Functional mitral regurgitation combined with increased early diastolic transmirtal velocity to early mitral annulus diastolic velocity ratio is associated with a poor prognosis in patients with shock

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Abstract

Background: Functional mitral regurgitation (FMR) is common in critically ill patients and may cause left atrial (LA) pressure elevation. This study aims to explore the prognostic impact of synergistic LA pressure elevation and FMR in patients with shock.

Methods: We retrospectively screened 130 consecutive patients of 175 patients with shock from April 2016 to June 2017. The incidence and impact of FMR and early diastolic transmirtal velocity to early mitral annulus diastolic velocity ratio (E/e′) ≥ 4 within 6 h of shock on the prognosis of patients were evaluated. Finally, the synergistic effect of FMR and E/e′ were assessed by combination, grouping, and trend analyses.

Results: Forty-four patients (33.8%) had FMR, and 15 patients (11.5%) had E/e′ elevation. A multivariate analysis revealed FMR and E/e′ as independent correlated factors for 28-day mortality (P = 0.043 and 0.028, respectively). The Kaplan-Meier survival analysis revealed a significant difference in survival between patients with and without FMR (χ² = 7.672, P = 0.006) and between the E/e′ ≥ 14 and E/e′ < 14 groups (χ² = 19.351, P < 0.010). Twenty-eight-day mortality was significantly different among the four groups (χ² = 30.141, P < 0.010). The risk of 28-day mortality was significantly higher in group 4 (E/e′ ≥ 14 with FMR) compared with groups 1 (E/e′ < 14 without FMR) and 2 (E/e′ < 14 with FMR) (P = 0.001 and 0.046, respectively).

Conclusions: Patients with shock can be identified by the presence of FMR. FMR and E/e′ are independent risk factors for a poor prognosis in these patients, and prognosis is worst when FMR and E/e′ ≥ 14 are present. It may be possible to improve prognosis by reducing LA pressure and E/e′.

Trial Registration: ClinicalTrials.gov, NCT03082326.

Keywords: Shock; Ultrasound; Functional mitral regurgitation; E/e′; Prognosis

Introduction

Mitrval regurgitation (MR) is defined as systolic retrograde flow from the left ventricle into the left atrium and is usually seen in critically ill patients. MR is the most common valvular disease[1] and the second most common valvular heart disease requiring surgery in Europe, and its incidence increases with age.[2][4]

Functional mitral regurgitation (FMR) is defined as MR associated with poor remodeling and dysfunction of the left ventricle or mitral annulus in the presence of a structurally normal mitral leaflet. The literature shows that FMR predicts a poor prognosis and is frequently associated with increased morbidity and mortality.[1][5][6] Approximately 35% to 50% of patients with heart failure develop FMR, and these patients have a poor prognosis.[5][8] MR results in increased left atrial (LA) volume and pressure.[9] Elevated LA pressure may make patients, particularly patients with arrhythmia, more susceptible to pulmonary edema during exacerbation of disease and to cardiogenic pulmonary edema if fluids are administered too quickly when fluid resuscitation is required. This may be associated with further LA pressure elevation, resulting in an increased afterload on the pulmonary circulation. At the same time, increased LA pressure may laterally respond to the increased pressure throughout the left heart. This can result in poor myocardial perfusion due to coronary artery compression as
a result of deformation and expansion of the left heart, thus affecting myocardial contraction and cardiac output. An obvious consequence of FMR is a further increase in LA pressure, the reasons for which are diverse. First, patients with FMR (FMR+) are prone to have a structural basis for LA pressure elevation. Second, MR itself can lead to a further elevation in LA pressure, resulting in significant hemodynamic consequences. Finally, early diastolic transmitral velocity to early mitral annulus diastolic velocity ratio (E/e') ≥ 14 is recommended as a cutoff value for LA pressure elevation on cardiac ultrasound.\(^\[10\]\)

Shock is a syndrome that affects approximately one-third of patients in the intensive care unit and is associated with high morbidity and mortality.\(^{[11,12]}\) Patients with shock usually have complications of FMR, such as excessive fluid resuscitation, which leads to left ventricular (LV) enlargement and MR [Figure 1A and 1B]. However, the relationship between patients with shock and FMR remains controversial. Depending on the pathophysiological mechanisms of shock, once FMR occurs, it may increase the risk of fluid resuscitation and pulmonary edema through increased LA and LV pressure, which may further lead to poor perfusion of the heart itself and of the whole body. This can result in a vicious cycle that has not been reported in an organized fashion in the literature. In this study, we aimed to elucidate the incidence of FMR and E/e' ≥ 14 in patients with shock and to illustrate the need for intervention for FMR and E/e' ≥ 14 by analyzing the prognostic impact of their synergistic effects in patients with shock.

**Methods**

**Ethical approval**

This study was conducted in accordance with the *Declaration of Helsinki*. The study was approved by the Ethics Committee of West China Hospital Review Board. All patients and/or their families provided written informed consent for participation.

**Patient selection**

We retrospectively screened 130 consecutive hospitalized patients within 6 h of shock onset from 175 patients with shock who underwent transthoracic echocardiography (TTE) at our hospital from April 2016 to June 2017 [Figure 2]. The inclusion criteria were as follows\(^{[11,12]}\): (1) age ≥ 18 years; (2) hypotension with a systolic arterial pressure < 90 mmHg, mean arterial pressure (MAP) < 70 mmHg, or a reduction in systolic blood pressure > 40 mmHg from baseline; (3) arterial lactate concentration > 2 mmol/L and urine output < 0.5 mL·kg\(^{-1}\)·h\(^{-1}\). Patients were excluded if they met one of the following criteria: (1) age < 18 years; (2) pregnant; (3) patients or family refused enrollment. As a teaching hospital, all included patients were treated according to the standard treatment protocol.

**Critical care ultrasound (CCUS) examination**

The CCUS examination was performed once within 6 h of shock onset. All CCUS examinations were performed by board certified physicians who had completed the full Chinese Critical Ultrasound Study Group training course and who had >6 months of experience in performing CCUS.

The CCUS study included two-dimensional, M-mode, and Doppler echocardiography and tissue Doppler imaging. TTE examinations were performed with a Philips CX50 (Philips Healthcare, Bothell, WA, USA) or Sonosite M-Turbo (SonoSite Industry, Bottle, WA, USA), which had an ordinary convex probe, and an array probe was used for data collection. Evaluation of valvular function was performed as follows\(^{[13-17]}\): Doppler color flow imaging showing regurgitant flow during systole in a parasternal long-axis view, a parasternal short-axis view, and apical four-chamber (A4CH) or five-chamber views suggested MR, tricuspid regurgitation, or aortic valve regurgitation.

Early diastolic transmitral velocity > 1.5 m/s suggested that transmitral flow had increased; early diastolic tricuspid velocity > 1 m/s suggested that tricuspid
flow had increased; and aortic peak velocity $>2$ m/s suggested that transaortic flow had increased. LA pressure was evaluated using the E/e’ ratio according to European Association of Echocardiography and American Society of Echocardiography recommendations updated in 2016, where E was measured using pulsed Doppler of mitral inflow in the A4CH, and e’ reflected the average septal and lateral mitral annular diastolic velocities using tissue Doppler imaging.$^{[10,18]}$ Lung ultrasound (LUS) was performed using a 2 to 4 MHz convex probe based on international evidence-based recommendations for point-of-care LUS$^{[19]}$ using a complete eight-zone LUS examination to evaluate lung ultrasound score (LUSS). Each zone was scored according to the LUS pattern as follows$^{[20]}$: (1) normal aeration (N); presence of lung sliding with A lines or fewer than two isolated B lines; (2) moderate loss of lung aeration: multiple well-defined B lines (B1 lines); (3) severe loss of lung aeration: multiple coalescent B lines (B2 lines); (4) lung consolidation (C): presence of a tissue pattern characterized by dynamic air bronchograms. For a given region of interest, points were allocated according to the worst ultrasound pattern observed: $N=0$, $B1$ lines $=1$, $B2$ lines $=2$, $C=3$. The total score was 24.$^{[21,22]}$

**Statistical analysis**

Data were analyzed using SPSS 24.0 statistical software (IBM Corp.; Armonk, NY, USA). Continuous variables are expressed as mean ± standard deviation or median quartile (first–third quartile) according to their distribution, and categorical variables are expressed as absolute values and percentages. A multivariate logistic regression analysis using stepwise forward elimination to identify factors with independent associations with 28-day mortality was performed. Survival was calculated using the Kaplan-Meier method to compare the relationship between the four groups in terms of 28-day mortality. The mortality rates of the four groups were compared using the log-rank test. A $P$ value of $<0.050$ was considered statistically significant.

**Results**

**Demographic, clinical, and echocardiographic characteristics of patients with shock**

Complete data were available for 130 patients with shock (77 males and 53 females) from April 2016 to June 2017. Table 1 outlines the demographic, clinical, and echocardiographic characteristics of the overall population at the time of enrollment. The mean age of patients was $57.4 \pm 17.9$ years, the mean heart rate was $115.6 \pm 22.5$ beats/min, and the MAP was $80.1 \pm 16.2$ mmHg. The median lactate concentration was $3.5$ mmol/L (interquartile range [IQR], $2.1$–$7.6$ mmol/L; range, $1.0$–$28.2$ mmol/L), and the average acute physiology and chronic health evaluation (APACHE) II score was $23.9 \pm 8.4$ (range, 2–
Table 1: Clinical, echocardiographic, and hemodynamic characteristics of patients with shock with and without FMR and with E/e’ ≥ 14 or < 14.

| Variable                          | All patients (n = 130) | FMR+ (n = 44) | FMR- (n = 86) | P     | E/e’ ≥ 14 (n = 15) | E/e’ < 14 (n = 115) | P     |
|-----------------------------------|------------------------|---------------|---------------|-------|-------------------|--------------------|-------|
| Sex (male/female)                 | 77/53                  | 26/18         | 51/35         | 0.981 | 87/7              | 69/46              | 0.621 |
| Age (years)                       | 57.4 ± 17.9            | 62.0 ± 18.0   | 56.0 ± 17.4   | 0.034 | 68.1 ± 14.9       | 55.9 ± 17.8        | 0.013 |
| HR                               | 115.6 ± 22.5           | 117.9 ± 24.1  | 114.4 ± 21.7  | 0.401 | 115.1 ± 23.4      | 115.6 ± 22.5       | 0.929 |
| MAP (mmHg)                        | 80.1 ± 16.2            | 85.9 ± 19.4   | 77.1 ± 13.4   | 0.003 | 74.0 ± 11.4       | 80.9 ± 16.5        | 0.123 |
| APACHE II                         | 23.9 ± 8.4             | 27.3 ± 7.8    | 22.1 ± 8.2    | 0.001 | 27.2 ± 10.4       | 23.4 ± 8.0         | 0.100 |
| Lactate (mmol/L)                  | 3.5 (2.1, 7.6)         | 4.3 (2.2, 9.1)| 3.0 (2.1, 6.8)| 0.141 | 7.0 (2.7, 17.0)   | 3.2 (2.1, 6.7)     | 0.003 |
| Length of mechanical ventilation (h) | 162.0 (88.5, 378.8) | 145 (95.0, 241.0) | 234 (111.8, 402.8) | 0.118 | 187.5            | 170.82             | 0.734 |
| PaO2/FiO2                          | 215.1 ± 115.9          | 214.7 ± 116.8 | 215.3 ± 116.1 | 0.978 | 207.1 ± 127.3     | 216.1 ± 114.9      | 0.779 |
| Main causes of distributive shock |                        |               |               |       |                   |                    |       |
| Pneumonia                         | 29 (35.8)              | 15 (51.7)     | 14 (48.3)     | 3 (10.3) | 6 (28.9)         | 26 (89.7)           |       |
| Abdominal infection               | 33 (40.7)              | 7 (21.2)      | 26 (78.8)     | 2 (6.1) | 31 (93.9)        |                    |       |
| Infections in other sites         | 16 (19.8)              | 8 (50.0)      | 8 (50.0)      | 2 (12.5) | 14 (87.5)       |                    |       |
| Brain herniation                  | 2 (2.5)                | 1 (50.0)      | 1 (50.0)      | 1 (50.0) | 1 (50.0)        |                    |       |
| Other                             | 1 (1.2)                | 0             | 1 (100.0)     | 0      | 1 (100.0)       |                    |       |
| Main causes of hypovolemic shock  |                        |               |               |       |                   |                    |       |
| Hemorrhagic shock                 | 38 (97.4)              | 8 (21.1)      | 30 (78.9)     | 4 (10.5) | 34 (89.5)       |                    |       |
| Excessive dehydration             | 1 (2.6)                | 1 (100.0)     | 0             | 0      | 1 (100.0)       |                    |       |
| Main causes of cardiogenic shock  |                        |               |               |       |                   |                    |       |
| Acute myocardial infarction       | 3 (37.5)               | 1 (33.3)      | 2 (66.7)      | 2 (66.7) | 1 (33.3)       |                    |       |
| Acute onset of chronic heart failure | 4 (50.0)             | 3 (75.0)      | 1 (25.0)      | 1 (25)  | 3 (75)          |                    |       |
| Neurogenic                        | 1 (12.5)               | 0             | 1 (100.0)     | 0      | 1 (100.0)       |                    |       |
| Main causes of obstructive shock  |                        |               |               |       |                   |                    |       |
| Acute pulmonary embolism          | 2 (100.0)              | 0             | 2 (100.0)     | 0      | 2 (100.0)       |                    |       |
| Valve hemodynamic changes         |                        |               |               |       |                   |                    |       |
| FMR                               | 44 (100)               | 0             | 40 (100.0)    | 0.000  | 6 (40.0)        | 38 (33.0)           | 0.592 |
| IMF                               | 18 (40.9)              | 21 (24.4)     | 32 (27.8)     | 0.134  |                  |                    |       |
| TR                                | 37 (84.1)              | 24 (27.9)     | 53 (46.1)     | 0.597  |                  |                    |       |
| ITF                               | 2 (4.5)                | 9 (10.5)      | 8 (53.3)      | 0.471  |                  |                    |       |
| AR                                | 6 (13.6)               | 6 (7.0)       | 9 (7.8)       | 0.126  |                  |                    |       |
| IAF                               | 4 (9.1)                | 4 (4.7)       | 6 (5.2)       | 0.219  |                  |                    |       |
| LUSs                              | 11.1 ± 5.9             | 9.4 ± 5.8     | 9.9 ± 5.9     | 0.783  |                  |                    |       |
| E/e’                              | 10.8 ± 5.1             | 8.8 ± 3.5     | 8.4 ± 2.4     | 0.000  |                  |                    |       |
| 28-day mortality                  | 28 (63.6)              | 33 (38.4)     | 48 (41.7)     | 0.001  |                  |                    |       |

Data are expressed as n (%), mean ± standard deviation or median quartile (first-third quartile). APACHE: acute physiology and chronic health evaluation; AR: Aortic regurgitation; E/e’: Early diastolic transmural velocity to early mitral annulus diastolic velocity ratio; FMR: Functional mitral regurgitation; FMR+/: Without FMR; FMR+: With FMR; HR: Heart rate; IAF: Increased transaortic flow; IMF: Increased transmural flow; ITF: Increased transtricuspid flow; LUSs: Lung ultrasound score; MAP: Mean arterial pressure; TR: Tricuspid regurgitation.

50). A total of 129 patients (99.2%) were mechanically ventilated, with the median time on ventilator support being 162.0 h (IQR, 70.0–273.0 h) and the mean ratio of partial pressure arterial oxygen and fraction of inspired oxygen PaO2/FiO2 was 215.1 ± 115.9 mmHg. Among the four sub-types of shock (distributive, hypovolemic, cardiogenic, and obstructive), distributive shock was the most common (n = 81 [62.3%]), followed by hypovolemic shock (n = 39 [30.0%]), cardiogenic shock (n = 8 [6.2%]), and obstructive shock (n = 2 [1.5%]). The median length of intensive care unit and hospital stay was 14.5 days (IQR, 7.0–27.3 days) and 21 days (IQR, 13.0–38.0 days), respectively. The 28-day mortality was 46.9% (61/130).

Patients were divided into four groups: FMR+, FMR−, E/e’ ≥ 14, and E/e’ < 14. The baseline demographic and hemodynamic characteristics are shown in Table 1. Of the 130 hospitalized patients with shock, 44 (33.8%) had FMR and 15 (11.5%) had E/e’ elevation. FMR+ patients were older compared with FMR− patients (P = 0.034).
had a significantly higher risk of 28-day mortality compared with patients with shock with E/e \(< 14\) (P \(= 0.013\)). Patients with shock with E/e \(\geq 14\) also had a higher lactate concentration and a higher 28-day mortality rate compared with those with E/e \(< 14\) (P \(= 0.003\) and 0.001, respectively).

### Outcome and survival analysis

Through a univariate correlation analysis, FMR+ patients, E/e \(\geq 14\), a higher LUSS, and a higher lactate concentration had a significantly higher risk of 28-day mortality (P \(= 0.007\), 0.001, 0.008, and 0.001, respectively) [Table 2].

According to the multivariate analysis [Table 3], FMR was independently associated with 28-day mortality (odds ratio [OR], 0.344; 95% confidence interval [CI], 0.123–0.965; P \(= 0.043\)), E/e \((\text{OR}, 1.156; 95\% \text{ CI}, 1.016–1.317; P \(= 0.028\)); LUSS (OR, 1.073; 95% CI, 1.001–1.151; P \(= 0.048\)), and lactate concentration (OR, 1.134; 95% CI, 1.032–1.246; P \(= 0.009\)) were also independently associated with 28-day mortality [Table 3].

The survival analysis revealed that FMR+ patients with shock had a lower survival rate (χ² = 7.672, P = 0.006) [Figure 3]. E/e \(\geq 14\) was also associated with a lower survival rate (χ² = 19.351, P < 0.010) [Figure 4]. Patients were divided into four groups: E/e \(< 14\) FMR− (group 1), E/e \(< 14\) FMR+ (group 2), E/e \(\geq 14\) FMR− (group 3), and E/e \(\geq 14\) FMR+ (group 4). The survival analysis revealed that FMR− patients with shock with E/e \(< 14\) had the highest survival rate, and FMR+ patients with E/e \(\geq 14\) had the lowest survival rate (χ² = 30.141, P < 0.010) [Figure 5].

The 28-day mortality rate for enrolled patients was 46.9% [Figure 6]. The 28-day mortality rate was 33.8%, 57.9%, 77.8%, and 100.0% in group 1, group 2, group 3, and group 4, respectively. Patients in group 4 had a significantly higher risk of 28-day mortality compared with patients in groups 1 and 2 (P \(= 0.001\) and 0.046, respectively).

### Discussion

In the present study, a total of 130 consecutive patients with shock were included. The prevalence of FMR was 33.8%, and 11.5% of patients with shock had E/e elevation. FMR+ patients were more likely to have a higher lactate concentration, a higher APACHE II score, a higher E/e value, and a higher 28-day mortality rate compared with FMR− patients. In addition, patients with E/e \(\geq 14\) were more likely to have a higher lactate concentration and a higher 28-day mortality risk compared with those with E/e \(< 14\). The multivariate analysis demonstrated that with

### Table 2: Univariate correlation analysis between FMR and clinical indices and 28-day mortality.

| Indexes | P     | OR   | 95% CI       |
|---------|-------|------|--------------|
| FMR     | 0.007 | 0.356| 0.168–0.755  |
| IMF     | 0.074 | 2.005| 0.936–4.296  |
| TR      | 0.235 | 1.522| 0.761–3.045  |
| ITF     | 0.087 | 3.321| 0.839–13.137 |
| AR      | 0.161 | 2.453| 0.700–8.594  |
| IAF     | 0.857 | 1.140| 0.273–4.769  |
| E/e<14  | 0.001 | 1.206| 1.075–1.333  |
| LUSS    | 0.008 | 1.087| 1.022–1.157  |
| Lactate | 0.001 | 1.152| 1.061–1.251  |

AR: Aortic regurgitation; CI: Confidence interval; E/e: Early diastolic transmitral velocity to early mitral annulus diastolic velocity ratio; FMR: Functional mitral regurgitation; IAF: Increased transaortic flow; IMF: Increased transmitral flow; ITF: Increased transtricuspid flow; LUSS: Lung ultrasound score; OR: Odds ratio; TR: Tricuspid regurgitation.

### Table 3: Multivariate analysis of independent correlated factors for 28-day mortality in patients with shock.

| Indexes | P     | OR   | 95% CI       |
|---------|-------|------|--------------|
| FMR     | 0.043 | 0.344| 0.123–0.965  |
| IMF     | 0.476 | 1.465| 0.513–4.185  |
| TR      | 0.310 | 1.651| 0.627–4.344  |
| ITF     | 0.213 | 0.334| 0.060–1.874  |
| AR      | 0.416 | 0.534| 0.117–2.425  |
| IAF     | 0.741 | 1.352| 0.226–8.074  |
| E/e<14  | 0.028 | 1.156| 1.016–1.317  |
| LUSS    | 0.048 | 1.073| 1.001–1.151  |
| Lactate | 0.009 | 1.134| 1.032–1.246  |

AR: Aortic regurgitation; CI: Confidence interval; E/e: Early diastolic transmitral velocity to early mitral annulus diastolic velocity ratio; FMR: Functional mitral regurgitation; IAF: Increased transaortic flow; IMF: Increased transmitral flow; ITF: Increased transtricuspid flow; LUSS: Lung ultrasound score; OR: Odds ratio; TR: Tricuspid regurgitation.

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Figures: 3, 4, 5, 6
FMR, E/e′ ≥ 14 was associated with a higher 28-day mortality rate. The highest survival rate of patients with shock was observed in group 1, while the highest 28-day mortality rate was observed in group 4.

Shock is widely regarded as one of the leading causes of death in the intensive care unit. MAP and lactate concentration are two valuable variables used to describe shock severity. In this study, a multivariate analysis demonstrated that FMR was an independent correlated factor for 28-day mortality, as well as E/e′, LUSS, and lactate concentration. This means that FMR is as important as lactate concentration to indicate the outcomes of patients with shock.

LA dilation and an increase in LA pressure may be caused by MR, which may further result in E/e′ elevation. This LA pressure increase may lead to elevated pulmonary capillary pressure and pulmonary edema. Interestingly, in this study, we observed no significant difference in LUSS between FMR+ patients and FMR− patients, or between patients with E/e′ ≥ 14 and those with E/e′ < 14. The reason was probably that elevated LUSS can be caused not only by cardiogenic pulmonary edema, but also by other pulmonary ventilation deficits, such as those due to conditions such as pneumonia and chronic interstitial pulmonary fibrosis..

LUSS is an independent correlated factor for 28-day mortality, indicating that LUSS is also a response to disease severity; the more severe the disease in critically ill patients, the more severe the inflammation and the more serious capillary leakage, leading to an increase in LUSS. FMR and E/e′, which are also independent correlated factors for 28-day mortality in patients with shock, both reflect disease severity and prognosis. Although there was no difference between the two groups in the presence of FMR and E/e′ ≥ 14, deterioration of pulmonary edema can cause LUSS to increase.

Up to now, no studies have elucidated the effect and incidence of FMR and E/e′ ≥ 14 in patients with shock and the synergistic effect of both on the prognosis of these patients. Our study showed that these two factors are independent correlated factors affecting the prognosis of patients with shock. Specifically, prognosis worsens with increased exposure to these two factors, with significant differences in 28-day mortality across exposure levels. In addition, patients with FMR or E/e′ ≥ 14 were significantly older compared with those without FMR or E/e′ < 14.

This study suggests that the occurrence of FMR should be of high concern in patients with shock, especially elderly patients. Further therapeutic interventions to adjust LA pressure need to be considered to improve the prognosis of patients with shock.
This study has some limitations that should be noted. Firstly, we only assessed E/e’ once within 6 h of shock onset; thus, we did not follow up on changes in E/e’. By repeatedly monitoring FMR and E/e’ values, we could provide better clinical guidance. Additionally, this was a retrospective cohort study; further large-scale, multicenter, and prospective cohort studies are required to confirm and extend our findings on the relationships between FMR, E/e’, and patient outcomes.

In summary, our data suggest that a certain percentage of patients with shock have FMR and E/e’ ≥ 14, both of which are independent correlated factors for 28-day mortality. Patients with shock have the worst prognosis when both FMR and E/e’ ≥ 14 are present. Therefore, monitoring patients with shock, especially the elderly, may be necessary to detect the presence of FMR in a timely manner and to improve prognosis by reducing LA pressure using treatments to lower E/e’. In hospitalized patients with shock, the pathophysiology of FMR and E/e’ and the mechanism that affects prognosis need to be further studied.

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Conflicts of interest

None.

References

1. Schmitto JD, Lee LS, Mokashi SA, Bolman RM 3rd, Cohn LH, Chen FY. Functional mitral regurgitation. Cardiol Rev 2010;18:283–291. doi: 10.1097/CRD.0b013e3181e6468.
2. Enriquez-Sarano M, Akkus CW, Vahanian A. Mitral regurgitation. Lancet 2009;373:1382–1394. doi: 10.1016/S0140-6736(09)60692-9.
3. Nikono VT, Gardin JM, Skelton TN, Gottsdiner JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart disease: a population-based study. Lancet 2006;368:1005–1011. doi: 10.1016/S0140-6736(06)69208-8.
4. Jung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, et al. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on Valvular Heart Disease. Eur Heart J 2002;23:1231–1243. doi: 10.1093/eurheartj/159.03.00201-X.
5. Ducas RA, White CW, Wassef AW, Farag A, Bhagirath KM, Freed DH, et al. Functional mitral regurgitation: current understanding and approach to management. Can J Cardiol 2014;30:173–180. doi: 10.1016/j.cjca.2013.11.022.
6. Watanabe N, Maluus S, Nishino S, O’Donoghue TA, Hung J. Functional mitral regurgitation: imaging insights, clinical outcomes and surgical principles. Prog Cardiovasc Dis 2017;60:351–360. doi: 10.1016/j.pcad.2017.11.006.
7. Di Salvo TG, Acker MA, Dec GW, Byrne JG. Mitral valve surgery in advanced heart failure. J Am Coll Cardiol 2010;55:271–282. doi: 10.1016/j.jacc.2009.08.059.
8. Punnoose L, Burkholof D, Cunningham L, Horn EM. Functional mitral regurgitation: therapeutic strategies for a ventricular disease. J Card Fail 2014;20:252–267. doi: 10.1016/j.cardfail.2014.01.019.
9. McCutcheen K, Manga P. Left ventricular remodelling in chronic primary mitral regurgitation: implications for medical therapy. Cardiovasc J Afr 2018;29:51–63. doi: 10.8380/CVJAA-2017-0009.
10. Nagush SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2016;17:1321–1360. doi: 10.1093/ehjci/jew082.
11. Vincent JL, De Backer D. Circulatory shock. N Engl J Med 2013;369:1726–1734. doi: 10.1056/NEJMra1208943.
12. Ithodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Perrr R, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med 2017;43:304–377. doi: 10.1007/s00134-017-4683-6.
13. Vahanian A, Task Force on Clinical Practice Guidelines. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 1: aortic and pulmonary regurgitation. Eur J Echocardiogr 2010;11:223–244. doi: 10.1093/ejechoc/eqp30.
14. Lancellotti P, Tribouilloy C, Hagendorff A, Moura L, Popescu BA, Aglicia E, et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). Eur J Echocardiogr 2010;11:307–332. doi: 10.1093/ejechoc/eqp31.
15. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Thorac Cardiovasc Surg 2014;148:e1–e132. doi: 10.1016/j.jtcs.2014.05.014.
16. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, et al. 2017 AHA/ACC focused update of the 2014 AHA/ ACC Guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2017;135:e1159–e1195. doi: 10.1161/CIR.0000000000000503.
17. Nagues SF, Appleton CP, Gilibeert TC, Marino PO, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2009;22:107–133. doi: 10.1016/j.echo.2008.11.023.
18. Volpicielli G, Elbarbary M, Blaivas M, Lichtenstein DA, Mathias G, Kirpatrick AW, et al. International evidence-based recommendations for point-of-care lung ultrasound. Intensive Care Med 2012;38:577–591. doi: 10.1007/s00134-012-2513-4.
19. Bouhemad B, Brisson H, Le-Guen M, Arbelot C, Lu Q, Rouby JJ. Bedside ultrasound assessment of positive end-expiratory pressure-induced lung recruitment. Am J Respir Crit Care Med 2011;183:341–347. doi: 10.1164/rccm.201003-0369OC.
20. Soummar A, Perbet S, Brisson H, Arbelot C, Constantin JM, Lu Q, et al. Ultrasound assessment of lung aeration loss during a successful weaning trial predicts postextubation distress. Crit Care Med 2012;40:2064–2072. doi: 10.1097/CCM.0b013e318246f6a8.
21. Yin W, Li Y, Zeng X, Qin Y, Wang D, Zou T, et al. The utilization of critical care ultrasound to assess hemodynamics and lung pathology on ICU admission and the potential for predicting outcome. PLoS One 2017;12:e0182881. doi: 10.1371/journal.pone.0182881.