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Incremental value of global longitudinal strain for predicting early outcome after cardiac surgery

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Aims Global longitudinal strain (GLS) seems accurate for detecting subclinical myocardial dysfunction, and may therefore be used to improve risk stratification for cardiac surgery.

Methods and results Longitudinal strain (by two-dimensional speckle tracking) was computed in 425 patients [mean age 67 ± 13 years, 69% male, left ventricular ejection fraction (LVEF) 51 ± 13%] referred for cardiac surgery [isolated coronary artery bypass graft (CABG) ($n = 155$), aortic valve surgery ($n = 174$), mitral surgery ($n = 96$)]. GLS (global-ε) was assessed for predicting early postoperative death. Despite a fair correlation between LVEF and global strain ($r = -0.73$, $P < 0.0001$), 40% of patients with preserved LVEF (defined as LVEF ≥50%) had abnormal global-ε (defined as global-ε > −16%): −12.8 ± 1.7%, range −15% to −8%. In patients with preserved LVEF, NT-proBNP level (983 vs. 541 pg/mL, $P = 0.03$), heart failure symptoms (NYHA class, 2.2 ± 0.9 vs. 1.9 ± 0.9, $P = 0.02$), and the need for prolonged (>48 h) inotropic support after surgery (33.3 vs. 21.2%, $P = 0.03$) were greater when global-ε was impaired. Importantly, despite similar EuroSCORE (9.7 ± 12 vs. 7.7 ± 9%, $P = 0.2$ for EuroSCORE I and 4.2 ± 6.2 vs. 3.4 ± 4.9%, $P = 0.4$ for EuroSCORE II), the rate of postoperative death was 2.4-fold (11.8 vs. 4.9%, $P = 0.04$) in patients with preserved LVEF when global-ε was impaired. Multivariate analysis showed that global-ε is an independent predictor for early postoperative mortality [odds ratio = 1.10 (1.01–1.21)] after adjustment to EuroSCORE.

Conclusion GLS has an incremental value over LVEF for risk stratification in patients referred for cardiac surgery.

Keywords Strain • Speckle tracking • Outcome • Cardiac surgery

Introduction

Left ventricular (LV) systolic function is a powerful predictor of cardiovascular outcome,[1] and the severity of LV systolic dysfunction is a main determinant in the decision to refer patients for cardiac surgery. In daily practice, LV systolic function is mainly assessed by LV ejection fraction (LVEF) based on two-dimensional (2D) echocardiographic imaging.[2] The logistic EuroSCORE models include LVEF to stratify operative risk in patients scheduled for cardiac surgery.[3] However, the accuracy and reproducibility of LVEF measurement remains dependent on image quality and the operator's experience.[4] Recently, the assessment of myocardial longitudinal function by 2D speckle tracking has been proposed to overcome these issues. Speckle-tracking analysis allows the three components of myocardial deformation to be studied. Several studies have consistently reported that longitudinal strain by 2D speckle tracking may provide an accurate and reproducible measurement of regional and global LV contractility,[5] fairly correlated with sonomicrometric data and cardiac magnetic resonance imaging (MRI).[6] Previous studies have demonstrated the prognostic value of global longitudinal strain (GLS) measurements in the setting of valvular diseases[7–9] or heart failure patients.[10–12] The

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present study sought to assess the incremental value of GLS by 2D speckle tracking for predicting early postoperative death after cardiac surgery.

Methods

Study population

Among 464 patients who underwent cardiac surgery at our institution between January 2009 and January 2010, all consecutive patients referred for coronary artery bypass graft (CABG) or/and left heart valve surgery were screened. Patients referred for cardiac tumour resection, isolated tricuspid surgery, cardiac transplantation, or cardiac assistance were excluded. Finally, 425 patients with CABG or left heart valve surgery and a comprehensive and analysable preoperative echocardiography (GE Healthcare, Vingmed System 7, Horton, Norway) were included in the study. All patients provided informed consent before the investigations and the study was approved by our local ethics committee.

Echocardiography

Comprehensive echocardiography was performed before surgery using commercially available Vivid 7 systems (GE Vingmed, Horton, Norway), including standard 2D apical four-, two-, and three-chamber views (4C, 2C, 3C) digitally stored at a high frame rate (>50 frames/s, mean 74 ± 17). All measurements were preformed off-line on a dedicated workstation (EchoPAC, GE Healthcare) by experienced sonographers blinded to patient's outcome. LV volumes and LVEF were computed using the Simpson biplane method from 2C and 4C apical views. Longitudinal strain was computed using 2D-speckle-tracking analysis by automated function imaging (AFI). For strain processing, the peak of the R-wave on the electrocardiogram was used as the reference time point for end-diastole and segments with poor-quality tracking were manually discarded.[13] GLS was only computed from patients with >81% of segments adequately tracked (≥14 segments for a 16-segment model). Given the average value of −18.6 ± 0.1% for normal GLS, any value assessed by AFI > −16% was considered as impaired GLS.[14]

The logistic EuroSCORE I and II

EuroSCORE I includes: age; sex; presence/absence of chronic pulmonary disease, extracardiac arteriopathy, neurological dysfunction, previous cardiac surgery, renal dysfunction, active endocarditis, critical preoperative state, unstable angina, recent myocardial infarction, or pulmonary hypertension; thoracic aortic surgery, valve surgery, or post-infarction septal rupture; and LVEF (preserved, >50%; moderately impaired, 30–50%; or severely impaired, <30%).[3] EuroSCORE II includes : age; sex; renal impairment; presence/absence of chronic lung disease, extracardiac arteriopathy, poor mobility, previous cardiac surgery, active endocarditis, critical preoperative state, diabetes on insulin, unstable angina, recent myocardial infarction, or pulmonary hypertension (moderate, 30–55 mmHg; or severe, >55 mmHg); NYHA level; thoracic aortic surgery, number of valve procedure or isolated CABG, the urgency of intervention; and LVEF (good, >50%; moderate, 31–50%; poor, 21–30%; or very poor, <20%). Patient's outcome data were obtained from medical records, by direct patient interviews, or from the referring physician.

Statistical analysis

Continuous variables with a normal distribution are expressed as mean ± standard deviation (SD). Dichotomous data are expressed as percentages. To compare numerical data between two groups, paired and unpaired Student's *t*-tests were used as appropriate. Nominal variables were compared using either the χ^2 or the Fisher tests. Linear correlation was used to compare longitudinal global

Table 1 Baseline patient's characteristics

	All patients (*n* = 425)
Age (years)	67 ± 13
Gender, female [no. (%)]	134 (31)
Diabetes [no. (%)]	124 (29)
Hypertension [no. (%)]	261 (61)
Atrial fibrillation [no. (%)]	40 (9)
NYHA class III–IV [no. (%)]	148 (35)
NT-proBNP (pg/mL)	1038
Creatinine (μmol/L)	103 ± 72
Surgery [no. (%)]	
Cardiopulmonary bypass duration (min)	138 ± 76 (30–720)
Indications [no. (%)]	
Aortic stenosis	152 (36)
Aortic regurgitation	22 (5)
Mitral regurgitation	96 (23)
Isolated CAD	155 (36)
Strain	
Global strain (%)	−14 ± 4 (−3 to −24)
Global strain [no. (%)]	
> −7%	24 (6)
−7% to −15%	234 (55)
≤ −16%	167 (39)
EuroSCORE II (%)	
LVEF by Simpson's biplane (%)	51 ± 13
LVEF [no. (%)]	
<20%	6 (1)
21–30	22 (5)
31–50%	123 (29)
>50%	274 (64)
Diabetes on insulin [no. (%)]	40 (9)
Previous cardiac surgery [no. (%)]	45 (11)
Chronic lung disease [no. (%)]	30 (7)
Extracardiac arteriopathy [no. (%)]	83 (20)
Severe renal impairment [no. (%)]	102 (24)
Angina at rest [no. (%)]	9 (2)
Recent myocardial infarction [no. (%)]	64 (15)
Pulmonary hypertension >55 mmHg [no. (%)]	38 (9)
Critical preoperative state [no. (%)]	18 (4)
Emergency [no. (%)]	45 (11)
Active endocarditis [no. (%)]	21 (5)
Valve surgery [no. (%)]	278 (65)
Surgery on thoracic aorta [no. (%)]	25 (6)

Values are mean ± SD. NYHA, New York Heart Association; CABG, coronary artery bypass graft; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; LGS, longitudinal global strain; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

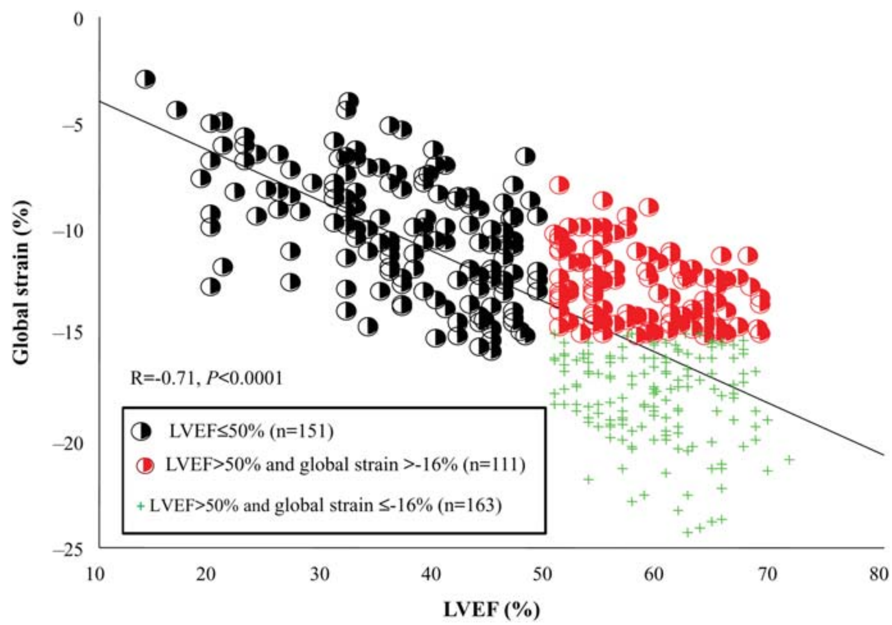

Figure 1 Correlation between LVEF and GLS assessed by 2D speckle tracking.

Table 2 Univariate predictors of death and the need for inotropic support

	Death (n = 36)	Survival (n = 389)	P-value	Inotropic support >48 h (n = 140)	No inotropic support (n = 285)	P-value
CPB duration (min)	186 ± 129	134 ± 68	<0.001	167 ± 94	123 ± 63	<0.001
Global Strain (%)	−12 ± 4%	−14 ± 4	0.006	−12 ± 4	−15 ± 4	<0.001
Nt-proBNP pg/mL (n = 299)	2757	934	<0.001	1469	797	<0.001
EuroSCORE I (%)	24 ± 23	9 ± 11	<0.001	15 ± 17	7 ± 8	<0.001
EuroSCORE II (%)	11 ± 13	4 ± 6	<0.001	7 ± 10	3 ± 5	<0.001
LVEF (%)	47 ± 14	52 ± 12	0.06	47 ± 14	54 ± 11	<0.001
<20%	3	1	0.04	1	1	<0.001
21–30%	14	4		9	3	
31–50%	22	29		38	24	
>50%	61	65		52	72	
Diabetes on insulin (%)	11	9	0.7	9	10	0.9
Previous cardiac surgery (%)	14	10	0.5	12	10	0.4
Chronic lung disease (%)	3	7	0.3	9	6	0.3
Extracardiac arteriopathy (%)	2	2	0.7	22	18	0.3
Severe renal impairment (%)	4	2	0.07	31	21	0.02
Angina at rest (%)	0	2	0.4	4	1	0.03
Recent myocardial infarction (%)	19	15	0.4	18	14	0.3
Pulmonary hypertension >55 mmHg (%)	17	8	0.09	9	8	0.7
Emergency (%)	22	9	0.01	18	7	<0.001
Active endocarditis (%)	14	4	0.01	7	4	0.1
Valve surgery (%)	81	64	0.04	73	61	0.02
Surgery on thoracic aorta (%)	17	5	0.004	7	5	0.5
Critical preoperative state (%)	17	3	<0.0001	11	1	<0.001

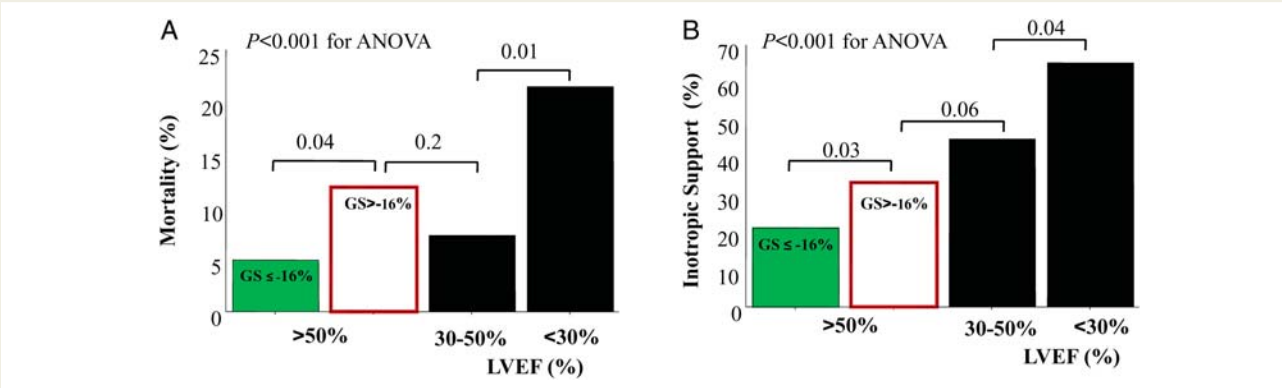

Figure 2 Postoperative outcome (*A* for mortality and *B* for the need for inotropic support >48 h) according to GLS and LVEF.

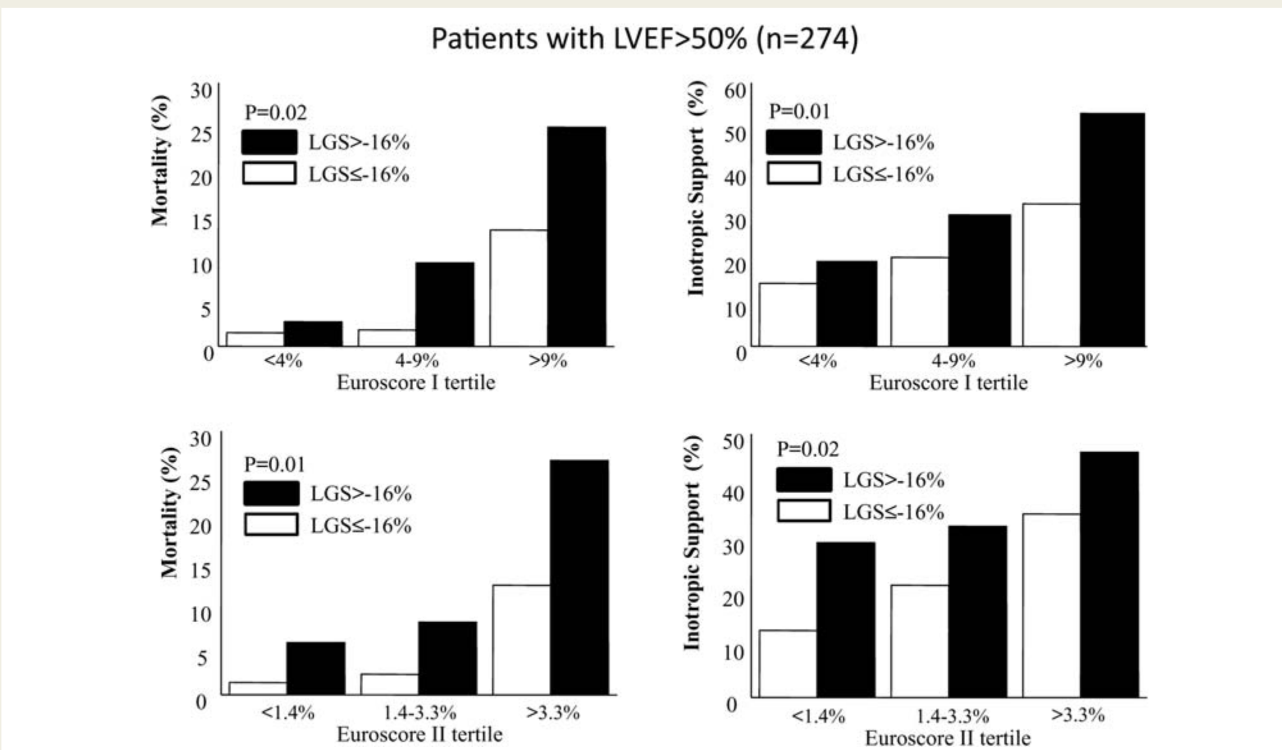

Figure 3 Incremental prognostic value of GLS adjusted to EuroSCORE II tertile (*A* for postoperative mortality and *B* for the need for inotropic support for >48 h).

strain with LVEF. The primary endpoint for analysis was in-hospital survival or 30-day postoperative survival among patients discharged from hospital.[3] The secondary endpoint was the need for prolonged inotropic support (>48 h) after cardiac surgery. Multivariable analysis included all variables for which the *P*-value from univariate analysis was <0.05. The incremental value of risk factors (global, EuroSCORE, and cardiopulmonary bypass duration) was assessed by comparing global χ^2 of the logistic model**.** Reproducibility for global strain and LVEF was assessed in 20 random patients, and expressed as the mean ratio of the difference over paired measurements. Two-tailed *P*-values of <0.05 were considered statistically significant.

Results

Study patients

Baseline characteristics of the whole group ($n = 425$ patients, mean age: 67 ± 13 years, 69% male) are shown in *Table 1*. Aortic valve surgery was performed in 174 patients [aortic stenosis ($n = 152$), aortic regurgitation ($n = 22$)]. Of these 174 patients, CABG was required in 59 patients and tricuspid ring annuloplasty was added in 6 patients. Mitral valve surgery for mitral regurgitation was performed in 96 patients (49% repaired) with associated tricuspid annuloplasty or CABG in 30 and 5 patients, respectively. Among patients with valve surgery, combined aortic and mitral valve intervention was performed in six patients. Isolated CABG was performed in 155 patients.

Preoperative longitudinal strain and LVEF

Ejection fraction averaged 51 ± 13% (range, 14–72%); LVEF was preserved (>50%) in 274 patients, it was moderately impaired (30–50%) in 123 patients, and severely depressed (<30%) in 28 patients. Overall, only 36 (8%) patients had one or two segments not analysable. Global strain was fairly correlated with LVEF ($r = -0.71$, $P < 0.0001$; *Figure 1*). However, among 274 patients with preserved LVEF, GLS was impaired in 111 (40.5%, *Figure 1*) cases (mean GLS = −13.8 ± 4.2%). Among patients with preserved LVEF, impaired GLS was observed in 53% of patients referred for aortic stenosis (53/99) vs. 38% of patients referred for CABG (33/87) and 27% of patients with mitral regurgitation (20/75, $P = 0.0002$ for inter-group comparison, see Supplementary data online, *Figure S1*). Despite similar EuroSCORE (9.7 ± 12 vs. 7.7 ± 9%, $P = 0.2$ for EuroSCORE-I and 4.2 ± 6.2 vs. 3.4 ± 4.9%, $P = 0.4$ for EuroSCORE-II), patients with preserved LVEF but impaired GLS had greater BNP serum levels (median value, 1025 vs. 503 pg/mL, $P = 0.01$) and more severe heart failure symptoms (NYHA functional class, 2.2 ± 0.9 vs. 1.9 ± 0.9, $P = 0.03$).

Postoperative outcomes

Postoperative death occurred in 36 patients (8.5%) and was mainly caused by refractory heart failure (57%). Death was more frequent if prolonged inotropic support was required (17.3 vs. 4.0%, $P < 0.0001$), or when LVEF was impaired (*Table 2*). Postoperative deaths were higher in patients with LVEF<30% (21%), when compared with those with LVEF ≥30% (21.4 vs. 7.6%, $P = 0.01$). There was no significant difference in the rate of postoperative deaths between patients with a 30–50% LVEF and those with LVEF >50% (7.3 vs. 7.7%). Interestingly, in patients with LVEF >50%, early postoperative mortality [odds ratio (OR) = 2.4, 11.8 vs. 4.9%, $P = 0.04$, *Figure 2*] and the need for prolonged inotropic support (OR = 1.6, 33 vs. 21%, $P = 0.03$, *Figure 2*) were greater if GLS was impaired, even after adjustment to EuroSCORE I and II (*Figure 3*). Finally, multivariate analysis demonstrated that GLS contributed to improve the accuracy of both logistic models for predicting early postoperative death [OR = 1.10 (95% confidence interval = 1.01–1.21)], the need for inotropic support or the combined endpoint of death, or the need for prolonged inotropic support (*Tables 3 and 4*). The incremental value of global strain for predicting early post-operative outcome is reported in *Figure 4*. The incremental value for predicting the combined endpoint defined by death and the need for prolonged inotropic support remained significant in all subgroup analysis (*Figure 5*).

Reproducibility of echocardiographic measurements

Intra- and inter-observer reproducibility averaged 3 and 6%, respectively, for global strain; and 7 and 12%, respectively, for LVEF by the Simpson biplane method.

Table 3 Independent predictors of post-operative outcome with EuroSCORE I

	OR	95% CI	*P*-value
Inotrope support>48 h			
Global strain (per %)	1.15	1.08–1.21	<0.001
CPB duration (per 30 min)	1.22	1.11–1.34	<0.001
EuroSCORE (per %)	1.04	1.02–1.07	<0.001
Mortality			
Global strain (per %)	1.10	1.01–1.21	0.03
CPB duration (per 30 min)	1.16	1.02–1.31	0.02
EuroSCORE (per %)	1.04	1.02–1.06	<0.001
Mortality + inotrope support >48 h			
Global strain (per %)	1.15	1.09–1.21	<0.001
CPB duration (per 30 min)	1.24	1.13–1.37	<0.001
EuroSCORE (per %)	1.05	1.02–1.07	<0.001

OR, odds ratio; CI, confidence interval.

Table 4 Independent predictors of post-operative outcome with EuroSCORE II

	OR	95% CI	*P*-value
Inotrope support>48 h			
Global strain (per %)	1.15	1.08–1.21	<0.001
CPB duration (per 30 min)	1.23	1.12–1.35	<0.001
EuroSCORE (per %)	1.07	1.02–1.11	0.002
Mortality			
Global strain (per %)	1.10	1.01–1.21	0.03
CPB duration (per 30 min)	1.17	1.04–1.32	0.009
EuroSCORE (per %)	1.07	1.03–1.11	0.001
Mortality + inotrope support >48 h			
Global strain (per %)	1.15	1.09–1.21	<0.001
CPB duration (per 30 min)	1.26	1.14–1.39	<0.001
EuroSCORE II (per %)	1.07	1.02–1.12	0.002

OR, odds ratio; CI, confidence interval.

Discussion

The assessment of LV myocardial function plays an important role in predicting mortality and complications after cardiac surgery.[3,15,16] The main result of our study is that myocardial longitudinal strain may improve risk stratification obtained by EuroSCORE, when compared with LVEF.

In daily practice, LVEF by 2D echocardiography is used to assess LV systolic function. However, this approach may be limited by operator experience and image quality, which impacts greatly on LVEF accuracy and reproducibility.[4] Accurate endocardial border delineation may be challenging in numerous patients because one or more segments of lateral or anterior wall cannot be adequately visualized. This may be overcome by extrapolating the tracing or the use of a foreshortened apical view that might lead to

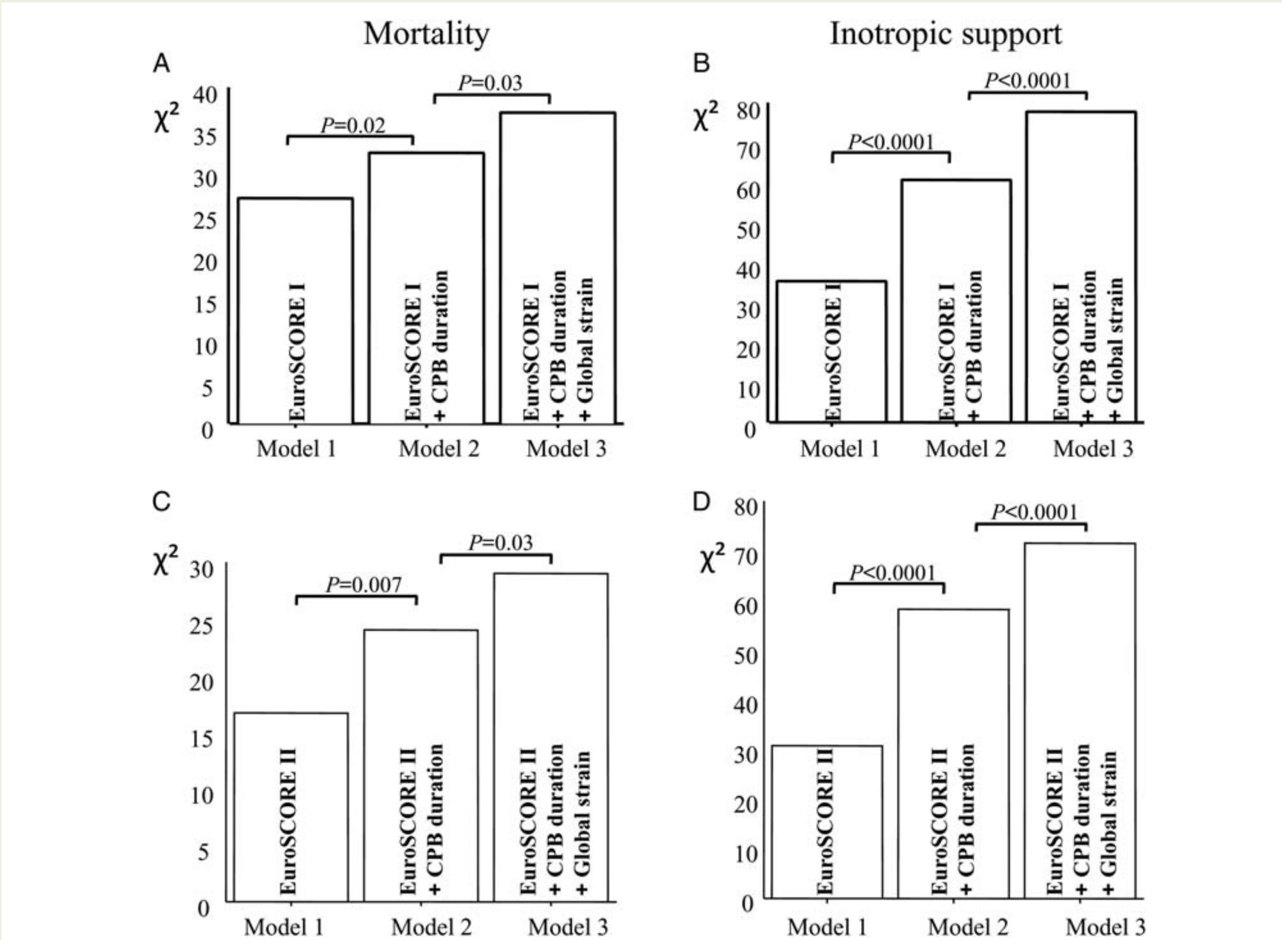

Figure 4 Incremental prognostic value of risk factor (global strain, EuroSCORE, and cardiopulmonary bypass duration) by logistic regression model presented as global χ^2 value.

underestimated LV volumes or overestimated LVEF. Recently, Macron *et al.*[17] demonstrated that GLS assessed by 2D speckle tracking is better correlated with LVEF assessed by MRI than LVEF assessed by echocardiography in patients with a poor acoustic window, probably because speckle-tracking imaging is less influenced by the quality of acoustic windows. The accuracy and reproducibility of GLS measurements, regardless of image quality, may be explained by the use of the whole stack of images for 2D speckle-tracking analysis and by the fact that endocardium–blood interface is less crucial for longitudinal strain analysis. In addition, GLS computed from the 16 segments of the myocardium may provide a more global and accurate assessment of myocardial function than the Simpson biplane model, which only includes 12 segments.

Unlike LVEF, the assessment of myocardial function by speckle tracking is not based on the measurement of LV volume changes, and thus does not rely on a geometric model that is unsuitable for patients with complex LV deformation. Indeed, this advantage of speckle tracking over the Simpson method has been demonstrated by Brown *et al.*[18] who reported that in patients with more than five abnormal contractile segments, GLS by 2D speckle tracking is better correlated with LVEF by MRI than LVEF derived from 2D echocardiography. However, GLS should not be assimilated to LVEF, because longitudinal myocardial deformation is mainly driven by the endocardial layers. This discrepancy is crucial because impaired myocardial contractility in several cardiac diseases seems to affect the endocardial layers first. This may explain the incremental value of GLS over LVEF for detecting early changes in myocardial function and for predicting cardiovascular outcome. Indeed, several studies have demonstrated that impaired GLS provides additional value in predicting outcome in chronic heart failure patients and in patients with ischaemic cardiac disease.[10–12,19–21] Longitudinal function seems to be a sensitive marker for the identification of subclinical deterioration of LV function in patients with asymptomatic valvular diseases. Lafitte *et al.*[7] demonstrated that in asymptomatic patients with severe aortic stenosis ($n = 65$), impaired GLS (reported in 57–64% of patients) was associated with abnormal exercise testing and with an increased risk of cardiac events during the follow-up. These data support our results, which show that early post-operative mortality may be increased by a factor 2.4 in patients with impaired GLS, despite preserved LVEF. This is in agreement with accumulating data demonstrating that asymptomatic patients

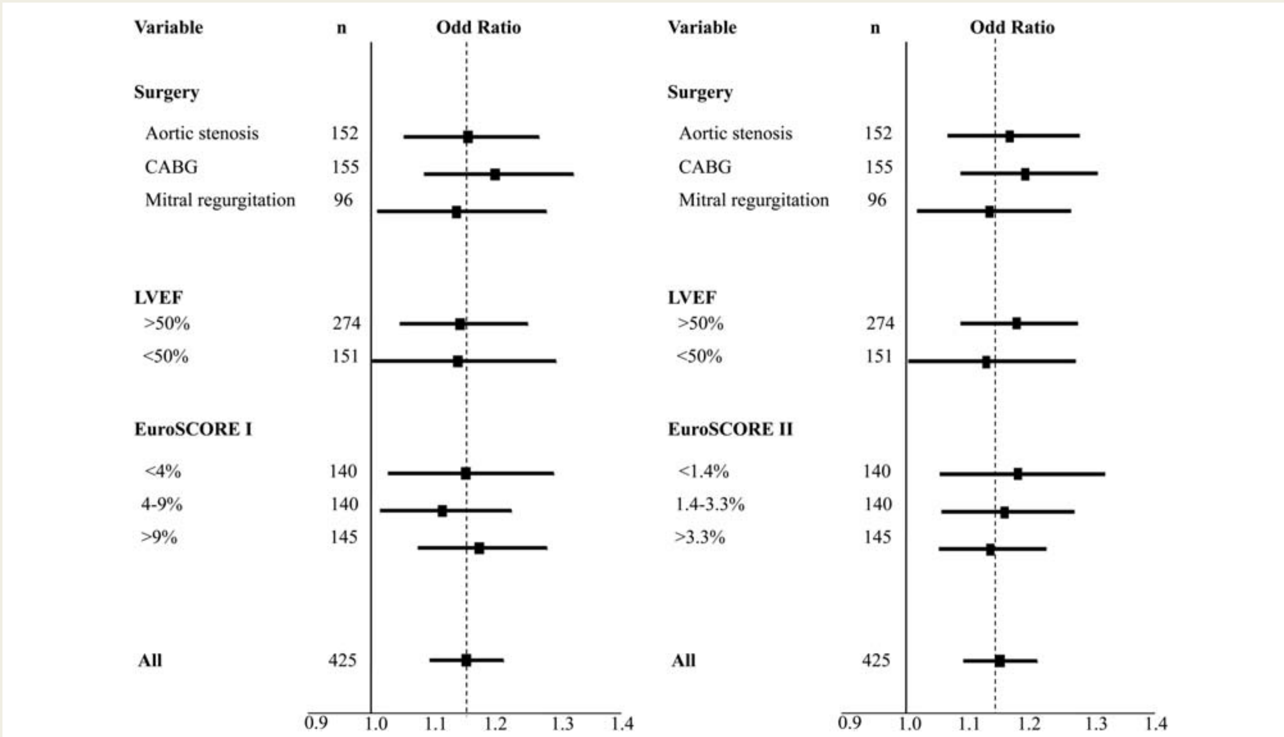

Figure 5 OR according to subgroup analysis; LVEF, left ventricular ejection fraction.

with preserved LVEF should benefit from early surgery when or before impaired global strain. This underlines the need for future study evaluating the exact timing of early surgery in this setting, especially in valvular diseases. We also believe that the assessment of longitudinal strain before cardiac surgery may contribute to improve the risk stratification of patients referred for left-sided cardiac surgery. The accurate assessment of the postoperative risk may lead to consider alternative treatment (i.e. transcatheter valve implantation in the setting of aortic stenosis) or to modify surgical strategy that should aim to reduce cardiopulmonary bypass duration.

A limitation of this study is heterogeneity and the limited sample size of the population study that prevents an accurate assessment of the optimal cut-off value for GLS in each type of surgery. To overcome this limitation, we used global strain as a continuous value in the multivariate analysis. In addition, strain data in this study were only computed from GE software and results cannot be extended to other systems, since differences in strain value may exist between different vendors.

In conclusion, GLS assessed by 2D speckle tracking has incremental value over LVEF for risk stratification in patients referred to cardiac surgery. Among patients with preserved LVEF, GLS enables further risk stratification for the risk of early postoperative death or prolonged inotropic support after left-sided cardiac surgery.

Supplementary data

Supplementary data are available at *European Heart Journal – Cardiovascular Imaging* online.

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IMAGE FOCUS

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Multimodality imaging of cardiac tumour

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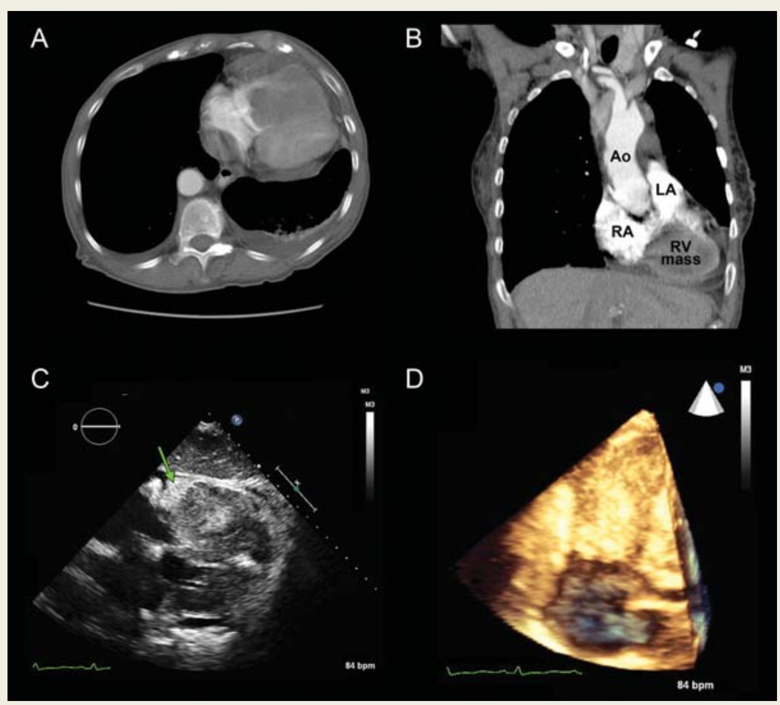

A 76-year-old woman with a history of poorly differentiated spindle cell carcinoma of the right iliac bone presented with worsening hip pain. Computed tomography of the chest, abdomen, and pelvis revealed a soft tissue mass within the right ventricle measuring ~5.8 × 3.5 cm (*Panels A* and *B*) and moderate pericardial thickening (*Panel A*). An echocardiogram confirmed the diagnosis of a large right ventricular (RV) mass and pericardium with heterogeneous features (*Panel C*, see Supplementary online data, *Video S1*), which was enhanced with agitated saline (see Supplementary online data, *Video S2*). Three-dimensional echocardiographic imaging reaffirmed the presence of the tumour filling the entire right ventricle (*Panel D*, see Supplementary online data, *Video S3*). Given the metastatic nature of her disease, a palliative approach was chosen.

Metastatic heart tumours are more common than primary tumours and usually represent a poor prognosis. Myocardial metastases, which are less frequent, are usually associated with melanoma or lymphoma but rarely have been reported from spindle cell carcinoma. Ao, aorta; LA, left atrium; RA, right atrium.

Supplementary data are available at *European Heart Journal – Cardiovascular Imaging* online.

Conflict of interest: none declared.