline demographic characteristics compared with our study. Besides, some clinical factors were also identified as independent risk factors for mortality in our study, and these included advanced age, history of CAD. Increasing age has been widely identified as a risk factor for mortality in hip fracture patients because the patient with advanced age has poor physiological reserve to cope with the surgery and trauma stress. Preexisting CAD was a risk factor for inhospital mortality in our study. In agreement with our result, Norring-Agerskov et al investigated the impact of cardiovascular disease on mortality among 113,211 patients with hip fracture, they showed that 30-day mortality was significantly increased in individuals with preexisting cardiac disease.

With our study, we have demonstrated that presence of AS, LVEF <50% had a negative impact on postoperative cardiac complications or mortality, which could be explained by the hemodynamic instability in these patients. AS causes a reduction in left ventricular compliance and in coronary reserve. In addition, patients with LVEF <50% have poor cardiac reserve. As a result, the hemodynamic changes appear to be more pronounced in patients undergoing surgical procedures.

This study had another clinical implication. A previous study showed concern about the surgery delay caused by TTE, but early operative treatment is generally advocated for patients with a hip fracture to minimize the potential morbidity. The physical examination (murmur), cardiac biomarkers, and electrocardiogram could provide some information associated with cardiac disease (CAD, severe AS), but it is less reliable compared with echo especially in the medical centers without co-management models pairing orthopedic surgeons with anesthesiologists or cardiologists. Cardiac abnormalities including aortic stenosis, cardiac failure, and pulmonary hypertension, are all reliably evaluated by echocardiography. Therefore, our study may propose a method to balance the surgery delay and TTE test. Among the different types of TTE abnormalities, aortic stenosis and LVEF were the dominant predictors of postoperative cardiac complications and in-hospital mortality in elderly hip fracture. So, we could simplify the TTE process by assessing aortic valve and LVEF specifically on focused echocardiography, which could decrease the waiting time for surgery.
However, further prospective studies with larger study population are required for better clarification.

To the best of our knowledge, this was the first study evaluating impact of the different types of TTE abnormalities on postoperative cardiac complications specifically and inhospital mortality. However, there are several limitations to our study. Firstly, this was a retrospective study with natural selection bias. However, we minimized the bias in patient enrollment by using data from an electronic medical record database. Secondly, the patients involved were elderly patients with preoperative TTE, so our results cannot be directly applied to all patients undergoing hip fracture surgery.

Conclusion
In elderly patients undergoing hip fracture surgery, presence of AS and history of CAD were the predictive factors of postoperative cardiac complications. In addition, advanced age, history of CAD, presence of AS and LVEF <50% were the independent predictive factors of in-hospital mortality. Therefore, we could simplify the TTE process by assessing aortic valve and LVEF specifically on focused echocardiography, which could avoid surgery delay.

Abbreviations
TTE, transthoracic echocardiography; LVEF, left ventricular ejection fraction; CAD, coronary artery disease; AS, aortic stenosis; ASA, American Society of Anesthesiologists; AMI, acute myocardial infarction; PAPS, systolic pulmonary artery pressure; CI, confidence interval; PFNA, proximal femoral nail anti-rotation; COPD, chronic obstructive pulmonary disease.

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Xuepan Chen and Yuanchen Ma are co-first authors in this study.

Author Contributions
All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure
The authors report no conflicts of interest in this work.

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