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iCONCEPTS

CONCEPTS ON THE VERGE OF TRANSLATION

Normalized End-Systolic Volume and Pre-Load Reserve Predict Ventricular Dysfunction Following Surgery for Aortic Regurgitation Independent of Body Size

Thomas L. Gentles, FRACP,* John K. French, MB, PhD,†‡ Irene Zeng, MSc,†
Paget F. Milsom, FRACS,§ A. Kirsten Finucane, FRACS,* Nigel J. Wilson, FRACP*
Auckland, New Zealand; and Sydney, New South Wales, Australia

Pre-operative end-systolic volume (ESV) is predictive of outcome after surgery for severe aortic regurgitation. ESV is influenced by body size and reflects function and afterload, but not pre-load. Left ventricular (LV) chamber size and function were measured in 40 patients (ages 10 to 64 years) by echocardiography before and 7 months after operation and expressed as *z*-scores in addition to simple indexing. A functional pre-load index, a marker of pre-load reserve, was calculated. Independent risk factors for post-operative LV dysfunction included higher post-operative ESV *z*-score (odds ratio [OR]: 3.3, $p = 0.006$) and lower functional pre-load index (OR: 0.3, $p = 0.03$). ESV per square meter had similar power to the ESV *z*-score. The ESV uncorrected for body size underestimated risk in smaller patients and overestimated risk in larger patients ($p < 0.002$). Pre-load reserve is an independent risk factor for LV dysfunction after aortic valve surgery in patients with severe aortic regurgitation. Failure to correct ESV for body size introduces systematic bias to risk assessment. (J Am Coll Cardiol Img 2012;5:626–33) © 2012 by the American College of Cardiology Foundation

Progressive left ventricular (LV) dilation and systolic dysfunction occur in the context of chronic severe aortic regurgitation (AR). Contractile dysfunction can present in the absence of symptoms, may persist despite valve replacement or repair, and carries a long-term risk of congestive heart failure and premature death (1).

Outcome after surgery for AR relates to pre-operative symptomatic status, the magnitude of regurgitation, and LV geometric and mechanical characteristics. The more robust of the latter include ejection fraction (EF), shortening fraction (SF), and end-systolic dimension (ESD) or volume (ESV). Afterload may also have an impact on post-operative outcome,

From the *Green Lane Paediatric and Congenital Cardiac Service, Starship Children's Hospital, Auckland, New Zealand; †Cardiology Department, Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand; ‡Liverpool Hospital, Sydney, New South Wales, Australia; and the §Cardiothoracic Surgery, Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand. This work was supported by a Project Grant from the National Heart Foundation of New Zealand, and salary (to Dr. Zeng) and secretarial support from the Green Lane Research and Education Fund. The authors have reported that they have no relationships relevant to the contents of this paper to disclose. Dr. Zeng currently works at the Center of Clinical Research and Effective Practice, Middlemore Hospital, Auckland, New Zealand.

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but the relationship between pre-load and outcome has not been assessed. Pre-load recruitment maintains LV function in the face of increasing afterload (2). In the severely dilated LV, pre-load recruitment may be limited by biomechanical constraints, restricting the capacity of the LV to accommodate progressive increases in afterload (2).

Guidelines for the timing of aortic valve surgery, developed on the basis of symptoms, LV end-systolic (ES) chamber size, and function have been validated in adult patients (3). There are few data to guide the timing of surgery in childhood. Moreover, women are more likely to present for surgery at a later stage in the disease process with a higher incidence of symptoms and a worse post-operative outcome than are men, despite having similar pre-operative LV size. In these groups, delaying surgery until standard adult male-based criteria are met may increase the risk of late LV dysfunction. Indexing volume (or dimension) to body surface area has been proposed as a solution to this problem (4). However, the relationship between body size and LV size is nonlinear and heteroscedastic (i.e., confidence intervals increase with increasing body size), so that simple indexing may increase rather than decrease body size–related variability.

In children, measures of cardiac size are typically expressed as z-scores that quantify the measured parameter in terms of its relationship to the expected range at a given body size in a normal population. Normalizing cardiac size in this way accounts for both nonlinearity and heteroscedasticity, and may be superior to simple linear indexing.

We sought to assess risk factors for poor outcome of the LV using z-scores to normalize cardiac chamber size to body size in addition to simple indexing in a patient population with a wide range of ages and body sizes. We also sought to assess the influence of pre-load on outcome, using a functional pre-load index (FPI), a measure of the relationship between a relatively pre-load–independent index of shortening (the mean velocity of shortening [VCFc]) and a pre-load dependent index (SF) (5) (Online Appendix).

Methods

Study population. The study population consisted of 40 patients with isolated severe AR who underwent aortic valve replacement. Subjects were recruited after they had been recommended for surgery based on standard clinical criteria consisting of symptoms and/or LV dysfunction in 29 and an end-diastolic dimension (EDD) >7 cm and/or an ESD >5 cm in 7 of the remaining 11. Those not in sinus rhythm were excluded. None had acute rheumatic fever. All had undergone pre-operative clinical assessment and echocardiography including phonography and indirect carotid pulse measurement. All had severe isolated AR as defined by a regurgitant jet width ≥65% of the LV outflow tract in association with holodiastolic flow reversal in the abdominal descending aorta. None had an aortic valve velocity ≥2.5 m/s, or more than mild mitral regurgitation or stenosis. A post-operative clinical assessment and echocardiogram were undertaken 6 to 12 months following operation. A normal population ($n = 158$, age range 6 to 62 years, 89 (56%) men, body surface area 1.6 ± 0.4 m^2, body mass index 22 ± 4.4 kg/m^2) was recruited for comparative purposes. None of the normal population had a history of cardiovascular disease or other chronic illness, and all had a normal cardiovascular examination including blood pressure measurement and a normal echocardiogram. The study was approved by the relevant ethical standards committee, and informed consent was obtained from patients, normal subjects, or their parents.

Echocardiogram measurements. Pre-operative variables recorded included short-axis dimensions, mass, ES fiber stress, sphericity, ejection time, and the pre-ejection period. The VCFc was calculated as SF/rate-corrected ejection time. LV volume was derived from 2-dimensional images using the area-length algorithm. In addition to simple indexing, LV size and function variables were expressed as z-scores in

ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation
CI = confidence interval
EDD = end-diastolic dimension
EDV = end-diastolic volume
EF = ejection fraction
ES = end-systolic
ESD = end-systolic dimension
ESV = end-systolic volume
FPI = functional pre-load index
LV = left ventricle
NYHA = New York Heart Association
OR = odds ratio
SF = shortening fraction
VCFc = rate-corrected mean velocity of circumferential fiber shortening

Table 1. Demographic and Clinical Characteristics

	Aortic Regurgitation (n = 40)
Age, yrs	35 (10–64)
Female	9 (23)
BSA, m^2	2.0 (1.2–2.4)
NYHA functional class 1/2/3/4	14 (35)/17 (43)/8 (20)/1 (2)
ACE inhibitor	27 (68)
Diuretic	14 (35)
Digoxin	6 (15)
RHD	24 (60)
CAD	1 (2)

Values are median, (range), or n (%).
ACE = angiotensin-converting enzyme; BSA = body surface area; CAD = coronary artery disease requiring coronary artery bypass grafting; NYHA = New York Heart Association; RHD = rheumatic heart disease.

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Table 2. Pre-Operative and Post-Operative LV Size and Function

	Pre-Operative	Post-Operative
EDV, ml	350 ± 88	188 ± 60*
Indexed EDV, ml/m²	178 ± 37	93 ± 25*
EDV, *z*-score	5.5 ± 1.2	1.5 ± 1.7*
ESV, ml	153 ± 53	86 ± 36*
Indexed ESV, ml/m²	78 ± 23	44 ± 16*
ESV, *z*-score	5.1 ± 1.4	2.0 ± 1.8*
EF, %	56 ± 8	55 ± 8
EF, *z*-score	−1.5 ± 2.1	−1.8 ± 1.8

Values are mean ± SD. *p < 0.001 compared with pre-operative measure.
EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; LV = left ventricular.

relation to body surface area (LV size) or age (LV function and fiber stress) with respect to the normal population (Online Appendix). The FPI was calculated as the difference between the SF *z*-score (pre-load dependent) and the VCFc *z*-score (pre-load independent) in order to estimate the contribution of pre-load to shortening (Online Appendix). The stress-velocity index was calculated as a *z*-score expressing VCFc adjusted for afterload (ES fiber stress). At the post-operative assessment, LV volume was measured using the same technique described previously. The primary endpoint was an abnormal EF at the post-operative assessment. As EF declines with age, an abnormal EF was defined as a measurement more than 2 SDs below the normal population mean for the given age. The lower limit of normal (*z*-score −2.0) was 56.7% for a 10-year-old and 52% for a 65-year-old.

Table 3. Comparison of Echocardiographic Parameters Between Patients With Impaired and Normal Post-Operative LV Function

Pre-Operative Variable	Impaired Post-Operative LV Function (n = 14)	Normal Post-Operative LV Function (n = 26)	Correlation Coefficient (vs. Post-Operative EF *Z*-Score)
EDD*z*	5.4 ± 1.4	4.7 ± 1.1	−0.237
ESD*z*	5.1 ± 1.1	4.0 ± 0.9*	−0.420*
SF*z*	−2.4 ± 1.5	−1.2 ± 1.6†	0.314†
EDth/D*z*	−0.9 ± 1.4	−0.4 ± 1.4	0.303
Mass*z*	4.5 ± 1.6	4.4 ± 1.6	0.113
VCFc*z*	−3.0 ± 1.5	−2.5 ± 1.2	0.132
ESFS*z*	2.7 ± 1.7	1.6 ± 1.6	−0.412†
SVI	−1.7 ± 1.4	−1.7 ± 1.1	0.177
FPI	0.5 ± 0.8	1.3 ± 0.7*	0.426*
ETc, ms	350 ± 31	374 ± 28†	0.380†
PEP, ms	81 ± 33	58 ± 20†	−0.413*
PEP/ET	0.26 ± 0.12	0.17 ± 0.07*	−0.434*
Sphericity	0.71 ± 0.07	0.70 ± 0.07	−0.095
EDV*z*	6.1 ± 1.1	5.2 ± 1.4†	−0.256
Indexed EDV, ml/m²	195 ± 39	169 ± 33†	−0.263
ESV*z*	6.1 ± 1.2	4.5 ± 1.1*	−0.506*
Indexed ESV, ml/m²	95 ± 23	68 ± 13*	−0.512*
EF*z*	−2.8 ± 2.3	−0.8 ± 1.6*	0.491*
ESV*z*/EF	12.7 ± 4.3	7.8 ± 2.4*	−0.560*

Values are mean ± SD. *p < 0.01 for categorical analysis (impaired vs. normal post-operative LV function), or continuous (regression) analysis; †p < 0.05.
EDD = end-diastolic dimension; EDth/D = end-diastolic wall thickness/dimension ratio; ESD = end-systolic dimension; ESFSc = end-systolic circumferential fiber stress; ETc = rate-corrected ejection time; FPI = functional pre-load index (see text for details); PEP = pre-ejection period; SF = shortening fraction; VCFc = rate-corrected mean velocity of circumferential fiber shortening; SVI = stress-velocity index; *z* = *z*-score (see text for details); other abbreviations as in Table 2.

Statistical analysis. Summary statistics are expressed as mean ± SD, or in the case of skewed distribution, as median and range. As the *z*-score records the number of SD a measurement is from the normal population mean, the normal population has a mean *z*-score of 0 ± 1. The Student *t* test was used for between-group comparisons of continuous measurements. Relationships between continuous variables were explored with linear regression. Dichotomous variables were compared using the Fisher exact test. Univariate logistic regression was applied to investigate the association between demographic, clinical, and echocardiographic variables and the primary endpoint (EF *z*-score <−2). Variables with p value <0.20 were entered into multiple logistic regression models. The best subset method was used to select the final model where Akaike information criterion was minimized and area under receiver-operating characteristic curve was maximized. Independency between variables in the model was checked by correlation coefficients. Two-sided tests were used and a p value <0.05 was considered significant. SAS version 9.1, (SAS Institute, Cary, North Carolina) and R version 2.1.1 (R Foundation for Statistical Computing, Vienna, Austria) was used in all analyses.

Results

Pre-operative assessment. Demographic and clinical characteristics are detailed in Table 1. Eleven patients were less than 20 years of age, and 10 had body surface areas <1.8 m². Rheumatic heart disease was the predominate etiology (60%), and coronary artery disease was present in only 1 patient, who had concomitant coronary artery bypass grafting.

Pre-operative LV mechanics were characterized by severe dilation (EDV *z*-score 5.5 ± 1.2 vs. normal population 0 ± 1, p < 0.0001), increased mass (*z*-score 4.4 ± 1.3, p < 0.0001), increased afterload (ES fiber stress *z*-score 2.0 ± 1.7, p < 0.0001), increased FPI (1.0 ± 0.8, p < 0.0001), decreased LV function (EF z-score −1.5 ± 2.1, p = 0.0001), and decreased contractile function (stress-velocity index −1.7 ± 1.2, p < 0.0001).

Post-operative assessment. Subjects were reviewed 7 ± 2 months after aortic valve surgery. New York Heart Association (NYHA) functional class improved compared with the pre-operative status in 24 (60%) subjects and was unchanged in the remaining 16, of whom 14 were in NYHA functional class I prior to surgery. All were in sinus rhythm. Cardiac medications included an angiotensin-converting enzyme inhibitor in 15 (38%) subjects, diuretic in 7 (18%), and an antiarrhythmic agent in 1 (3%). There was a significant decrease in EDV and ESV, with no change in EF overall (Table 2). LV dysfunction (EF z-score <−2) was evident in 14 (35%) subjects, 9 (23%) of whom had an EF z-score <−3.

Pre-operative determinants of impaired post-operative function. Pre-operative factors associated with post-operative LV dysfunction by univariate analysis included z-scores for ESD and ESV, SF and EF, indexed ESV (ESV/body surface area), and the ratio of the ESV z-score to EF (Table 3). Of those with post-operative LV dysfunction, 13 of 14 subjects had an ESV z-score >4.5 or an indexed ESV >65 ml/m^2, compared with 12 of 26 of those without (p = 0.004, sensitivity 93%, specificity 54%) (Fig. 1). There was a significant correlation between pre- and post-operative EF (r = 0.49, p = 0.001) (Fig. 2). Nevertheless, in those with normal LV function before surgery, LV dysfunction was present at follow-up in 5 of 27 (18.5%) subjects, 4 of whom had a pre-operative ESV z-score >4.5. In the subgroup who had no symptoms and normal LV function before surgery, 3 of 11 had LV dysfunction after operation, all 3 having a pre-operative ESV z-score >4.5. There was an overall improvement in EF at follow-up in those with LV dysfunction before surgery (change in EF z-score +1.6 ± 1.1). Although 10 of 13 subjects experienced an absolute improvement, post-operative function normalized in only 4 (30.8%).

A lower FPI was associated with post-operative LV dysfunction, as was a longer pre-ejection period, shorter ejection time, and lower pre-ejection period: ejection time ratio (Table 3). Similar associations were found when post-operative EF z-score was treated as a continuous variable (Table 3).

Sensitivity was similar for ESV z-score >4.5 and ESV index >65 ml/m^2, whereas current American Heart Association/American College of Cardiology guideline parameters (EDD ≥7.5 cm, ESD ≥5.5 cm, or EF ≤50%) (1) were less discriminatory (Table 4). Symptoms before surgery were poorly predictive of post-operative LV dysfunction (p = 0.2), and LV dysfunction was not related to pre-operative mass, sphericity, or to the thickness/dimension ratio, nor was it related to patient age, sex, etiology of the regurgitant lesion, or medication use before operation.

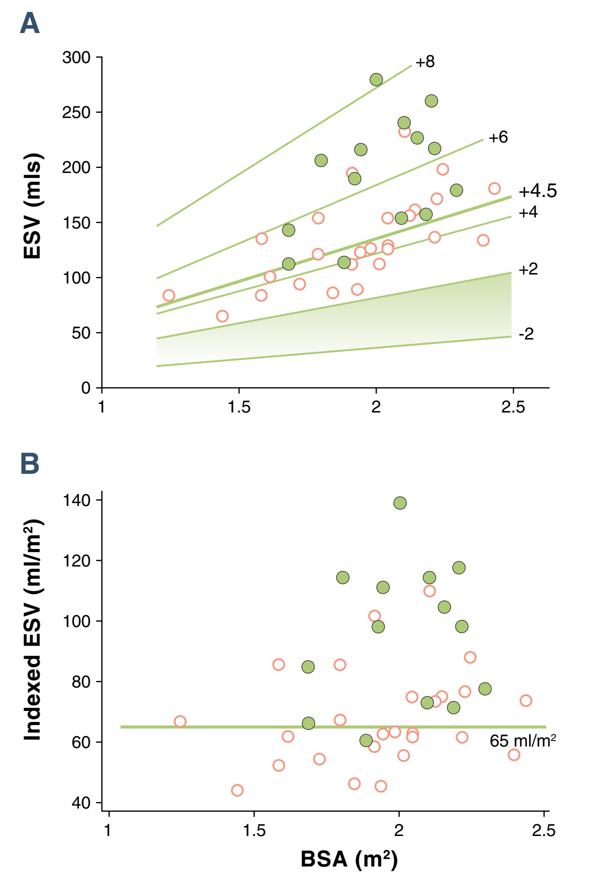

Figure 1. ESV Versus BSA

(A) The **lines** represent the z-score distribution with numbers indicating the number of SD above or below the normal population mean (see text for details). The **shaded area** defines the "expected" or normal values (z-score: −2 to +2). The **thicker line** is at the cutoff z-score (+4.5). **(B)** Indexed end-systolic volume (ESV) versus body surface area (BSA). The **horizontal line** indicates the cutoff (65 ml/m^2). **Green circles** = post-operative left ventricular (LV) dysfunction, **red circles** = no post-operative LV dysfunction.

Multiple logistic regression identified pre-operative ESV z-score (p = 0.006, odds ratio [OR]: 3.3, 95% confidence interval [CI]: 1.4 to 7.9) and FPI (p = 0.03, OR: 0.3, 95% CI: 0.08 to 0.9) to be independently associated with LV dysfunction after operation. The impact of alterations in FPI on risk through a range of ESV z-scores is illustrated in Figure 3. In order to identify parameters associated with minimal risk of post-operative LV dysfunction, models were developed using cutoffs that

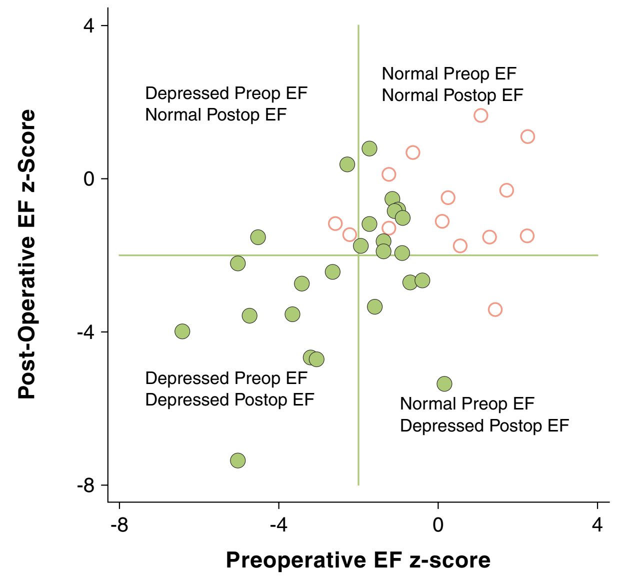

Figure 2. The Relationship Between Pre- and Post-Operative EF

The **vertical** and **horizontal lines** indicate a *z*-score of −2 for the pre-operative (preop) and post-operative (postop) ejection fraction (EF), respectively. **Green circles** indicate end-systolic volume (ESV) *z*-score >4.5, **red circles** indicate ESV *z*-score <4.5.

maximized sensitivity (Table 5). Receiver-operating characteristics were not statistically different between models. However, the ESV *z*-score FPI model had a higher specificity than the ESV *z*-score/EF ratio or the ESV *z*-score alone. Substituting the indexed ESV for the ESV *z*-score resulted in a model with similar specificity, whereas ESV uncorrected for body size was less strongly associated with post-operative LV dysfunction (Fig. 4). Interestingly, risk scores generated from models incorporating ESV uncorrected for body size were related to body surface area ($p < 0.0001$), as well as post-operative LV dysfunction, as were those using the indexed ESV, although to a lesser extent ($p = 0.02$). In both instances, a smaller body surface area was associated with a lower risk score and vice versa. Conversely, risk scores generated from the ESV *z*-score were independent of body surface area. Hence, ESV uncorrected for body size systematically underestimated risk in smaller patients and overestimated risk in larger patients, whereas indexed ESV had a similar, although less marked, bias. There was no relationship between risk scores and patient age or sex independent of outcome.

Discussion

This study demonstrates that LV dysfunction is common 7 months after surgery for chronic AR. Factors independently associated with post-operative LV dysfunction were ESV normalized to body surface area, and FPI, which is the difference between the normalized SF and mean velocity of shortening. The association between ESV and clinical outcome is well recognized and most probably reflects its relationship to both function and afterload. LV ESD was less strongly associated with outcome, likely reflecting the nonlinear relationship between short-axis dimension and volume in the dilated LV (5).

In addition to simple indexing, we normalized ESV to body surface area using methodology that accounted for the nonlinearity and heteroscedasticity inherent in the relationship between these variables. The 2 methods had similar predictive ability and were superior to ESV uncorrected for body size. The risk score generated from the latter was lower in smaller patients, and higher in larger patients despite outcome being unrelated to body size. This indicates a systematic misrepresentation of risk in both these patient groups. A similar but more subtle bias exists with the indexed ESV. Normalizing chamber size to body size using *z*-scores removes this bias, as is readily illustrated in the normal population (Fig. 5). However, the incremental value of *z*-scores over simple indexing was minor and of no clinical significance in this patient population. This most probably relates to the near-linear relationship between body size and cardiac chamber size over the range of body surface area studied.

To date, decision making around timing of surgery in younger and smaller patients has been hindered by a lack of age- or size-specific guidelines. In the current study, an ESV *z*-score <4.5, or an ESV index of <65 ml/m^2 carried a low risk of post-operative LV dysfunction. These ESV cutoffs predicted LV dysfunction with a greater degree of sensitivity than the cutoffs in the current American Heart Association/American

Table 4. Comparison With Conventional Measures

Pre-Operative Variable and Cutoff	n (%) of 14 With Post-Operative LV Dysfunction Predicted by Cutoff (Sensitivity)
Symptoms	6 (43)
EDD ≥7.5 cm	6 (43)
ESD ≥5.5 cm	7 (50)
EF ≤50%	8 (57)
EF *z*-score <−2	9 (64)
ESV index >65 ml/m^2	13 (93)
ESV *z*-score >4.5	13 (93)

Values are n (%). Cutoffs for EDD, ESD and EF as per American Heart Association/American College of Cardiology guidelines (1).
Abbreviations as in Tables 2 and 3.

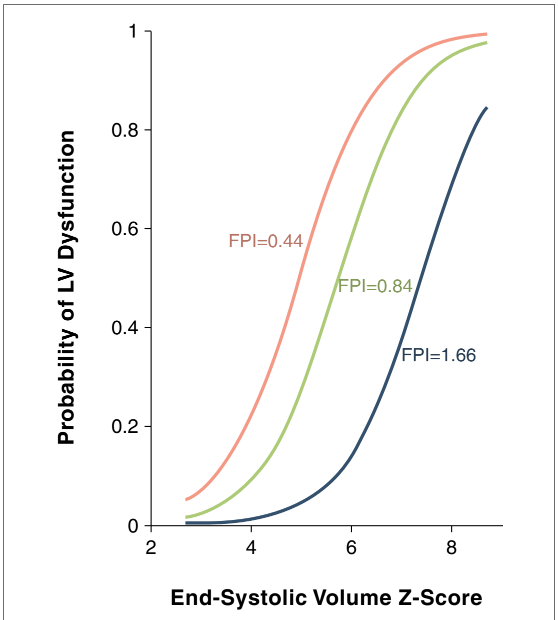

Figure 3. The Probability of Ventricular Dysfunction at Given Levels of Pre-Load According to the ES *Z*-Score

The plots are derived from the logistic regression equations in Table 4. ES = end-systolic; FPI = functional pre-load index.

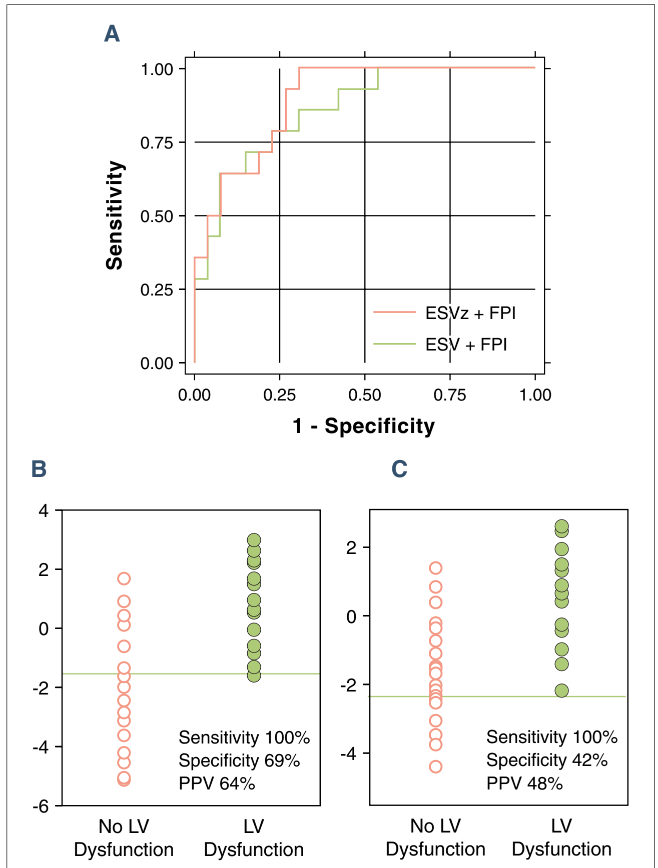

Figure 4. Prediction of LV Dysfunction After Surgery for Aortic Regurgitation

(A) Receiver-operating characteristics. **(B)** Risk scores for the ESVz + FPI. **(C)** Risk scores for ESV + FPI. **Green circles** = post-operative LV dysfunction. ESVz = pre-operative end-systolic volume *z*-score; other abbreviations as in Figures 1 and 3.

College of Cardiology guidelines (1) and, together with the risk score combining the FPI, represent an enhancement in the assessment of risk in smaller patients with severe AR.

The FPI was independently associated with LV dysfunction after operation. This finding can be explained within the conceptual framework of afterload mismatch and pre-load reserve (2). Elevated pre-load and afterload stimulate myocardial remodeling. Myofibers increase in length and width, thus normalizing end-diastolic and ES fiber stress. As the disease progresses, remodeling fails to normalize myofiber load. Afterload increases, and LV function is maintained through pre-load recruitment. Pre-load reserve is eventually exhausted, and progressive ventricular dysfunction ensues.

Quantification of pre-load is challenging. Simple noninvasive measures such as EDV are poorly representative of myofiber length, which is influenced by pressure and compliance at the chamber level, and by myocyte and interstitial remodeling. FPI does not measure pre-load directly, but ex-

Table 5. Comparison of Predictive Accuracy Across Different Models

Risk Score Equation	AUC	Risk Score Cutoff	Specificity	PPV
0.03 × ESV − 5.0	0.81 (0.66–0.95)	−2.00	27%	42%
0.07 × Indexed ESV − 6.0	0.82 (0.68–0.96)	−1.95	31%	44%
1.1 × ESVz − 6.6	0.83 (0.69–0.96)	−2.10	35%	45%
0.5 × ESVz/EF − 5.2	0.83 (0.69–0.97)	−2.12	27%	42%
0.025 × ESV − 1.05 × FPI − 3.7	0.86 (0.74–0.98)	−2.90	42%	48%
0.067 × Indexed ESV − 1.25 × FPI − 5.0	0.89 (0.79–0.99)	−1.7	65%	61%
1.2 × ESVz − 1.3 × FPI − 5.9	0.89 (0.80–0.99)	−1.44	69%	64%

Sensitivity and negative predictive value set at 100% for all models (see text for details).
AUC = area under receiver-operating characteristic curve; PPV = positive predictive value; other abbreviations as in Tables 2 and 3.

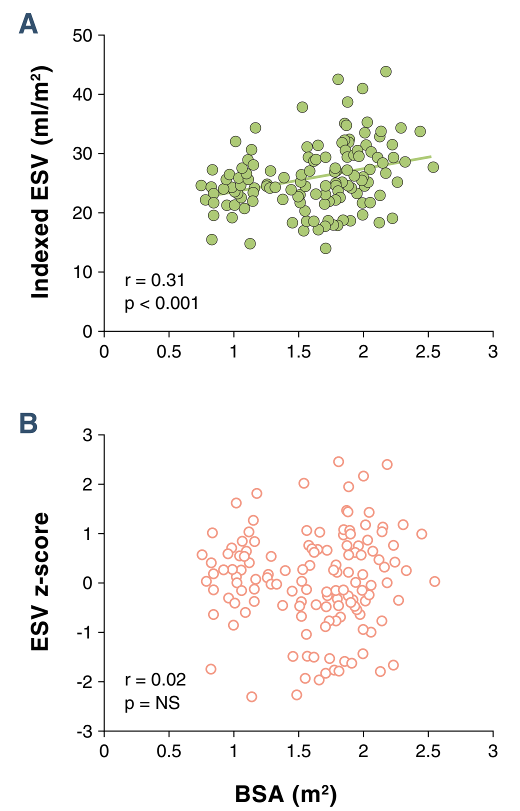

Figure 5. Normal Population: Relationship Between BSA and Normalized ESV

(A) BSA versus indexed ESV, and **(B)** versus ESV z-score. Abbreviations as in Figure 1.

presses the relative contribution of ejection time to shortening, on the understanding that SF is influenced by diastolic fiber length to a greater extent than is VCFc (5). FPI thus reflects the degree of shortening augmentation that relates to factors other than afterload and contractility. Validation of this index in the context of chronic volume load and ongoing remodeling is problematic. Regardless of the mechanism, post-operative recovery is less likely to occur once the LV is unable to augment function by further increasing ejection time. This is a recognized feature of the failing myocardium, as is prolongation of isovolumic contraction and an increasing pre-ejection period/ejection time ratio.

Symptoms were not associated with post-operative LV dysfunction. The high prevalence of younger patients in the current study may account for this lack of association, as severe AR is often well tolerated in children and young adults, despite significant LV dilation and borderline function. Importantly, absence of symptoms was not protective if the ESV *z*-score was >4.5 before surgery, even when function was normal. In the current series with relatively short follow-up, symptomatic status improved in all with NYHA functional class III or IV symptoms before surgery. However, the long-term prognosis is less certain, and those with LV dysfunction have an increased risk of death and cardiovascular events at late follow-up. Persistent LV dysfunction is of particular concern in younger patients with a potential life expectancy of many decades and a high risk of late reoperation. Because of this, we used a cutoff for risk-score analysis that returned 100% sensitivity; our interest was to identify a risk score below which there was minimal risk of LV dysfunction.

Study limitations. We were unable to account for the duration of regurgitation, and although the etiology of AR was not related to outcome, the small numbers in each subgroup precluded identification of an association. Furthermore, this study was not designed to detect any difference related to angiotensin-converting enzyme inhibitor use, and we cannot discount an influence of this or other medication on post-operative LV function.

There was no relationship between post-operative EF and the timing of assessment after operation, but remodeling may continue past the point of post-operative assessment (median: 7 months). An improvement in EF has been reported between observations 6 to 8 months and 3 to 7 years after operation. Nevertheless, improvement was largely confined to those with a normal EF at the earlier examination, so later remodelling is unlikely to change the conclusions of the current study. The sample size is small with respect to the number of variables and there is a risk of overfitting, particularly in relation to the multivariate models.

Future Directions

The conclusions of this report should remain tentative until supported by larger series with longer follow-up. Prospective validation of the risk score in larger cohorts with differing AR etiology, particularly in younger patients without rheumatic heart disease, would also be useful. Normalizing cardiac size across populations with differing sex, ethnicity, and body composition is a challenge and deserving of further investigation. In the current study, there was no interaction between sex and risk scores generated from the multivariate model, and an analysis using sex-specific *z*-scores made no material difference to the analysis presented in this report. However, *z*-scores are likely to be advantageous at extremes of body size—especially in smaller children—where the relationship between body surface area and cardiac size is nonlinear and confidence intervals are quite different to those with average adult body size. Whether by *z*-score or simple indexing, the use of body surface area to adjust for cardiac size assumes a normal weight/height relationship. Its utility in those with a disparate weight/height ratio will become an increasing issue given the current epidemic of obesity.

Although perhaps simplistic, the concept of preload limitation may have clinical application. The impact of contractile dysfunction on the FPI requires further investigation, as does comparison of this index to similar measures including systolic time intervals and the myocardial performance index.

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Reprint requests and correspondence: Dr. Tom Gentles, Green Lane Paediatric and Congenital Cardiac Service, Starship Children's Hospital, Private Bag 92 024, Auckland 1142, New Zealand. *E-mail: tomg@adhb.govt.nz*.

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Key Words: aortic regurgitation ■ contractility ■ echocardiography ■ pre-load ■ prognosis surgery ■ valvular heart disease.

▶ APPENDIX

For an explanation of FPI and *z*-score derivation, please see the online version of this article.