The International Journal of Cardiovascular Imaging (2019) 35:1019–1026
https://doi.org/10.1007/s10554-019-01599-5

ORIGINAL PAPER

The value of a simplified approach to end-systolic volume measurement for assessment of left ventricular contractile reserve during stress-echocardiography

Marco A. R. Torres[1] · Thais F. Texeira[1] · Ana C. Camarozano[2] · Clarissa C. A. Bellagamba[1] · Natalia M. Quevedo[2] · Altair I. Heidemann Junior[1] · Carolina Bertoluci[1] · Tonino Bombardini[3] · Michele De Nes[3] · Quirino Ciampi[4] · Eugenio Picano[3] on behalf of the Stress Echo 2020 study group of the Italian Society of Cardiovascular Imaging

Received: 10 January 2019 / Accepted: 6 April 2019 / Published online: 11 April 2019
© Springer Nature B.V. 2019

Abstract
The peak stress/rest ratio of left ventricular (LV) elastance, or LV force, is a load-independent index of left ventricular contractile reserve (LVCR) with stress echo (SE). To assess the accuracy of LVCR calculated during SE with approaches of different complexity. Two-hundred-forty patients were referred to SE for known or suspected coronary artery disease or heart failure and, of those, 200 patients, age 61 ± 15, 99 females, with interpretable volumetric SE were enrolled. All readers had passed the upstream quality control reading for regional wall motion abnormality (RWMA) and end-systolic volume (ESV) measurement. The employed stress was dipyridamole (0.84 mg, 6 min) in 86 (43%) and dobutamine (up to 40 mcg/kg/min) in 114 (57%) patients. All underwent SE with evaluation of RWMA and simultaneous LVCR assessment with stress/rest ratio of LV force (systolic blood pressure by cuff sphygmomanometer/ESV). ESV was calculated in each patient by two of three methods: biplane Simpson rule (S, in 100 patients), single plane area-length (AL, apical four-chamber area and length, in 100 patients), and Teichholz rule (T, from parasternal long axis and/or short axis view, in 200 patients). RMWA were observed in 54 patients. Success rate for ESV measurement was 76% (100/131) for S, 92% (100/109) for AL, and 100% (240/240) for T. There were 100 paired measurements (rest and stress) with S versus T, and 100 with AL versus T. The analysis time was the shortest for T (33 ± 8 s at rest, 34 ± 7 s at stress), intermediate for AL (70 ± 22 s at rest 67 ± 21 s at stress), and the longest for S (136 ± 24 at rest 129 ± 27 s at stress, $p < 0.05$ vs. T and AL). ESV absolute values were moderately correlated: T versus S (r rest = 0.746, $p < 0.01$, n = 100; r stress = 0.794, $p < 0.01$, n = 100); T vs. AL (r = 0.603 $p < 0.01$, n = 100, at rest and r = 0.820 $p < 0.01$ n = 100 at peak stress). LVCR values were tightly correlated independently of the method employed: T versus S (r = 0.899, $p < 0.01$, n = 100), and T versus AL (r = 0.845, $p < 0.01$, n = 100). LVCR can be accurately determined with all three methods used to extract the raw values of ESV necessary to generate the calculation of Force. Although S is known to be more precise in determining absolute ESV values, the relative (rest-stress) changes can be assessed, with comparable accuracy, with simpler and more feasible T and AL methods, characterized by higher success rate, shorter imaging and analysis time.

Keywords Left ventricular contractility · Echocardiography · Stress

Abbreviations

AL	Area-length method
CAD	Coronary artery disease
EF	Ejection fraction
ESV	End-systolic volume
HF	Heart failure
LV	Left ventricle
LVCR	Left ventricular contractile reserve
RWMA	Regional wall motion abnormalities
S	Simpson method
SE	Stress echocardiography
T	Teichholz method
TTE	Transthoracic echocardiography
WMSI	Wall motion score index

✉ Eugenio Picano
picano@ifc.cnr.it

Extended author information available on the last page of the article

Introduction

The assessment of regional wall motion abnormalities (RWMA) is the cornerstone of stress echocardiography (SE) for the evaluation of patients with coronary artery disease (CAD) and/or heart failure (HF) [1, 2]. The evaluation of global left ventricular (LV) contractile reserve (LVCR) is also possible during stress and is usually defined as an increase by ≥ 5 points in ejection fraction (EF) from rest to peak stress [3]. An alternative approach is the calculation of Force, also known as elastance [4], which allows to apply noninvasively in the SE lab the concept originally developed by Suga and Sagawa in the experimental laboratory with an invasive approach [5]. Force is expressed as the ratio of peak systolic blood pressure by cuff sphygmomanometer and end-systolic volume (ESV) by 2-D echocardiography [6]. Force is simpler to measure than EF, since it requires only ESV, rather than both ESV and end-diastolic volumes as EF. Differently from EF, Force is not dependent on heart rate, preload and afterload changes [7, 8]. The robust pathophysiological basis translates into better prognostic performance when compared to EF in patients undergoing SE [9–12]. Ideally, Force measured with the modified Simpson (S) rule requires biplane view of the left ventricle (LV) with integration of 4- and 2-chamber apical view to calculate ESV with the method of disks [13]. However, the possibility to obtain images suitable for volumetric assessment with S method decreases at peak stress which degrades image quality for increased heart rate, hyperventilation and hypercontractility [14].

Aim of this prospective two-center study was to assess the feasibility and relative accuracy of LVCR based on rest-stress Force variations with three different methods of different complexity for estimating ESV: S (the gold standard), apical single plane area-length (AL), and linear Teichholz (T) method from parasternal long- or short-axis.

Methods

Study population

In this prospective two-center study, we initially screened 240 patients. From this series, 200 patients were enrolled (99 female, 101 male; age 60 ± 15 years). They were referred to the SE laboratories of two university hospitals (Porto Alegre and Curitiba, Brazil). The inclusion criteria were: 1) Age > 18 years; 2) referral to dipyridamole or dobutamine SE for known or suspected CAD or HF, with any degree of resting left ventricular function (preserved or reduced); 3) no severe primary valvular or congenital heart disease; 4) wall motion imaging by TTE of acceptable quality at rest; 5) willingness to give their written informed consent allowing scientific utilization of observational data, respectful of privacy rights. Exclusion criteria were: 1- acoustic window of unacceptable quality at rest for regional wall motion assessment (n = 10); 2- unwillingness to give informed consent (n = 0).

The recruitment started in August, 2017 and lasted until November, 2018.

All patients underwent SE testing as part of a clinically-driven work-up and according to the referring physician's indications. The study protocol was reviewed and approved by the institutional ethics committees as a part of the SE 2020 study (148—Comitato Etico Lazio-1, July 16, 2016; Clinical Trials.Gov Identifier NCT 030.49995). The local center chapters of SE 2020 were approved in August, 2017 (in Porto Alegre, CAAE: 63787417.2.1001.5327) and July, 2018 (in Curitiba, CAAE: 63787417.2.2005.0096).

Transthoracic echocardiography

We used commercially available ultrasound machines: Philips EPIQ 7 model with transducer X5-1 5 MHz, IE 33 and Affinity 70 (Philips, Medical Systems, Andover, MA, USA) with a 2.5–3.5 and 4 MHz phased-array sector scan probe; Vivid 7 (GE Healthcare, USA, manufactured in Horten, Norway), with standard transducers.

All patients underwent comprehensive TTE at rest, and SE according to the protocol recommended by the European Association of Cardiovascular Imaging guidelines [2]. We used dipyridamole up to 0.86 mg/kg over 6′ or dobutamine starting from 5 up to 40 mcg/kg/min with atropine co-administration up to 1 mg. Electrocardiogram and blood pressure were monitored continuously. Criteria for interrupting the test were severe chest pain, diagnostic ST-segment shift, excessive blood pressure increase (systolic blood pressure ≥ 240 mmHg, diastolic blood pressure ≥ 120 mmHg), limiting dyspnea, maximal predicted heart rate, significant arrhythmias or limiting side effects. Echocardiographic imaging was performed from parasternal long axis view, short axis view, and apical 4-, 3- and 2-chamber view, using conventional two-dimensional echocardiography. Wall-motion score index (WMSI) was calculated in each patient at baseline and peak stress, in a four-point score ranging from one (normal) to four (dyskinetic) in a 17-segment model of the LV [2, 3]. All doctors and nurses involved were trained in Basic Life Support and Advanced Cardiac Life Support.

A test was considered positive for ischemia when at least two adjacent segments of the same vascular territory of the LV showed an increment of at least one point of WMSI during SE.

Volume analysis

By design, at least 2 methods were initially applied to assess ESV in all 240 recruited patients. Of these 240, Teichholz rule (T, from parasternal long axis and/or short axis view) was attempted and successfully completed in all 240. Biplane Simpson (S) method was attempted in 131 consecutive patients and successfully completed in 100. Single plane area-length (AL, apical four-chamber area and length) was attempted in 109 patients (not evaluated with S) and successfully completed in 100.

LV EDV and ESV were measured from apical four- and two-chamber views, using the biplane S method. Only representative cycles with optimal endocardial visualization were measured and the average of three measurements was taken. The endocardial border was traced, excluding the papillary muscles. The frame captured at the R wave of the ECG (or the first frame after mitral valve closure when ECG trace was unreadable) was considered to be the end-diastolic frame, and the frame with the smallest left ventricular silhouette (usually the first frame before mitral valve opening) the end-systolic frame [13]. All cardiac volumes were normalized to body surface area, yielding their respective indexes.

In the AL method, four-chamber view, the LV area is traced as above and the long-axis length is measured from the furthest point of the apex to the midpoint of the straight line crossing the mitral valve annulus [15] (Fig. 1).

In the T method, linear measurements of the LV end-diastolic and end-systolic internal diameter are obtained from 2D echocardiographic images perpendicular to the LV long-axis and measured at or immediately below the level of the mitral valve leaflets tips [13, 16] (Fig. 1).

LVCR criteria of positivity were stress-specific and based on previous data analyzing the prognostic impact of this parameter:: < 2.0 for dobutamine [10] and < 1.1 for dipyridamole [12].

Quality control for RWMA and ESV reading

On a set of 20 video-clips selected from eight different laboratories as a part of the quality control process of the SE 2020-RWMA subproject, the accredited readers all had ≥ 90% concordance with core lab reading on presence of RWMA [17, 18]. The cardiologist-echocardiographer performing the test interpreted the RWMA. The procedure for acquisition between centers was standardized through a web-based learning module before starting data collection.

With the same approach, the reading of ESV implied readings of a different set of 20 clips selected from seven different laboratories [19]. The accepted threshold was 80% concordance with area measurement (from apical 4- and 2-chamber views). The gold standard was the average reading of two experienced observers of the coordinating centers. For each clip, the measurement was considered concordant when the reading was ± 20% from the gold standard.

In order to assess intraobserver reproducibility, the same observer (TT) measured the ESV measures in a set of 20 (rest or stress) clips with three methods. On the same clips, a different independent observer (MAT) repeated the same measurements.

Statistical analysis

The statistical analyses included descriptive statistics (frequency and percentage of categorical variables and mean and standard deviation of continuous variables). Data are expressed as mean ± standard deviation (normally distributed data) or per cent frequency (categorical data) [20]. Parametric Pearson's correlation coefficient analysis was used to assess the absolute values of ESV and the relative (stress-rest) changes of LVCR with ESV assessed with different methods (S vs. T and AL vs. T). For analysis of concordance between LVCR of the three methods we used Kappa statistics. The intra-class correlation coefficient was calculated to assess inter-rater and intra-rater variability of

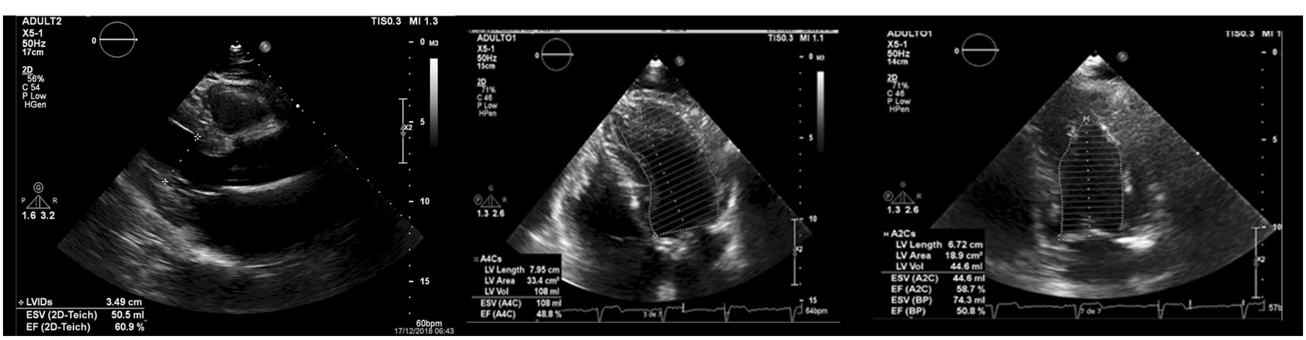

Fig. 1 Methodology of ESV calculation. The measurement of ESV was obtained in each patient with two of three methods: parasternal view with Teichholz method (left panel); area-length monoplane from apical four-chamber view (middle panel); biplane modified Simpson (middle and right panel)

measurements with different methods. Statistical significance was set at $p < 0.05$. All analyses were conducted with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL,USA, version 12).

Results

The main clinical characteristics of the study patients are described in Table 1. The employed stress was dipyridamole in 86 (43%) and dobutamine in 114 (57%) patients.

Qualitative analysis: WMSI and RWMA

Interpretable images were obtained in all patients at peak stress, with an overall feasibility of 100% for interpretation of RWMA and calculation of WMSI. In the overall population, WMSI increased slightly at peak stress (Table 2). Stress-induced ischemic RWMA were present in 54 patients (27%).

Quantitative analysis: ESV, EF and LVCR

Images were considered interpretable for quantitative analysis with at least one method in all patients. The feasibility rate (at rest and peak stress) was 100% for T (240/240), 92% for AL (100/109) and 76% for S (100/131). A paired evaluation was available in 200 patients: 100 with T and S and an additional 100 with T and AL.

For those with interpretable images, the analysis time for ESV was the shortest for T (33 ± 8 s at rest 34 ± 7 s at stress), intermediate for AL (70 ± 22 s at rest 67 ± 21 s at stress), and the longest for S (136 ± 24 s at rest 129 ± 27 s at stress), $p < 0.05$ versus T and S at rest and stress.

For ESV intra-rater variability, the ICC was 0.964 for S, 0.953 for A-L and 0.981 for T at rest. For ESV inter-rater variability, the ICC was 0.965 for S, 0.989 for A-L and 0.998 for T at rest. For LVCR, the ICC was 0.812 (inter-rater) and 0.629 (intra-rater) for S, 0.907 and 0.936 for AL, and 0.958 (inter-rate) and 0.954 (intra-rater) for T.

Considering the absolute values of ESV, the correlation was good for both S and T (r rest = 0.746, $p < 0.01$, n = 100; r stress = 0.794 n = 100, $p < 0.01$), and AL and T (r = 0.603, $p < 0.01$, n = 100, at rest and r = 0.820, $p < 0.01$, n = 100 at peak stress).

Considering LVCR (based on relative changes between rest and stress), the correlation was moderate for both S and T (n = 100, r = 0.899, $p < 0.01$), and AL and T (r = 0.845, n = 100, $p < 0.01$) (Fig. 2**).**

Table 1 Study patients

Sex (F/M)	99/101
Age (years)	60.6 ± 14.9
BSA (m^2)	1.7 ± 0.5
Hypertension	142 (71%)
Diabetes	72 (36%)
Previous MI	32 (16%)
CABG/PCI	28 (14%)
NYHA class	140 (I) 50 (II) 10 (III)
Beta-blocker	87 (43.5%)
Nitrates	10 (5%)
Calcium channel blockers	58 (29%)
Statin	107 (53.5%)
ACE	63 (31.5%)
Anti-platelet therapy	80 (40%)

ACE angiotensin-enzyme inhibitors, *CABG* coronary artery bypass surgery, *MI* myocardial infarction, *PCI* percutaneous coronary intervention

Table 2 Echocardiographic and hemodynamic findings

EF rest % (S)	49 ± 13
EF stress % (S)	54 ± 13
WMSI rest	1.2 ± 0.4
WMSI stress	1.1 ± 0.3
Force rest (S) (mmHg/mL)	3.5 ± 2.6
Force stress (S) (mmHg/mL)	5.1 ± 5.2
ESV index rest (mL/m^2) (S)	35 ± 18
ESV index stress (mL/m^2) (S)	31 ± 22
HR rest (beats/m)	73 ± 14
HR stress (beats/m)	113 ± 26
DBP rest (mmHg)	77 ± 15
DBP stress (mmHg)	83 ± 14
SBP rest (mmHg)	149 ± 30
SBP stress (mmHg)	157 ± 38
LVCR (S)	1.4 ± 0.5

DBP diastolic blodd pressure, *EF* ejection fraction, *ESV* end-systolic volume, *HR* heart rate, *LVCR* left ventricular contractile reserve, *S* Simpson rule, *WMSI* wall motion score index

Correlation among WMSI, EF and LVCR values

In all 200 patients we obtained measurable WMSI and LVCR. Δ(stress-rest)-WMSI was poorly correlated with LVCR obtained with T (n = 200, r = 0.16, p = NS), AL (n = 100, r = 0.047, p = NS) or S (n = 100, r = 0.138, p = NS).

In the 200 patients with both EF and LVCR obtained with T, a moderate correlation was observed between LVCR and Δ (stress-rest) EF (r = 0.523, $p < 0.01$).

Patterns of response combining WMSI and LVCR

The rest and stress values of WMSI, EF, Force and LVCR are shown in Table 2. At individual patient analysis, the

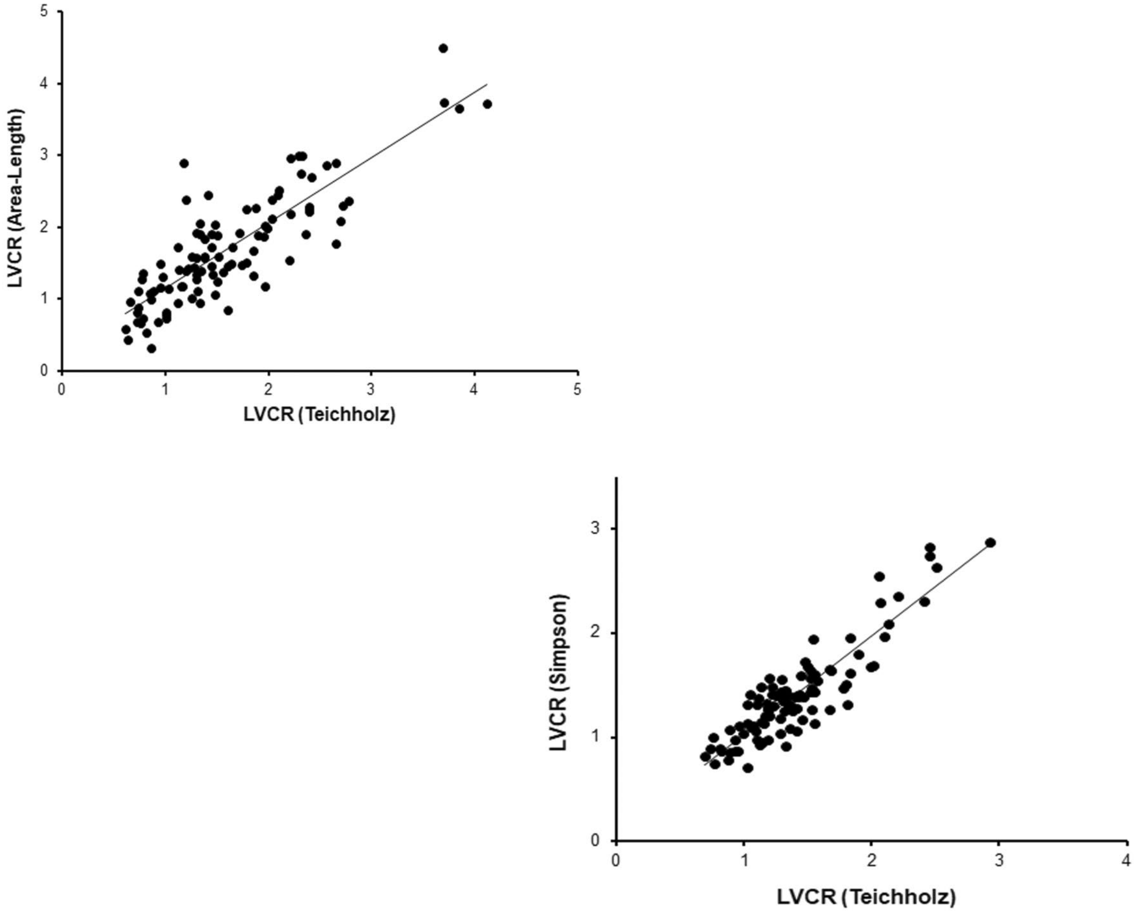

Fig. 2 The correlation between LVCR with different methods. There is a good correlation between LVCR with AL and T (upper panel) and S and T (lower panel)

combination of RWMA and LVCR using the T method identified 4 separate patterns of response: non-ischemic and strong heart (with no inducible RWMA and normal LVCR) found in 71 patients (38%); non-ischemic and weak heart in 74 patients (37%); ischemic and strong heart in 15 patients (7.5%); ischemic and weak heart in 39 patients (20%).

The level of concordance for positivity or negativity between the LVCR calculated of the three methods were 89% for S versus T and 87% for T versus AL (Kappa values were 0.768 and 0.742, respectively).

Discussion

LVCR can be measured in all patients with a combined use of S (first choice), AL (second choice) and T (third choice) methods. As expected the correlation between the 3 methods is only moderate for absolute values of ESV, due to the recognized greater accuracy of S method in presence of distorted and dilated LV. S method remains therefore the gold standard. When it is not feasible for presence of images of suboptimal quality, AL and even T provide a suitable surrogate, with the clear advantage of being substantially simpler and less time-consuming than S. The integrated stepwise use of S, AL and T for volumetric SE allows to gain in virtually all patients insight into force-based assessment of LVCR, more informative than EF-based LVCR.

Comparison with previous studies

Our findings are in agreement with previous studies showing that LVCR can be evaluated during all forms of physical, pharmacological and pacing stress [6, 9, 12, 21].

We found a high success rate at rest, but in 30% of patients the biplane view was not optimal and therefore the apical 4-chamber view was analyzed with the A-L approach. The success rate increases from 70% to 90% when only one apical view is needed and becomes 100% when the less accurate but technically easiest parasternal view is needed as in T method. Interestingly, the success rate did not decrease during stress, possibly due to the use of pharmacological stresses.

The improvement of technical feasibility and success rate during stress is essential for exploiting at the fullest the potential merits of Force in the clinical arena. The advantages of force-based LVCR over ejection fraction-based LVCR are convincingly rooted in theoretical and pathophysiological grounds and proven, to date, in selected populations. Previous studies showed that LVCR based on Force is simpler, faster and better for risk stratification than EF [9–12]. It is simpler from the computational aspect because it does not require the measurement of EDV needed, in addition to ESV, for EF. It is more reproducible because EF requires the manual tracing of the endocardial contours in end-diastole and end-systole in two projections. As these values are summed and multiplied to calculate EF, any measurement error is compounded [22]. It is also simpler because the myocardial backscatter reflectors decrease their intensity at end-systole compared to end-diastole, and therefore specular endocardial boundaries in end-systole are easier to visualize [23]. Due to consolidation of the ventricular mass and architecture in systole, endocardial boundaries are better delineated at end-systole than at end-diastole [22]. The reproducibility of measurements from 2D without contrast is substantially better for ESV than for EDV [24, 25].

Clinical implications

Volumetric echocardiography is important at rest and during stress, but its practical impact has been severely limited by the well-supported notion that they are "too time consuming", even nowadays that the dedicated software is on board of every commercially available machines [26]. This is especially important during stress, which is a battle against time, with so many parameters to see and so little time available [27]. However, ultrasound images can be stored for off-line processing and the extra-time required for volume analysis is of a few minutes for S, and of a few seconds for T method.

LVCR expands the potential of integrated SE and offers an information which is complementary and additive to RWMA. It can be measured in all patients with a combination of 3 methods: S when both apical 4 and 2-chamber views are measurable at rest and during stress (as it happens in most, but not all, patients); AL when only apical four-chamber view is measurable; and T when only parasternal views are available. The extra-analysis time is minimal with the simplest T, and still very reasonable with the gold standard S method.

In this way, LVCR and volumetric stress echocardiography can become an integral part of the state-of-the-art SE protocol, and may add surprising dividends to RWMA. In fact, a weak heart can be present in absence of ischemic RWMA, and a strong heart can coexist with RWMA—and they offer independent and incremental information over RWMA and superior to EF also in applications beyond CAD [25]. It is good that we can measure the force-based LVCR in virtually all patients referred to SE lab.

Limitations

We measured ESV at the smallest cavity size, as suggested by current guidelines [12]. However, this measurement is not always so obvious in populations with conduction delays and asynchronous contraction, not infrequent in patients with CAD or HF as those enrolled in the present study [28].

We used pharmacological stress only because this is the standard clinical practice in our labs, where only recently a supine cyclo-ergometer became available. Generalization of results to exercise stress test is not straightforward because an intrinsic limitation of the technique is the required quality of ultrasound scans. However, the measurement on images of degraded quality might further emphasize the value of the simplified T method, less affected by image degradation than S [29]. Accordingly, cyclo-ergometer stress test can have a huge impact on the quality of scans.

We compared volumetric SE with single plane vs biplane methods, but the real gold standard would be real time 3D echocardiography, which is however more technically demanding and less feasible during stress and requires additional hardware and software cost [12].

Within this study, several different ultrasound devices were used from two vendors, and certainly differences in image quality and features can account for accuracy and success of measurement between the compared approaches. In particular, the feasibility and accuracy of S and A–L drop considerably in presence of image quality intermediate-to-poor, whereas T is much less affected. In a study with real time three-dimensional echocardiography as the gold standard, the correlation of ESV with transoesophageal echo-based T was worse than S with high quality images, but significantly better with poor-quality images [29].

We compared T with S in 100 patients and T with A–L in another set of 100 patients. In order to have a full comparison, the three techniques might have been measured in the full population.

Conclusions

LVCR can be accurately determined with all three methods used to extract the raw values of ESV necessary to generate the calculation of Force: S, AL and T. Although S is known to be more precise in determining absolute ESV values, the relative (rest-stress) changes can be assessed, with comparable accuracy, with simpler and more feasible T and AL methods, characterized by higher success rate, shorter imaging and analysis time. Dual imaging of RWMA and LVCR can be integrated in all patients, with all pharmacological stresses, in the comprehensive new standard of quadruple imaging SE with ABCD protocol [30].

Funding Ageing project of Italian national Research Council (GAE P001328).

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

References

1. Pellikka PA, Nagueh SF, Elhendy AA, Kuehl CA, Sawada SG (2007) American Society of Echocardiography recommendations for performance, interpretation, and application of stress echocardiography. J Am Soc Echocardiogr 20(9):1021–1041
2. Sicari R, Nihoyannopoulos P, Evangelista A, Kasprzak J, Lancellotti P, Poldermans D (2008) Stress echocardiography expert consensus statement: european Association of Echocardiography (EAE) (a registered branch of the ESC). Eur J Echocardiogr 9:415–437
3. Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, Edvardsen T, Garbi M, Ha JW, Kane GC, Kreeger J, Mertens L, Pibarot P, Picano E, Ryan T, Tsutsui JM, Varga A (2016) The clinical use of stress echocardiography in non-ischaemic heart disease: recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. Eur Heart J Cardiovasc Imaging 17:1191–1229
4. Ginzton LE, Laks MM, Brizendine M, Conant R, Mena I (1984) Noninvasive measurement of the rest and exercise peak systolic pressure/end-systolic volume ratio: a sensitive two-dimensional echocardiographic indicator of left ventricular function. J Am Coll Cardiol 4:509–516
5. Sagawa K, Suga H, Shoukas AA, Bakalar KM (1977) End-systolic pressure/volume ratio: a new index of ventricular contractility. Am J Cardiol 40:748–753
6. Bombardini T, Correia MJ, Cicerone C, Agricola E, Ripoli A, Picano E (2003) Force-frequency relationship in the echocardiography laboratory: a noninvasive assessment of Bowditch Treppe? J Am Soc Echocardiogr 16:646–655
7. Cikes M, Solomon SD (2016) Beyond ejection fraction: an integrative approach for assessment of cardiac structure and function in heart failure. Eur Heart J 37:1642–1650
8. Bombardini T, Mulieri LA, Salvadori S, Costantino MF, Scali MC, Marzilli M, Picano E (2017) Pressure-Volume relationship in Stress echocardiography laboratory: does (left ventricular end-diastoli) size matter? Rev Esp Cardiol 70:96–104
9. Grosu A, Bombardini T, Senni M, Duino V, Gori M, Picano E (2005) End-systolic pressure/volume relationship during dobutamine stress echo: a prognostically useful non-invasive index of left ventricular contractility. Eur Heart J 26:2404–2412
10. Cortigiani L, Bombardini T, Corbisiero A, Mazzoni A, Bovenzi F, Picano E (2009) The additive prognostic value of end-systolic pressure-volume relation in patients with diabetes mellitus having negative dobutamine stress echocardiography by wall motion criteria. Heart 95:1429–1435
11. Bombardini T, Costantino MF, Sicari R, Ciampi Q, Pratali L, Picano E (2013) End-systolic elastance and ventricular-arterial coupling reserve predict cardiac events in patients with negative stress echocardiography. Biomed Res Int 2013:235194
12. Cortigiani L, Huqi A, Ciampi Q, Bombardini T, Bovenzi F, Picano E (2018) Integration of Wall Motion, Coronary Flow Velocity, and Left Ventricular Contractile Reserve in a Single Test: prognostic Value of Vasodilator Stress Echocardiography in Patients with Diabetes. J Am Soc Echocardiogr 31:692–701
13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU (2015) Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 28:1–39. e14
14. Martin TW, Seaworth JF, Johns JP, Pupa LE, Condos WR (1992) Comparison of Adenosine, Dipyridamole, and Dobutamine in Stress Echocardiography. Ann Intern Med 116:190–196
15. Wahr DW, Wang YS, Schiller NB (1983) Left ventricular volumes determined by two-dimensional echocardiography in a normal adult population. J Am Coll Cardiol 1:863–868
16. Teichholz LE, Kreulen T, Herman MV, Gorlin R (1976) Problems in echocardiographic volume determinations: echocardiographic-angiographic correlations in the presence of absence of asynergy. Am J Cardiol 37:7–11
17. Picano E, Ciampi Q, Citro R, D'Andrea A, Scali MC, Cortigiani L, Olivotto I, Mori F, Galderisi M, Costantino MF, Pratali L, Di Salvo G, Bossone E, Ferrara F, Gargani L, Rigo F, Gaibazzi N, Limongelli G, Pacileo G, Andreassi MG, Pinamonti B, Massa L, Torres MAR, Miglioranza MH, Daros CB, de Castro e Silva Pretto JL, Beleslin B, Djordjevic-Dikic A, Varga A, Palinkas A, Agoston G, Gregori D, Trambaiolo P, Severino S, Arystan A, Paterni M, Carpeggiani C, Colonna P (2017) Stress echo 2020: the international Stress Echo study in ischemic and non-ischemic heart disease. Cardiovasc Ultrasound. https://doi.org/10.1186/s12947-016-0092-1
18. Ciampi Q, Picano E, Paterni M, Borguezan Daros C, Simova I, de Castro e Silva Pretto JL, Scali MC, Gaibazzi N, Severino S, Djordjevic-Dikic A, Kasprzak J, Zagatina A, Varga A, Lowenstein J, Merlo PM, Amor M, Celeutkiene J, Perez J, Di Salvo G, Galderisi M, Mori F, Costantino FM, Massa L, Dekleva M, Quesada Chavez D, Trambaiolo P, Citro R, Colonna P, Rigo F, Torres ARM, Monte I, Stankovic I, Neskovic A, Cortigiani L, Re F, Dodi C, D'Andrea A, Villari B, Arystan A, De Nes M, Carpeggiani C, on behalf of Stress Echo 2020 study group of the Italian Society of Cardiovascular Echography (2017) Quality Control of Regional Wall Motion Analysis in Stress echo 2020. Int J Cardiol 249:479–485
19. Carpeggiani C, Ciampi Q, Paterni M, De Nes M, Zagatina A, Simova I, Djordievic-Dikic A, Citro R, Colonna P, Picano E (2019) Multi-step Web-based Training: the road to Stress echo 2020. Arg J Cardiol 86(6):404–409
20. Hinkle DE, Wiersma W, Jurs SG (2003) Applied statistics for the behavioral sciences. Houghton Mifflin College Division, Boston, p 756
21. Bombardini T, Agrusta M, Natsvlishvili N, Solimene F, Pap R, Coltorti F, Varga A, Mottola G, Picano E (2005) Noninvasive assessment of left ventricular contractility by pacemaker stress echocardiography. Eur J Heart Fail 7:173–181
22. Turakhia MP, McManus DD, Whooley MA, Schiller NB (2009) Increase in end-systolic volume after exercise independently predicts mortality in patients with coronary heart disease: data from the Heart and Soul Study. Eur Heart J 30:2478–2484
23. Picano E, Faletra F, Marini C, Paterni M, Danzi GB, Lombardi M, Campolo L, Gigli G, Landini L, Pezzano A, Distante A (1993) Increased echodensity of transiently asynergic myocardium in humans: a novel echocardiographic sign of myocardial ischemia. J Am Coll Cardiol 21:199–207

24. Kataoka A, Scherrer-Crosbie M, Senior R, Gosselin G, Phaneuf D, Guzman G, Perna G, Lara A, Kedev S, Mortara A, El-Hajjar M, Shaw LJ, Reynolds HR, Picard MH (2015) The value of core lab stress echocardiography interpretations: observations from the ISCHEMIA Trial. Cardiovasc Ultrasound 13(1):47
25. Thavendiranathan P, Popović ZB, Flamm SD, Dahiya A, Grimm RA, Marwick TH (2013) Improved interobserver variability and accuracy of echocardiographic visual left ventricular ejection fraction assessment through a self-directed learning program using cardiac magnetic resonance images. J Am Soc Echocardiogr 26:1267–1273
26. Schiller NB (2012) Gaining respect for echocardiographic volumetric quantitation: observations on a study of the baseline echocardiography data from the STICH echocardiography core laboratory. J Am Soc Echocardiogr 25:337–340
27. Picano E, Pellikka PA (2014) Stress echo applications beyond coronary artery disease. Eur Heart J 35:1033–1040
28. Mada RO, Lysyansky P, Daraban AM, Duchenne J, Voigt J-U (2015) How to define end-diastole and end-systole? JACC Cardiovasc Imaging 8:148–157
29. Grossgasteiger M, Hien MD, Graser B, Rauch H, Motsch J, Gondan M, Rosendal C (2014) Image quality influences the assessment of left ventricular function: an intraoperative comparison of five 2-dimensional echocardiographic methods with real-time 3-dimensional echocardiography as a reference. Ultrasound Med. 33(2):297–306. https://doi.org/10.7863/ultra.33.2.297
30. Picano E, Ciampi Q, Wierzbowska-Drabik K, Urluescu ML, Morrone D, Carpeggiani C (2018) The new clinical standard of integrated quadruple stress echocardiography with ABCD protocol. Cardiov Ultrasound 16:22. https://doi.org/10.1186/s12947-018-0141-z

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Affiliations

Marco A. R. Torres[1] · Thais F. Texeira[1] · Ana C. Camarozano[2] · Clarissa C. A. Bellagamba[1] · Natalia M. Quevedo[2] · Altair I. Heidemann Junior[1] · Carolina Bertoluci[1] · Tonino Bombardini[3] · Michele De Nes[3] · Quirino Ciampi[4] · Eugenio Picano[3] on behalf of the Stress Echo 2020 study group of the Italian Society of Cardiovascular Imaging

Marco A. R. Torres
mtorres@hcpa.edu.br

Thais F. Texeira
thaisftexeira@gmail.com

Ana C. Camarozano
camarozano@yahoo.com.br

Clarissa C. A. Bellagamba
clarissabellagamba@gmail.com

Natalia M. Quevedo
natykevv@gmail.com

Altair I. Heidemann Junior
aijunior@hcpa.edu.br

Carolina Bertoluci
carolinabertoluci@gmail.com

Tonino Bombardini
tbombardini@yahoo.it

Michele De Nes
denesm@ifc.cnr.it

Quirino Ciampi
qciampi@gmail.com

[1] Hospital de Clinicas de Porto Alegre - Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil

[2] Hospital de Clinicas UFPR, Medicine Department, Federal University of Paranà, Curitiba, Brazil

[3] Biomedicine Department, Institute of Clinical Physiology, CNR, CNR Research Campus, Via Moruzzi, 1, 56124 Pisa, Italy

[4] Cardiology Division, Fatebenefratelli Hospital, Benevento, Italy