Clinical and Prognostic Impact of a New Left Ventricular Ejection Index in Primary Mitral Regurgitation Because of Mitral Valve Prolapse

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Background—To prevent left ventricular dysfunction (LVD), surgery is recommended in patients with severe primary mitral regurgitation as soon as ejection fraction (EF) ≤60% or LV end-systolic diameter ≥40 mm. However, LVD may be concealed behind preoperative normal LVEF and LV end-systolic diameter. We sought to identify whether a new composite echocardiographic Doppler marker of the LV ejection according to the LV dilatation may predict postoperative LVD and outcome after mitral valve repair in patients with primary mitral regurgitation.

Methods and Results—Between 1991 and 2010, patients who underwent mitral valve repair for primary mitral regurgitation were studied. From preoperative echocardiography, we calculated LV ejection index (LVEI) using following formula: LVEI=indexed LV end-systolic diameter/LV outflow tract time–velocity integral. In the 278 patients included, the best correlation with postoperative LVEF was found with LVEI (r=−0.40; P<0.0001), even in patients with preoperative LVEF≥60% (r=−0.46; P<0.0001). In multivariable analysis, LCEI>1.13 was an independent predictor of postoperative LVD (P<0.0001). During a mean follow-up of 10±4.6 years, 67 (29%) deaths occurred. When compared with patients with preserved LVEI, those with LVEI>1.13 had significantly lower both survival and cardiac death–free survival (P=0.017 and P=0.008, respectively). Similar results were found in patients with preoperative LVEF≥60% (P=0.049 and P=0.016, respectively). In Cox proportional hazard model, after meticulous adjustment for cofactors, LVEI>1.13 remains independently associated with death (hazard ratio, 1.64; P=0.039) and cardiac-related death (hazard ratio, 3.27; P=0.026).

Conclusions—After mitral valve repair for primary mitral regurgitation, the preoperative LVEI is a new and simple composite parameter of both LV dilatation and LV forward flow able to accurately predict postoperative LVD and outcome.
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Key Words: echocardiography ■ general surgery ■ mitral valve ■ mitral valve insufficiency ■ ventricular dysfunction, left

Primary mitral regurgitation (MR) is the most frequent valvular heart disease in Western countries and frequently requires surgery.[1] To avoid left ventricular dysfunction (LVD) and its harmful outcome consequences, current both European Society of Cardiology[2] and American College of Cardiology/American Heart Association[3] guidelines recommend surgery in patients with severe MR in the presence of LV ejection fraction ≤60%[4–6] and LV dilatation.[7] However, LV ejection fraction may remain in normal range for long time,[8] delaying surgery, whereas subclinical myocardial LVD may be present.[9] Similarly, in patients with significant primary MR, cardiac magnetic resonance study recently shows that LV dilatation generally occurs in the mid apical section of the ventricle and only later, at an advanced stage of disease process, at the LV base.[10] Using echocardiography, this may lead to underestimation of the impact of MR on LV dimension, which may, in turn, delay surgical decision making and thus decrease the expected benefits of the intervention, more particularly on postoperative LV function. Given the limitation of LVD/dilatation as trigger for surgery, there is a profound need to identify complementary parameter assessing the consequences of MR on the ventricle. Recently, LV global longitudinal strain was quantified using 2-dimensional (2D) speckle tracking. Nevertheless, this parameter is load and geometry dependent,[11] may have technical limitation, and requires excellent image quality in the 3 apical views.[12]

See Editorial by Delling
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The aim of this study was to identify whether a new composite echocardiographic marker of LV dilatation according to the quality of LV ejection may predict postoperative LVD and outcome in patients with primary MR.

Methods

Population

Between January 1991 and December 2010, 335 patients who underwent mitral valve repair for severe chronic primary MR because of leaflet prolapse were studied (University Hospital of Amiens, Amiens, France). Patients underwent comprehensive preoperative (within 3 months before surgery) and postoperative (between 9 and 12 months after surgery) echocardiographic evaluation. The postoperative LV ejection fraction was not available in 29 patients.

Exclusion criteria were (1) MR caused by ischemic heart disease or dilated cardiomyopathy, rheumatic heart disease, active infective endocarditis, and congenital heart disease; (2) previous cardiac surgery; (3) concomitant aortic valve or aortic root surgery; (4) patients with history of myocardial infarction or recent acute coronary syndrome; and (5) patients (n=53, 16%) with missing preoperative LV ejection fraction, LV end-systolic diameter data, or LV outflow tract time–velocity integral ($LVOT_{TVI}$). These results are from a whole cohort of 278 patients, out of which the postoperative LV ejection fraction was available and assessed in 249 patients.

Baseline clinical characteristics, comorbidity, symptoms, and operative data were collected from patients' medical records. The Charlson index was calculated and used as comorbidity score. The standard EuroSCORE was calculated retrospectively for each patient using the calculator available online at http://www.euroscore.org. We obtained institutional review board authorization before conducting the study. The study was conducted in accordance with institutional policies, national legal requirements, and the revised Helsinki declaration.

Echocardiographic Measurements

Diagnoses of leaflet prolapse and flail leaflets were identified according to the recommended criteria.[13,14] LV dimensions were assessed from parasternal long-axis views by 2D-guided M-mode using the leading edge methodology at end diastole and end systole. All LV dimension were indexed for body surface area. LV ejection fraction was estimated by the Simpson biplane method or, in a minority of cases, visually (<5%). Preoperative LVD was defined as LV ejection fraction <60% and postoperative LVD as ≤50%. The $LVOT_{TVI}$ was obtained using pulsed wave Doppler. Severity of MR was assessed by Doppler echocardiography, as recommended.[15] The LV ejection index was calculated as the following ratio:

$$\text{LV ejection index} = \frac{\text{Indexed LV end} - \text{systolic diameter}}{\text{LVOT TVI}}$$

End Points Study

End points of the study were postoperative overall mortality and cardiovascular mortality. During follow-up, patients were monitored by their personal general practitioners or cardiologists. The deaths were ascertained by review of medical records, clinical interviews, or by telephone calls to physicians, patients, and (when necessary) next of kin.

Statistical Analysis

The data are presented as mean±SD or percentages and absolute number. The distribution of continuous data was tested for normality using the Kolmogorov–Smirnov test and skewed variables were presented using median (25th and 75th percentiles). The population

Table 1. Demographic and Clinical Data

Variables	Whole Cohort, n=278*	Postoperative LVEF>50%, n=185, 74%	Postoperative LVEF≤50%, n=64, 26%	*P* Value
Demographic data				
Age, y	65±11	65±11	68±10	0.075
Male sex, n (%)	194 (70)	127 (67)	46 (72)	0.63
Body surface area, m²	1.82±0.19	1.83±0.20	1.80±0.18	0.38
Body mass index, kg/m²	24.6±4.3	26.2±4.3	23.5±3	0.002
Risk factors and comorbidities				
Hypertension, n (%)	107 (38)	74 (40)	23 (36)	0.63
Dyslipidemia, n (%)	96 (34)	67 (36)	21 (33)	0.66
Smoking, n (%)	93 (33)	63 (34)	23 (36)	0.72
Obesity, n (%)	26 (9)	20 (15)	5 (11)	0.57
Diabetes mellitus, n (%)	20 (7)	15 (8)	5 (3)	0.17
Chronic lung disease, n (%)	27 (10)	19 (10)	5 (8)	0.57
Renal failure, n (%)	7 (2.5)	3 (2)	4 (6)	0.074
Hepatic disease, n (%)	3 (1)	2 (1)	1 (2)	0.59
Atrial fibrillation, n (%)	66 (24)	42 (23)	20 (31)	0.17
NYHA functional class ≥III, n (%)	139 (50)	91 (49)	34 (53)	0.67
Risk score				
Charlson index†	0.50 (0–1)	0 (0–1)	0.50 (0–1)	0.28
Logistic Euroscore†	2.1 (1.0–3.7)	2.0 (1.0–3.8)	2.3 (1.2–3.6)	0.56

LVEF indicates left ventricular ejection fraction; and NYHA, New York Heart Association.

*The whole cohort was composed of 278 patients, out of which postoperative LV ejection fraction assessment was available in 249 patients.

†Variable with normal distribution test failure.

Table 2. Preoperative LV Echocardiographic Data

Preoperative Variables	Whole Cohort, n=278*	Postoperative LVEF>50%, n=185, 74%	Postoperative LVEF≤50%, n=64, 26%	*P* Value
LV dimension				
LVES diameter, mm	37±7	36±6	40±7	<0.0001
LVED diameter, mm	61±6.5	61±6	63±7	0.064
Indexed LVES diameter, mm/m^2	20±4	20±4	22±4	<0.0001
Indexed LVED diameter, mm/m^2	34±4	34±4	35±4	0.018
LV function				
$LVOT_{TVI}$, cm	17±4	18±4	16±3	<0.0001
LV stroke volume, mL	65.5±20	68±20	61±18	0.009
Indexed LV stroke volume, mL/m^2	36±10	37±10	34±11	0.024
LVEF, %	68±8.5	69±7	66±9	0.003
LV ejection index	1.23±0.38	1.13±0.32	1.47±0.39	<0.0001
TR grade ≥3, n (%)	14 (5)	12 (6.5)	2 (3)	0.11
Systolic PAP, mm Hg	46±15	46±15	47±16	0.74

LVED indicates left ventricular end-diastolic; LVEF, LV ejection fraction; LVES, end-systolic; $LVOT_{TVI}$, left ventricular outflow tract time–velocity integral; PAP, pulmonary arterial pressure; and TR, tricuspid regurgitation.

*The whole cohort was composed of 278 patients, out of which postoperative LV ejection fraction assessment was available in 249 patients.

was first studied according to the presence of postoperative LVD, resulting in 2 groups. Comparison between the 2 groups was performed with the Student *t* test, Mann–Whitney *U* test, χ^2 test, or Fisher exact test, as appropriate. The relationship between postoperative LV ejection fraction and preoperative variables was assessed using Pearson or Spearman correlation. The multivariable relationship between LV ejection index and postoperative LVD was assessed using logistic regression. In addition, receiver operating characteristics curve was used to derive the best cutoff value to predict postoperative LVD using the Youden index.

Survival was estimated using Kaplan–Meier curves, and statistical difference between impaired and preserved preoperative LV ejection index group was assessed using log-rank test. Univariable and multivariable Cox proportional hazard regression analyses were performed to evaluate predictors of mortality, and hazard ratio (HR) and 95% of confidence interval (95% CI) were reported.

A *P* value of 0.05 was considered significant for all statistical tests. Data were analyzed with SPSS 17.0 (SPSS Inc, Chicago, IL).

Results

Among the 278 patients included in the study (age, 65±11 years; 70% of male), 249 have available postoperative LV ejection fraction and 26% (n=64) have developed postoperative LVD. Demographic, clinical, and preoperative echocardiographic data are reported in Tables 1 and 2.

The LV ejection index ranged from 0.46 to 2.73 (mean, 1.23±0.38; median, 1.17). There was a weak correlation between preoperative LV ejection index and preoperative LV ejection fraction (r=−0.32; P<0.0001).

Postoperative LVD

Compared with patients without postoperative LVD (n=185), those with LVD (n=64) had significantly lower weight (P=0.04) and body mass index (P=0.002), and there was a trend for significant older age (P=0.075) and higher rate of renal failure (P=0.054; Table 1). There was no other significant difference between these 2 groups regarding demographic and clinical data, and risk scores. Compared with patients without postoperative LVD, the group with postoperative LVD had significant higher preoperative LV dimension (Table 2) and lower LV stroke volume (P=0.009) and LV ejection fraction (P=0.003). The LV ejection index was markedly and significantly higher in patients with postoperative LVD (1.47±0.39 versus 1.13±0.32, P<0.0001). Excluding patients with preoperative LV ejection fraction <60% from the analysis led to similar results than in the whole population (Table 3).

Predictor of Postoperative LVD

The postoperative LV ejection fraction (available in n=249) was significantly correlated with preoperative LV size and function (Table 4). Among all other possible ratios combining LV stroke volume or $LVOT_{TVI}$ and LV diameters (r≤0.25, P value from 0.15 for indexed LV stroke volume/$LVOT_{TVI}$ to <0.0001 for LV end-systolic diameter/$LVOT_{TVI}$) as well as single parameters (all r≤0.28, P value from 0.019 to 0.0001; Table 4), including body surface area indexation, the best correlation was reported with LV ejection index (r=−0.40; P<0.0001). There was a nonsignificant correlation between postoperative LV ejection fraction and age and weight (P=0.059 and P=0.06, respectively).

Focusing only on patients with preoperative LV ejection fraction ≥60% (n=222 from 249 available postoperative LV ejection fraction) resulted in similar findings except for indexed LV end-diastolic diameter and LV ejection fraction that were no longer significantly correlated with postoperative LV ejection fraction (Table 4). In this subset, LV ejection index remained the best univariable predictor of postoperative LVD (r=−0.46; P<0.0001).

Using receiver operating characteristic curve analysis, LV ejection index showed good sensitivity and specificity in identifying postoperative LVD (area under the curve=0.75, cutoff value=1.13, sensitivity=0.80, and specificity=0.64).

Table 3. Demographic, Clinical, and Echocardiographic Data in Patients With Preserved Preoperative LVEF (≥60%)

Variables	Postoperative LVEF>50%, n=171, 77%	Postoperative LVEF≤50%, n=51, 23%	*P* Value
Demographic data			
Age, y	64±11	68±10	0.051
Male sex, n (%)	120 (70)	35 (69)	0.83
Body surface area, m^2	1.83±0.18	1.78±0.18	0.13
Body mass index, kg/m^2	26.0±4.2	23.6±3.2	0.011
Risk factors and comorbidities			
Hypertension, n (%)	69 (40)	19 (38)	0.76
Dyslipidemia, n (%)	63 (37)	17 (34)	0.69
Smoking, n (%)	60 (35)	14 (28)	0.35
Obesity, n (%)	18 (14)	2 (4)	0.18
Diabetes mellitus, n (%)	14 (8)	2 (4)	0.31
Chronic lung disease, n (%)	17 (10)	3 (6)	0.37
Renal failure, n (%)	3 (2)	3 (6)	0.14
Hepatic disease, n (%)	1 (1)	1 (2)	0.41
Atrial fibrillation, n (%)	37 (22)	17 (33)	0.09
NYHA functional class ≥III, n (%)	84 (49)	27 (52)	0.40
Risk score			
Charlson index*	0 (0–1)	0 (0–1)	0.88
Logistic Euroscore*	1.8 (0.9–3.8)	2.5 (1.2–3.7)	0.24
LV dimension			
LVES diameter, mm	35±6	38±5	0.004
LVED diameter, mm	61±6	62±7	0.33
Indexed LVES diameter, mm/m^2	19±3	21±3	<0.0001
Indexed LVED diameter, mm/m^2	33±4	35±4	0.037
LV function			
$LVOT_{TVI}$, cm	18±4	16±3	<0.0001
LV stroke volume, mL	68±20	59±18	0.004
Indexed LV stroke volume, mL/m^2	37±10	33±10	0.016
LVEF, %	70±6	69±6	0.298
LV ejection index	1.11±0.31	1.41±0.37	<0.0001
TR grade ≥3, n (%)	8 (5)	2 (4)	0.14
Systolic PAP, mm Hg	46±15	49±17	0.37

LVED indicates left ventricular end-diastolic; LVEF, LV ejection fraction; LVES, end-systolic; $LVOT_{TVI}$, left ventricular outflow tract time–velocity integral; and NYHA, New York Heart Association.

*Variable with normal distribution test failure.

The other ratios identified as predictor of LVD were LV end-systolic diameter/$LVOT_{TVI}$ ratio (area under the curve=0.74, cutoff value=2.35, sensitivity=0.64, and specificity=0.76) and LV end-systolic diameter/LV stroke volume ratio (area under the curve=0.69, cutoff value=0.74, sensitivity=0.52, and specificity=0.84).

On multivariable analysis, LV ejection index remained a significant independent predictor of postoperative LVD both considered as continuous variable or according to the threshold of 1.13, even after adjustment for preoperative age, sex, weight, LV end-systolic diameter, and LV ejection fraction (Table 5). In patients with preoperative LV ejection fraction ≥60%, the multivariable analysis also identified LV ejection index as an independent predictor of postoperative LVD. Consistently, the LV end-systolic diameter/$LVOT_{TVI}$ ratio was also independently associated with postoperative LVD with similar predictive value (both χ^2=42). See Figure I in the Data Supplement.

The presence of preoperative tricuspid regurgitation grade 3 or 4 (5%) and pulmonary hypertension (34%, ie, systolic pulmonary arterial pressure >50 mm Hg) was not associated with postoperative LVD, neither in univariable nor in multivariable analysis (all P>0.17).

At the last available follow-up, 23 patients depicted recurrent grade 3+ or 4+ MR, resulting in MR recurrence rates of 6±1%, 9±2%, and 15±4% at 6, 12, and 15 years, respectively. There was no significant relationship between postoperative LVD and recurrent MR (P=0.152).

Table 4. Correlation With Postoperative LVEF

	All Available Postoperative LVEF, n=249		Preoperative LVEF≥60%, n=222	
Variables	*r*	*P* Value	*r*	*P* Value
Demographic data and risk score				
Age	−0.12	0.059	−0.12	0.06
Body surface area	0.06	0.33	0.09	0.20
Body mass index	0.10	0.20	0.12	0.13
Weight	0.14	0.06	0.18	0.02
Charlson index*	−0.02	0.75	−0.01	0.88
Logistic Euroscore*	−0.06	0.33	−0.07	0.30
Preoperative LV dimensions				
LVES diameter	−0.25	<0.0001	−0.15	0.025
LVED diameter	−0.09	0.17	−0.02	0.74
Indexed LVES diameter	−0.27	<0.0001	−0.19	0.005
Indexed LVED diameter	−0.13	0.038	−0.09	0.16
Preoperative LV function				
$LVOT_{TVI}$	0.28	<0.0001	0.26	<0.0001
LV stroke volume	0.17	0.009	0.18	0.007
Indexed LV stroke volume	0.15	0.019	0.16	0.019
LVEF	0.25	<0.0001	0.10	0.14
LV ejection index	−0.40	<0.0001	−0.46	<0.0001
Preoperative systolic PAP	−0.05	0.44	−0.10	0.22

LVED indicates left ventricular end-diastolic; LVEF, LV ejection fraction; LVES, end-systolic; and LVOT VTI, left ventricular outflow tract – time-velocity integral.

*Variable with normal distribution test failure.

Postoperative Mortality and Cardiovascular-Related Mortality

During a mean postoperative follow-up of 10±4.6 years (median, 10 years [6–13 years]), 85 deaths occurred and 23 were from cardiovascular cause, resulting in overall survival of 86±2% at 6 years, 68±3% at 12 years, and 56±4% at 15 years, and in cardiovascular death-free survival of 96±1% at 6 years, 90±2% at 12 years, and 83±4% at 15 years.

Patients with a LV ejection index >1.13 had significant higher rate of death (36% versus 24%; *P*=0.021) and cardiovascular death (12% versus 4%, *P*=0.011) than those with preserved LV ejection index (ie, >1.13).

The 15-year survival and cardiovascular death-free survival were significantly lower (*P*=0.017 and *P*=0.008, respectively) in patients with increased LV ejection index (ie, >1.13; Figure 1). Similar results were found when patients with preoperative LV ejection fraction <60% were excluded (Figure 2). In patients (n=225) with combined preserved preoperative LV ejection fraction (≥60%) and LV end-systolic diameter <45 mm, the 15-year survival

Table 5. Univariable and Multivariable Analysis to Identify Predictors Postoperative LVD in Both Cohort With Available Postoperative LV Ejection Fraction (n=249) and Only in Patients With Preserved Preoperative LV Function (n=222)

	LV Ejection Index (per 0.1 increase)			LV Ejection Index >1.13		
Variables	Odds Ratio	95% CI	*P* Value	Odds Ratio	95%CI	*P* Value
Whole cohort						
Univariable	1.56	1.32–1.82	<0.0001	4.9	2.5–9.7	<0.0001
Age-, sex-, and weight-adjusted	1.69	1.35–2.08	<0.0001	5.1	2.6–10.1	<0.0001
+LVES diameter	1.56	1.23–2.00	<0.0001	5.1	2.6–10.1	<0.0001
+LV ejection fraction	1.56	1.23–2.00	0.001	4.4	2.2–9.0	<0.0001
Preoperative LV ejection fraction ≥60%						
Univariable	1.54	1.28–1.82	<0.0001	4.2	2.1–8.5	<0.0001
Age-, sex-, and weight-adjusted	1.72	1.33–2.22	<0.0001	5.1	2.1–12.5	<0.0001
+LVES diameter	1.56	1.19–2.04	0.001	3.3	1.3–8.5	0.015
+LV ejection fraction	1.59	1.2–2.08	0.001	3.2	1.2–8.4	0.016

CI indicates confidence interval; ES, end-systolic; and LV, left ventricular.

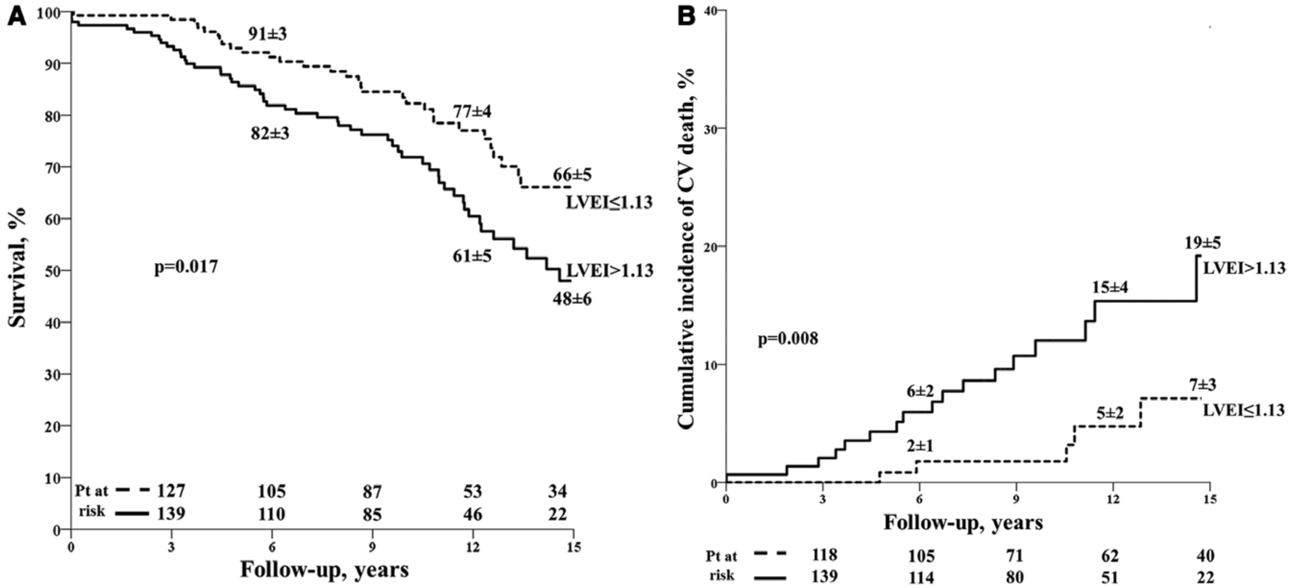

Figure 1. Overall survival (**A**) and cumulative incidence of cardiovascular (CV) death (**B**) according to left ventricular ejection index (LVEI) in the whole cohort (n=278).

and cardiovascular death-free survival were significantly lower (P=0.043 and P=0.015, respectively) in patients with increased preoperative LV ejection index (ie, >1.13; Figure 3). When only considering patients in normal sinus rhythm (n=213), high LV ejection index (ie, >1.13) remained associated with significantly lower survival and cardiovascular death-free survival than those with preserved LV ejection index (6 years: 83±4% versus 94±2%; 12 years: 66±6% versus 82±4%; 15 years: 51±8% versus 69±6%; P=0.029 and 6 years: 93±3% versus 98±1%; 12 years: 86±4% versus 96±2%; 15 years: 80±7% versus 93±3%, P=0.021).

Predictor of Long-Term Postoperative Mortality and Cardiovascular Mortality

Preoperative impaired LV ejection index was significantly associated with postoperative death and cardiovascular death, independently of age and sex (Table 6). Further multivariable adjustments (model 1) for advanced New York Heart Association functional class, Charlson index, LV end-systolic dilatation, and impaired LV ejection fraction identified that preoperative LV ejection index (ie, >1.13) was an independent predictor of death (HR, 1.64; 95% CI, 1.02–2.64; P=0.039) and of cardiovascular death (HR, 3.27; 95% CI, 1.15–9.28; P=0.026). The addition of renal failure to the model 1 (Table 6) resulted in a significant association between preoperative

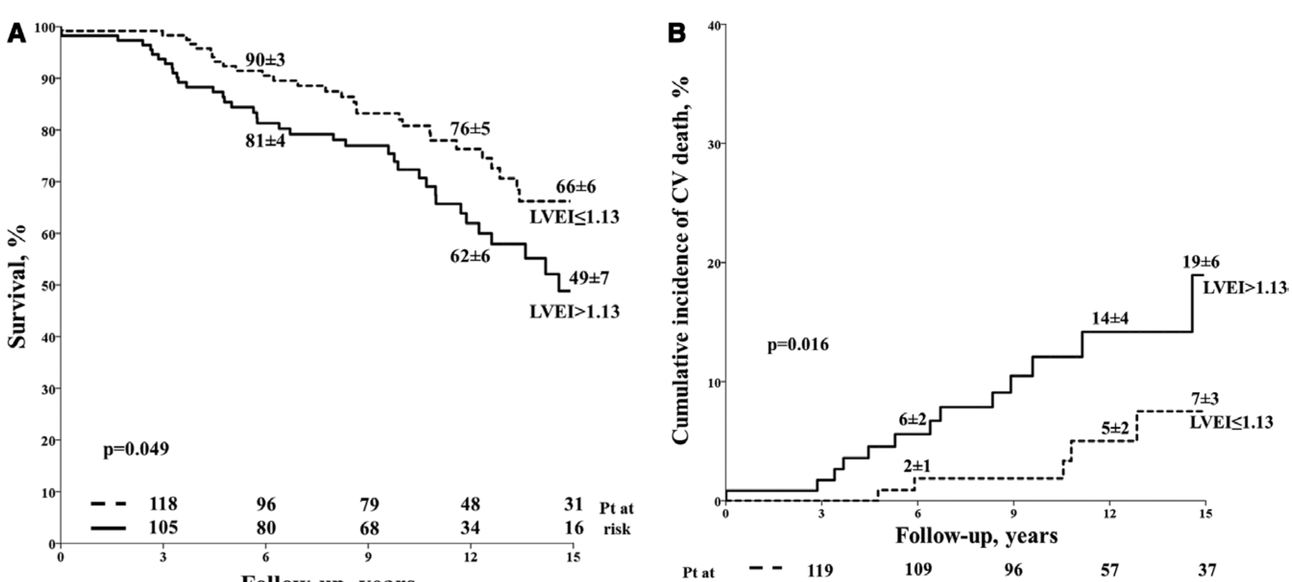

Figure 2. Overall survival (**A**) and cumulative incidence of cardiovascular (CV) death (**B**) according to left ventricular ejection index (LVEI) in patients with preoperative preserved LV systolic function (ie, ejection fraction ≥60%).

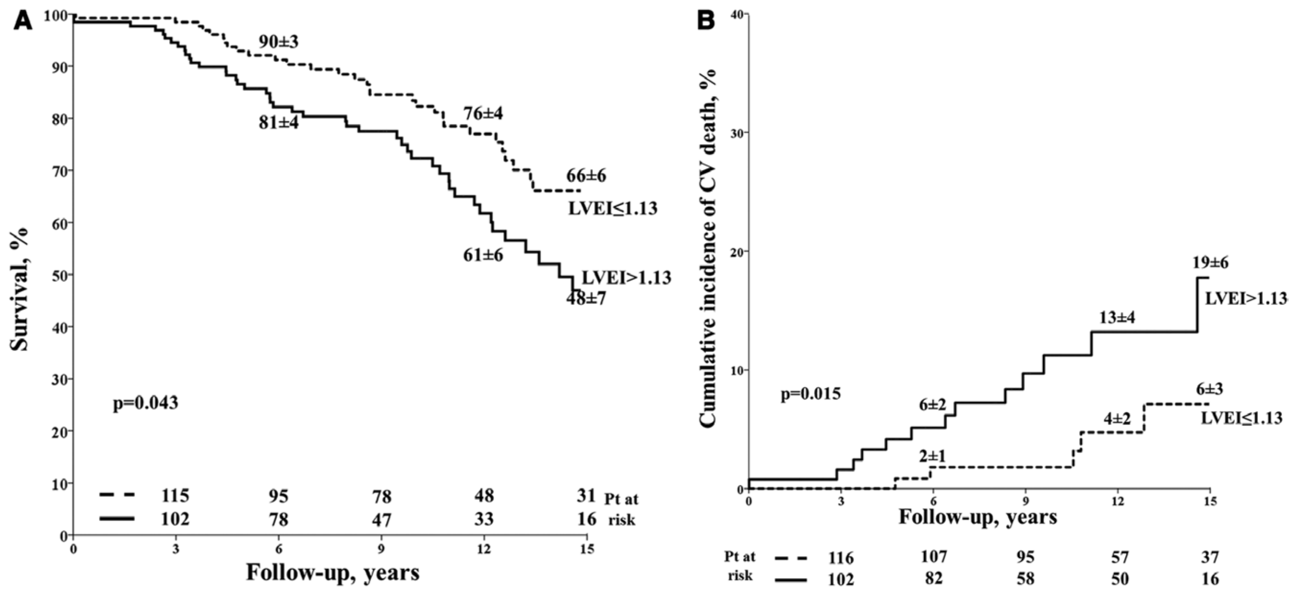

Figure 3. Overall survival (**A**) and cumulative incidence of cardiovascular (CV) death (**B**) according to left ventricular ejection index (LVEI) in patients (n=225) with both preoperative preserved LV systolic function (ie, ejection fraction≥60%) and no left ventricular dilatation (left ventricular end-systolic diameter <45 mm).

LV ejection index (ie, >1.13) and mortality (HR, 1.67; 95% CI, 1.03–2.71; *P*=0.036) and cardiovascular mortality (HR, 2.99; 95% CI, 1.03–8.67; *P*=0.044). Of interest, in patients with preoperative LV ejection fraction ≥60%, increased LV ejection index remained independently associated with death (HR, 1.67; 95% CI, 1.02–2.79; *P*=0.043) and cardiovascular death (HR, 4.68; 95% CI, 1.44–15.2; *P*=0.01). In patients (n=225) with combined preoperative preserved LV ejection fraction and LV end-systolic diameter <45 mm, LV ejection index was an independent predictor of death (HR, 1.75; 95% CI, 1.06–2.87; *P*=0.028) and cardiovascular death (HR, 4.01; 95% CI, 1.23–13; *P*=0.021).

Multivariable adjustment (model 1) reported a significant association between nonindexed LV end-systolic diameter/$LVOT_{TVI}$ ratio and mortality or cardiovascular mortality (mortality: HR, 1.34; 95% CI, 1.02–1.78; *P*=0.038; cardiovascular mortality: HR, 1.77; 95% CI, 1.70–2.91; *P*=0.024). However, when compared with LV ejection index, the LV end-systolic diameter/$LVOT_{TVI}$ ratio, although significant, was less predictive of both mortality and cardiovascular mortality (model χ^2: 30.9 versus 28.8 and model χ^2: 14.9 versus 13.1, respectively). Moreover, the ratio of LV end-systolic diameter/LV stroke volume was not associated with mortality or cardiovascular mortality in univariable analysis

Table 6. Impact of LV Ejection Index (>1.13) on Mortality and Cardiovascular-Related Mortality in Cox Proportional Hazard Model in Both Whole Cohort and Only in Patients With Preserved Preoperative LV Function

	Death			Cardiovascular Death		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Whole cohort						
Univariable	1.73	1.11–2.69	0.015	3.52	1.30–9.48	0.013
Age- and sex-adjusted	1.75	1.13–2.73	0.013	3.51	1.30–9.47	0.013
Model 1*	1.64	1.02–2.64	0.039	3.27	1.15–9.28	0.026
Model 2†	1.67	1.04–2.78	0.036	2.99	1.03–8.67	0.044
Preoperative LV ejection fraction ≥60%						
Univariable	1.62	1.00–2.60	0.05	3.65	1.78–11.3	0.025
Age- and sex-adjusted	1.68	1.03–2.73	0.036	3.77	1.21–11.7	0.022
Model 1*	1.67	1.02–2.79	0.043	4.68	1.44–15.2	0.01
Model 2†	1.67	1.04–2.78	0.033	3.86	1.24–12.0	0.02

CI indicates confidence interval; and LV, left ventricular.

*The model 1 included age, sex, New York Heart Association functional class ≥III, comorbidity index, preoperative LV end-systolic diameter >40 mm, and preoperative LV ejection fraction ≥60%.

†The model 2 is model 1+renal failure.

(P=0.09 and P=0.29). The use of various cutoff values of LV end-systolic diameter/LV stroke volume ratio resulted in similar nonsignificant results.

Discussion

The results of this study show that in patients with primary MR undergoing mitral valve repair: (1) increased preoperative LV ejection index (ie, >1.13) is an independent predictor of postoperative LVD and (2) a powerful determinant of postoperative survival and cardiovascular mortality, even in those with preserved preoperative LV ejection fraction and without severe LV dilatation. In addition, the LV ejection index seems superior to other ratios combining LV stroke volume or $LVOT_{TVI}$ and LV diameter in the prediction of both postoperative LVD and survival. Nonetheless, the use of nonindexed LV end-systolic diameter in the calculation of LV ejection index (ie, >2.35) is also significantly associated with outcome and could be preferred in obese patients in whom LV indexation is not suitable.

LV Ejection Index

The LV ejection index is an easy-to-obtain surrogate marker of the impact of MR on both LV dilatation and LV systolic function (ie, ejection). With MR worsening and LV contractility impairment, the $LVOT_{TVI}$ may decreases. In parallel, LV volume overload, because of chronic MR, progressively lead to LV dilatation. Together, these harmful consequences of MR will be highlighted by a marked increase in LV ejection index. Of note, $LVOT_{TVI}$ and indexed LV end-systolic diameter are unrelated in our series (r=−0.08; P=0.21), suggesting that these 2 parameters independently reflect the impact of MR on ejection and dilatation, respectively. Consequently, the impact of MR on only 1 of these 2 components will be detected by LV ejection index, explaining, at least in part, its strong relationship with postoperative LV function and outcome. For a given indexed LV end-systolic diameter, reduced LV TVI will result in increased LV ejection index. Similarly, for a given LV TVI, progressive LV dilatation and increase in indexed LV end-systolic diameter will also produce increased LV ejection index.

Our data showed almost similar prognostic value of nonindexed LV end-systolic diameter/$LVOT_{TVI}$ ratio. This suggests that in obese patients, in whom indexation may lead to erroneous conclusion, the use of nonindexed ratio could be an appropriate alternative.

LV Ejection Index Versus LV Ejection Fraction

In our series, despite significant, the relationship between LV ejection index and LV ejection fraction is notably weak. This may suggest that LV ejection index could be a good complementary parameter to LV ejection fraction for the risk stratification and the management of patients with primary MR. Although LV ejection fraction is a powerful determinant of poor prognosis[16] and an accurate marker of LV systolic dysfunction,[6] it often underestimates the degree of dysfunction in volume overload disease such as MR. Indeed, in patients with significant MR, LV ejection fraction if often normal or mildly reduced despite marked alteration of LV myocardial function, as suggested by recent series using speckle-tracking analysis.[9,17] In addition, preserved LV ejection fraction ≥60% does not necessarily imply absence of risk of cardiac event.[9,17,18] LV ejection fraction is not a pure marker of myocardial contractility. It is also highly influenced by LV geometry, the loading conditions, and the MR severity.[19] Indeed, for a given level of contractility, a significant increase in LV preload, which is common in chronic MR, and a decrease in LV afterload will yield to higher LV ejection fraction. This mechanism may explain why LV ejection fraction is often preserved in patients with severe primary MR, despite myocardial impairment.

Hence, LV ejection fraction grossly underestimates the extent of myocardial impairment in patients with MR. In patients with primary MR, the LV ejection fraction is often maintained within normal range owing to increased preload and reduced afterload. However, following mitral valve repair, the preload and afterload are normalized and LV ejection fraction drops thereby revealing the existence of myocardial dysfunction, which was masked before surgery.[6] Furthermore, the LV ejection fraction may also be artificially maintained within normal range or close to normal range by the presence of the MR itself.[19] The LV ejection fraction is the result of LV stroke volume divided by LV end-diastolic volume. However, LV stroke volume is the sum of LV forward stroke volume ejected through the LV outflow tract+the regurgitant volume. Hence, when the regurgitant volume increases, LV ejection fraction may increase, although myocardial contractility and LV forward stroke volume may be reduced. This close relationship between MR and LV ejection fraction underlines the usefulness of complementary parameter, such as LV ejection index, which is free of the impact of MR in its measurement.

LV Ejection Index Versus LV Longitudinal Function Parameters

The LV longitudinal function assessment, derived from tissue Doppler imaging, was found to be associated with the severity of MR in a cohort of patients including a majority of preserved LV ejection fraction.[20] Nevertheless, this technique requires high frame rate, narrow sector images, high-quality recording, and is particularly time consuming. In addition, tissue Doppler imaging strain and strain rate–derived parameters remain highly angle dependent.

More recently, LV longitudinal function was also assessed in patients with MR using 2D speckle-tracking analysis, both at rest[9] and during exercise.[17] Although the quantification of LV global longitudinal strain seems appealing and clinically useful, owing to its relationship with outcome, it also remains time consuming and required high-quality images. Furthermore, the measurement of LV global longitudinal strain is geometry and load dependent.[11,21] In opposition, LV ejection index is rapid to calculate and only requires measurement and images mandatory in routine echocardiographic examination.

Limitations

This study is retrospective, suggesting that all the results reported are limited by bias related to this design. The LV volumes were only available in a small sample of the studied population precluding subsequent analysis. In addition, the LV myocardial performance index, right ventricular, and diastolic function are lacking from our database. Furthermore, the postoperative LV ejection fraction was not available in 29 patients.

Because of the period of inclusion, the LV longitudinal strain parameters were not available in this cohort. The direct comparison between these parameters and LV ejection index was, thus, not performed.

Quantitative assessment of severity of MR using the proximal flow convergence method was not systematically performed in the current cohort. Nevertheless, MR was quantified as grade 3+ or grade 4+ in all these patients considered for surgery using an echocardiographic multiparametric approach or LV angiography. The LV ejection index is subject to drawbacks that required to be mentioned. First, as indexed, LV end-systolic is used as numerator, all limitations related to this parameter (eg, load dependency, single dimensional) may also be apply to LV ejection index. In addition, $LVOT_{TVI}$ is also limited by angle dependency. Nevertheless, the close independent relationship reported between LV ejection index and postoperative outcome may suggest that these limitations do not depreciate the usefulness of this new parameter.

Conclusions

After mitral valve repair for primary MR because of mitral valve prolapse, the preoperative LV ejection index is a new and simple composite parameter of both LV dilatation/forward flow able to accurately predict postoperative LVD. In addition, increased LV ejection index (ie, >1.13) is strongly associated with reduced long-term survival and markedly increased risk of cardiac death, independently of symptom, comorbidity, and LV parameters currently used in guidelines (ie, LV ejection fraction and LV end-systolic diameter). Consequently, LV ejection index may be used as an accurate complementary parameter to stratify the risk and guide decision making in patients with primary MR. Prospective large study is, however, required to confirm these findings.

Disclosures

None.

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CLINICAL PERSPECTIVE

The use of left ventricular (LV) dysfunction/dilatation as a trigger for surgery in patients with primary mitral regurgitation (MR) remains subject to obvious limitations. There is a profound need to identify complementary parameter assessing the consequences of MR on the ventricle. In a retrospective analysis of 278 patients who underwent mitral valve repair, we identified that preoperative LV ejection index, a new and simple composite parameter of both LV dilatation and forward flow, was able to accurately predict postoperative LV dysfunction and, when markedly elevated (ie, >1.13), was associated with increased risk of overall and cardiac-related death, independently of symptom, comorbidity, and LV parameters currently used in guidelines. The LV ejection index is easy and rapid to obtain and is the ratio of the indexed LV end-systolic diameter divided by the LV outflow tract time–velocity integral. With MR worsening and/or LV contractility impairment, the LV outflow tract time–velocity integral may decrease. In parallel, chronic MR progressively leads to LV dilatation. Together, these harmful consequences of MR will be highlighted by a marked increase in LV ejection index. Consequently, in addition to classical LV parameters, LV ejection index should be systematically calculated in patients with primary MR to comprehensively assess LV function and to help risk stratification. Furthermore, when considering early surgery in these patients, the LV ejection index may be useful in decision making by unmasking a subset of patients with higher risk of postoperative LV dysfunction and reduced survival than conventionally identified.

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Supplemental Material

Figure 1. Receiver operative characteristics curves analysis to predict postoperative LV dysfunction