ORIGINAL ARTICLE

Multi-step Web-based Training: the Road to Stress Echo 2020

Entrenamiento por etapas basado en la web: el camino hacia el Ecoestrés 2020

CLARA CARPEGGIANI[1], QUIRINO CIAMPI[2], MARCO PATERNI[1], MICHELE DE NES[1], ANGELA ZAGATINA[3], IANA SIMOVA[4], ANA DJORDIEVIC-DIKIC[5], RODOLFO CITRO[6], PAOLO COLONNA[7], EUGENIO PICANO[1]; ON BEHALF OF STRESS ECHO 2020 STUDY GROUP OF THE ITALIAN SOCIETY OF ECHOCARDIOGRAPHY AND CARDIOVASCULAR IMAGING (SIECVI).

ABSTRACT

Background: A standardized training platform helps to achieve reading harmonization in stress echocardiography (SE) beyond regional wall motion abnormalities (RWMA).
Objective: To harmonize SE reading criteria across different laboratories.
Methods: The core lab prepared for readers an obligatory 2-hour web-based learning module for 5 parameters: RWMA; B-lines; coronary flow velocity reserve (CFVR) based on peak diastolic flow velocity on the left anterior descending coronary artery; left ventricular contractile reserve (LVCR, from raw measurements of end-systolic volume, ESV); systolic arterial pulmonary pressure (from raw measurements of peak tricuspid regurgitant jet velocity, TRV). The quality control test consisted of 20 cases selected by the coordinating center. The a priori determined pass threshold was 18/20 (≥90%) with intra-class correlation coefficient between the coordinating lab and the peripheral reader >0.90.
Results: The certification was completed by 84 readers for RWMA, 65 for B-lines, 30 for CFVR, 24 for ESV and 20 for TRV. The mean reading time per attempt was shorter for TRV (9±4 min), CFVR (13±6 min) and B-lines (17±3 min), intermediate for ESV (24±7 min), and longer for RWMA (29±12 min, p <0.01). The success rate of the first attempt was higher for CFVR (85%), intermediate for TRV (75%) and B-lines (43 %), lower for ESV (35%) and lowest for RWMA (28 %, p <0.01).
Conclusions: A web-based learning platform improves image interpretation skills without need for expensive imaging equipment or a patient to scan. The road to certification is longer for RWMA, intermediate for ESV, and shorter for TRV, CFVR and B-lines.

Key Words: Stress Echocardiography - Web-based Platform - Quality Control.

RESUMEN

Introducción: Una plataforma de entrenamiento estandarizada ayuda a armonizar la lectura de la ecocardiografía de estrés (EE) más allá de las anormalidades en la motilidad parietal regional (AMPR)
Objetivo: Armonizar los criterios de lectura del EE a través de diferentes laboratorios.
Métodos: El laboratorio central preparó para los lectores de ecocardiografía un módulo obligatorio de 5 parámetros basado en la web de 2 horas de duración: AMPR; líneas B, reserva de la velocidad de flujo coronario (RVFC) evaluada mediante la velocidad pico del flujo diastólico en la arteria coronaria descendente anterior; reserva contráctil ventricular izquierda (RCVI, evaluada a partir de mediciones crudas del volumen de fin de sístole, VFS); y presión sistólica de la arteria pulmonar (basada en mediciones crudas de la velocidad del jet de regurgitación tricuspídea, VRT). La prueba de control de calidad consistió en 20 casos seleccionados por el centro coordinador. El umbral de aprobación determinado a priori fue de 18/20 (≥ 90%) con un coeficiente de correlación intraclase entre el laboratorio coordinador y el lector periférico > 0.90
Resultados: Ochenta y cuatro lectores completaron la certificación para las AMPR, 65 para las líneas B, 30 para la RVFC, 24 para el VFS y 20 para la VRT. El tiempo de lectura medio por intento fue más corto para la VRT (9 ± 4 min), la RVFC (13 ± 6 min) y las líneas B (17 ± 3 min), intermedio para el VFS (24 ± 7 min), y más prolongado para las AMPR (29 ± 12 min, p < 0.01). La tasa de acierto del primer intento fue más alta para la RVFC (85%), intermedia para la VRT (75%) y las líneas B (43%), menor para el VFS (35%) y más baja para las AMPR (28%, p < 0.01).
Conclusiones: La plataforma de aprendizaje basada en la web mejora las habilidades de interpretación de imágenes sin necesidad de un equipamiento de imágenes costoso o de estudiar un paciente. El camino hacia la certificación es más largo para las AMPR, intermedio para el VFS y más corto para la VRT, la RVFC y las líneas B.

Palabras clave: Ecocardiografía de estrés - Plataforma basada en la web - Control de calidad

Rev Argent Cardiol 2018;86:385-390. http://dx.doi.org/10.7775/rac.v86.i6.14286

Received: 09/28/2018 – *Accepted:* 10/18/2018

Address for reprints: Eugenio Picano, MD, PhD. CNR Institute of Clinical Physiology, Pisa. Via Moruzzi, 1 - CNR Research Campus - 56124 - Pisa Tel: +390503152398. Twitter: ≠eupic58. Fax: +390503152374. E-mail: picano@ifc.cnr.it

[1] CNR Institute of Clinical Physiology, Pisa, Italy
[2] Cardiology Division, Fatebenefratelli Hospital, Benevento, Italy
[3] Cardiology Department, Saint Petersburg State University, Russian Federation
[4] Acibadem City Clinic Cardiovascular Center, University Hospital, Sofia, Bulgaria
[5] Cardiology Clinic, Clinical Center of Serbia, Medical School, University of Belgrade, Serbia
[6] Cardiology Department and Echocardiography Lab, University Hospital "San Giovanni di Dio e Ruggi d'Aragona", Salerno, Italy
[7] Cardiology Hospital, Policlinico di Bari, Italy

Abbreviations

CAD	Coronary artery disease	**RWMA**	Regional wall motion abnormalities
CFVR	Coronary flow velocity reserve	**SE**	Stress echocardiography
ESV	End systolic volume	**TRV**	Tricuspid regurgitant velocity
LV	Left ventricle	**SPAP**	Systolic pulmonary arterial pressure

INTRODUCTION

Stress echocardiography (SE) is a cost-effective technique for diagnosis and risk stratification in patients with known or suspected coronary artery disease (CAD). (1-3) In recent years, the technique underwent a methodological and conceptual mutation and the classical approach based on regional wall motion abnormalities (RWMA) has changed into a more comprehensive assessment of several variables of pathophysiological and established prognostic interest within and beyond CAD. (4, 5) Four parameters now converge conceptually, logistically and methodologically in the integrated quadruple imaging SE protocol. (6) They are: RWMA, B-lines at lung ultrasound (7-11), left ventricular contractile reserve (LVCR) assessed as the stress/rest ratio of force [systolic blood pressure by cuff sphygmomanometer/end-systolic volume (ESV), by 2D echocardiography] (12-15); and coronary flow velocity reserve (CFVR) on the left anterior descending coronary artery. (16-18) Altogether they are fused in the so-called ABCD protocol allowing a synoptic functional assessment of epicardial coronary artery stenosis (wall motion), lung water (B-lines), myocardial function (LVCR) and coronary small vessels (CFVR). In the "ABCD" protocol, A stands for Asynergy; B for B-lines; C for Contractile reserve (LVCR); and D for Doppler-based assessment of CFVR. In addition, the routine assessment of tricuspid regurgitant jet velocity also offers insight into pulmonary hemodynamics (19, 20) and is integrated in the core quadruple imaging SE protocol in the presence of heart failure with reduced or preserved ejection fraction. (6)

Although promising and effective, the new SE protocol needs to be substantiated by large scale, prospective, multicenter, effectiveness studies necessary prior to large scale acceptance in the clinical arena. To fill this evidence gap, the Stress Echo 2020 (SE2020) study was designed and gathers to date the experience of over 50 laboratories from 20 countries. (21) Upstream to entering the study, the reader from each center has to pass a web-based course and a specific quality control test as detailed elsewhere for RMWA (22) and B-lines. (23) Here we present the extended experience on quality control test results on RWMA and B-lines and the initial results obtained with three additional steps of the quality control road to SE2020: ESV (the raw measurement necessary for LVCR); peak diastolic flow velocity (the raw measurement necessary for CFVR); and TRV (the raw measurement necessary for systolic pulmonary arterial pressure).

METHODS

The computer scientist team of the SE2020 study at IFC-CNR coordinated the procedures of the quality control assessment. The study was supported with institutional funding of the Italian National Research Council and with travel grants of the Italian Society of Cardiovascular Echography for dedicated sessions during national meetings. No support was received from the industry.

A web-based educational platform was developed to facilitate the training process. Participating cardiologists were invited by email to join the platform, which was protected by user-specific passwords. The platform includes files and videos with detailed instructions on how to start the training and allows downloading and uploading of external files, as previously described in detail. (22, 23)

Study reader population

All participants were clinical cardiologists and expert echocardiographists with ongoing high volume (>100 tests per year) SE activity.

Reading sessions and pass threshold

For each step, we selected 20 video clips. The privacy of patients was protected during acquisition, storage, and transmission of the SE study. All images were anonymized, and the identity of patients was not disclosed at any time to the readers.

Web-based learning module

For each step, the 2-hour web-based training module consisted of five sequential learning blocks: a- Selected readings of recent guidelines; b- A power-point file of 25 to 50 slides summarizing key points, and specific literature supporting the proposed reading policy, illustrating tips and tricks; c- A theory self-assessment test of five questions with four answers each (only one correct) preliminary to the video clip reading; d- Short (< 15 s) video clips of SE examinations with the same format as the official test reading. After completing the web-based module the reader could take the test (maximum three attempts). After the first attempt, the sequence of videos was mixed in the other attempts.

After the pass or fail response

The response was pass (≥ 90% accuracy) or fail. With pass, the reader received a certificate of accreditation and could start recruiting with a written informed consent signed by each patient and after clearance by the local Ethics Committee. With failure, the unsuccessful reader could retake the test at 1 month after passing the web-based module (this time obligatory). After the second failure, the reader could undergo training in a recommended center and try again after 1 year.

Step 1: Regional wall motion analysis

Absence or lesser degree RWMA at rest were the positivity criterion based on evaluation of the wall motion score index

with a 17-segment model of the LV (24). The pass threshold was ≥90 % concordance between the peripheral reader and the coordinating center reading. (22, 23)

Step 2: B-lines

B-lines were counted (from 0 to 10) in each video clip. The answer was considered correct if concordant with the reference standard reading±1. The pass threshold was ≥90% concordance between the peripheral reader and the coordinating center reading with intra-class correlation coefficient ≥0.90 and coefficient of variability <10%. (23)

Step 3-Left ventricular end-systolic volume

Left ventricular ESV was measured from apical four- and two-chamber views, using the biplane Simpson method (24). The endocardial border was traced, excluding the papillary muscles. The frame with the smallest left ventricular silhouette was the end-systolic frame. For each video clip, the planimetric area measurement in each projection was considered concordant when the reading was ±20% from the gold standard. The wider tolerance limits accepted in comparison with other parameters are due to the recognized measurement variability of this parameter even among experienced observers. (25, 26) The pass threshold was ≥90% concordance of area measurement between the peripheral reader and the coordinating center reading with intra-class correlation coefficient ≥0.90 and coefficient of variability <20%. (23)

Step 4: Peak diastolic flow velocity

Coronary flow velocity reserve is defined as the ratio between peak hyperemic and peak basal diastolic coronary flow velocities. In each video clip, peak diastolic Doppler flow velocities were measured. For each video clip, the measurement was considered concordant when the reading was ± 10% from the gold standard. The pass threshold was ≥90% concordance of peak diastolic flow measurement between the peripheral reader and the coordinating center reading with intra-class correlation coefficient ≥0.90 and coefficient of variability <10%.

Step 5- Tricuspid regurgitant jet velocity

Systolic pulmonary arterial pressure (SPAP) is calculated through the simplified Bernoulli equation (with TRV in m/s when substituted into the formula): SPAP= 4 TRV ^{2} + estimated right atrial pressure. In each video clip, TRV was derived from the application of continuous wave Doppler on the tricuspid regurgitant jet, from the apical four chamber view or from the parasternal right ventricular inflow view, finally choosing the highest measured TRV value. Peak velocity was measured in cm/s.

The gold standard was the average peak TRV flow velocity reading by two experienced observers of the coordinating centers (EB and FF). For each video clip, the measurement was considered concordant when the reading was ±10% from the gold standard. The pass threshold was ≥90% concordance with intra-class correlation coefficient >0.90 and coefficient of variability <10%.

Statistical analysis

Values are expressed as percentages or mean and standard deviation. Comparison between different steps was tested with analysis of variance and inter-group comparisons with the Newman-Keuls test. A p value < 0.05 was considered significant.

Ethical considerations

The study protocol was reviewed and approved by the institutional Ethics Committee as part of the SE2020 study (1487-CE Lazio-1, July 20, 2016).

RESULTS

A total of 112 readers from 54 centers in 17 countries (Argentina, Bosnia-Herzegovina, Brazil, Bulgaria, Costa Rica, Hungary, Italy, Lithuania, Mexico, Poland, Portugal, Romania, Qatar, Russia, Serbia, UK, and USA) entered the web-based training as per October 20th, 2018. The certification was completed by 84 readers for RWMA, 65 for B-lines, 30 for CFVR, 24 for ESV and 20 for TRV. The mean reading time per successful attempt was shorter for TRV (9± 4 min), CFVR (13± 6 min) and B-lines (17±3 min), intermediate for ESV (24±7 min), and longer for RWMA (29±12 min, p <0.01 vs. all the other groups) (Figure 1). The first attempt success rate was higher for CFVR (85%), intermediate for TRV (75%) and B-lines (43 %), lower for ESV (35%) and lowest for RWMA (28 %, p<0.01 vs. all the other groups) (Figure 2).

DISCUSSION

A modular web-based system for training and accreditation is a feasible, low cost and high efficiency option to obtain the accreditation of readers, standardize methods of execution and analysis, and harmonize reading criteria with an acceptable consistency, allowing data collection for scientific purposes in an effectiveness study.

Comparison with previous studies

Our study confirms and expands the findings of previous studies showing the feasibility of a web-based training and quality control platform for the essential steps of SE reading. We have separately reported the experience with regional wall motion analysis (on 63 readers) and B-lines (on 60 readers). The present study reports the updated experience on RWMA and B-lines and for the first time presents the experience obtained with TRV, ESV and CFVR. We accepted a priori (and found a posteriori) greater variability for ESV compared with other parameters. This is consistent with previous literature showing that the coefficient of variability for ESV is substantially lower than that for EDV (25, 26) but still higher than other echocardiographic indices used in SE.

To achieve the difficult task of echocardiographic data collection quality control, one possible approach is the use of a core lab which analyzes centrally images sent from all the recruiting sites. This approach is typically the preferred choice in a clinical trial and minimizes the sources of measurement variability suggested, but requires dedicated economic and human resources, and is more suitable for an efficacy study than for an effectiveness analysis aimed at evaluating the performance of the test in the field (27, 28). Another approach is to include all data without any

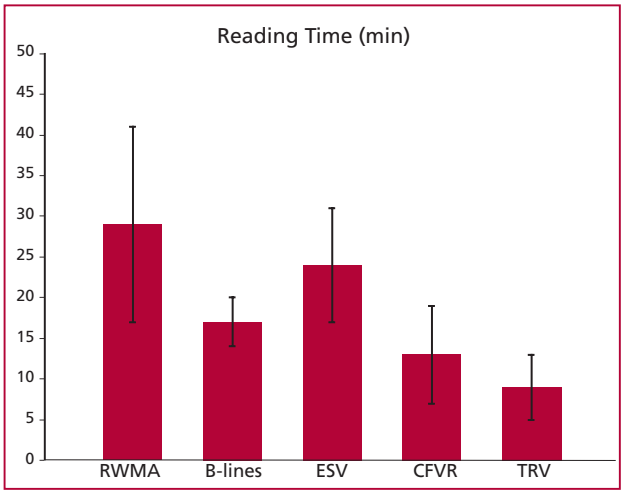

Fig. 1. Mean reading time for each of the 5 tested parameters. RWMA: Regional wall motion abnormalities; ESV: End systolic volume; CFVR: Coronary flow velocity reserve; TRV: Tricuspid regurgitant velocity.

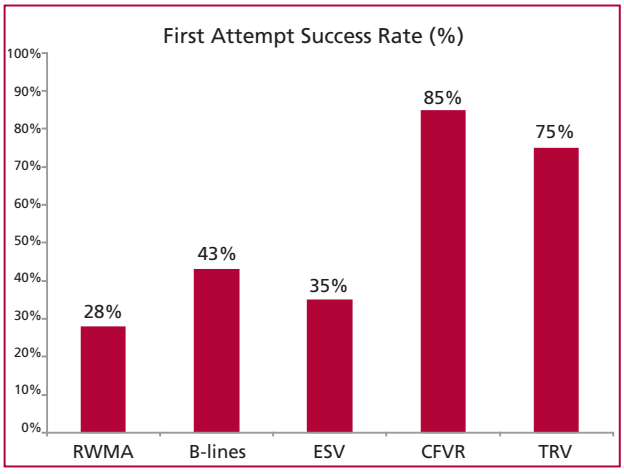

Fig. 2. Mean percentage of successful attempts at the first reading for each of the 5 tested parameters. Abbreviations as in Fig.1.

a priori quality control. This leads to collection of a large amount of data in a relatively short time, but can be very risky for a technique such as SE, which is operator-dependent with substantial variability, even among experienced readers, in the absence of a priori agreement of reading criteria and strict standardization of execution, image acquisition and interpretation criteria. (29, 30)

Clinical implications

A web-based training platform is a feasible and flexible approach for continuing education, methodology standardization and reading harmonization. It helps to spell-out reading criteria and to discuss in advance fine tuning of the project with a bottom-up approach more fruitful than a top-down approach which may have important limitations. For instance, the original B-line scan approach consisting of the classical 28-site approach (9), required 3 minutes of time, which resulted in many centers abandoning it for feasibility problems. This led to a reassessment of the method with the intra-network validation of different protocols, and at the end the simplified 4-site scan which was finally adopted by the network was proven to be the best trade-off between complexity and feasibility. (31) Along the network, the information and innovation does not fall vertically and unidirectionally from the coordinating center to the recruiting centers, but streams horizontally across the centers. This was only possible due to the strong experience, solid motivation, and intellectual generosity of the members of the network. The image bank used for quality control came from 19 different centers which sent typical cases for selection. In this way, the samples collected for quality control were representative of the garden variety of technologies, patients and stresses found in the real world.

Limitations

We restricted our web-based training to 5 key items, which obviously does not include the whole spectrum of parameters necessary for a thorough examinations in any patient under any condition. The full completion of the training road to SE2020 will include other steps, currently under construction, addressing specific parameters such as diastolic function (E/e' ratio and E wave deceleration time); right ventricular function (TAPSE); left atrial volume index; mitral regurgitation and aortic stenosis quantification. More than the single step, it is important that the SE2020 community accepted the underlying principle: those who have more experience in a particular field will share their knowledge and trace the path for others, accurately avoiding to convey academically sweet information without clear clinical correlate.

CONCLUSIONS

Web-based training is a pre-requisite to certification in specific aspects of SE reading, necessary to achieve the inter-center methodological standardization and reading harmonization required to build a SE lab without walls. The learning platform is suitable to improve image interpretation skills regardless of time and space, without the need for expensive imaging equipment or a patient to scan. The road to certification is longer and more difficult for RWMA ("the university of SE education"), intermediate for ESV ("the primary school" for acquisition, but the "secondary school" for analysis) and TRV ("the primary school" for analysis, but the "secondary school" for acquisition), and simpler for B-lines ("the kindergarten") (Figure 3). CFVR is elementary to measure but may be difficult to acquire, requires a higher standard of technology than other parameters, and therefore it might be called the PhD degree of the SE *cursus stu-*

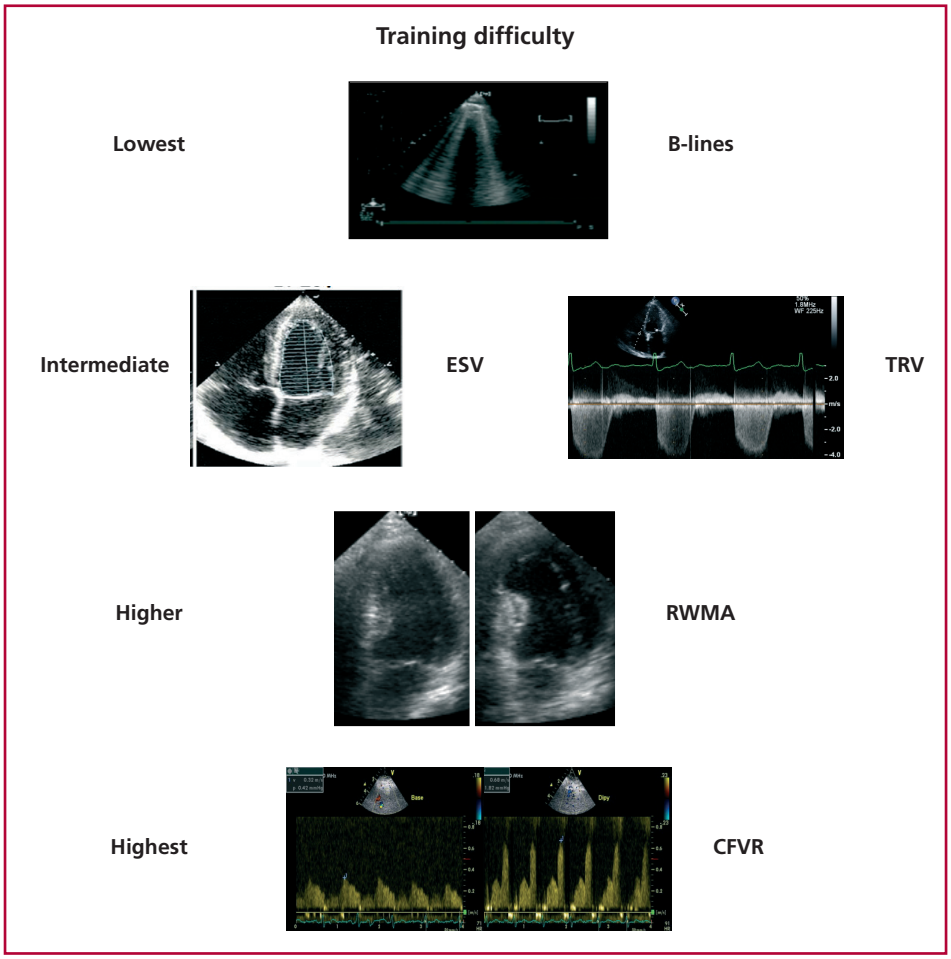

Fig. 3. The training difficulty of the 5 different parameters: lowest for B-lines, intermediate for ESV and TRV, higher for RWMA, and highest (for acquisition, not for reading) for CFVR. Abbreviations as in Fig.1.

diorum.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

REFERENCES

1. Picano E. Stress echocardiography. From pathophysiological toy to diagnostic tool. Point of view. Circulation 1992;85:1604-612. http://doi.org/bkgp

2. Pellikka PA, Nagueh SF, Elhendy AA, Kuehl CA, Sawada SG; American Society of Echocardiography, American Society of Echocardiography recommendations for performance, interpretation, and application of stress echocardiography. J Am Soc Echocardiogr. 2007; 20:1021-41. http://doi.org/bn7jkf

3. Sicari R, Nihoyannopoulos P, Evangelista A, Kasprzak J, Lancellotti P, Poldermans D, et al; on behalf of the European Association of Echocardiography. Stress echocardiography expert consensus statement. European Association of Echocardiography (EAE) (a registered branch of the ESC). Eur J Echocardiogr. 2008;9:415-37. http://doi.org/dvxvq8

4. Picano E. Stress echocardiography: a historical perspective. Special article. Am J Med 2003; 114:126-30. http://doi.org/dkdbrv

5. Picano E, Pellikka PA. Stress echo applications beyond coronary artery disease. Eur Heart J. 2014;35:1033-40. http://doi.org/cv9d

6. Picano E, Ciampi Q, Wierzbowska-Drabik K, Urluescu L-M, Morrone D, Carpeggiani C. The new clinical standard of integrated quadruple stress echocardiography with ABCD protocol. Cardiovasc Ultrasound 2018;16:22. http://doi.org/cv9d

7. Agricola E, Picano E, Oppizzi M, Pisani M, Meris A, Fragasso G, Margonato A. Assessment of stress-induced pulmonary interstitial edema by chest ultrasound during exercise echocardiography and its correlation with left ventricular function. J Am Soc Echocardiogr 2006:19;457-63. http://doi.org/drwhcn

8. Picano E, Pellikka PA. Ultrasound of extravascular lung water: a new standard for pulmonary congestion. Eur Heart J 2016;14:2091-104. http://doi.org/f8wbv4

9. Scali MC, Cortigiani L, Simionuc A, Gregori D, Marzilli M, Picano E. Exercise-induced B-lines identify worse functional and prognostic stage in heart failure patients with depressed left ventricular function. Eur J Heart Fail 2017;19:1468-78. http://doi.org/f9qch4

10. Picano E, Scali MC, Ciampi Q, Lichtenstein D. Lung ultrasound for the cardiologist. JACC imaging 2018;12:381-90.

11. Scali MC, Zagatina A, Ciampi Q, Cortigiani L, D'Andrea A, Djordjevic-Dikic A, et al, on behalf of the Stress Echo 2020 study group of the Italian Society of Cardiovascular Imaging. The Functional Meaning of B-profile During Stress Lung Ultrasound JACC imaging. In Press

12. Bombardini T, Correia MJ, Cicerone C, Agricola E, Ripoli A, Picano E. Force-frequency relationship in the echo lab: a non invasive assessment of Bowditch Treppe? J Am Soc Echo 2003;17:832-41.

13. Bombardini T, Agrusta M, Natsvlishvili N, Solimene F, Papp R, Coltorti F, et al. Noninvasive assessment of left ventricular contractility by pacemaker stress echocardiography. Eur J Heart Fail 2005;7:173-81. http://doi.org/dk2wj7

14. Grosu A, Bombardini T, Senni M, Duino V, Gori M, Picano E. End-systolic pressure/volume relationship during dobutamine stress echo: a prognostically useful non-invasive index of left ventricular contractility. Eur Heart J 2005;26:2404-12. http://doi.org/cmhzr6

15. Rigo F, Richieri M, Pasanisi E, Cutaia V, Zanella C, Della Valentina P, et al. Usefulness of coronary flow reserve over regional wall motion when added to dual-imaging dipyridamole echocardiography. Am J Cardiol 2003; 91:269-73. http://doi.org/cmhzr6

16. Lowenstein J, Tiano C, Marquez G, Presti C, Quiroz Cl. Simultaneous analysis of wall motion and coronary flow reserve of the left anterior descending coronary artery by transthoracic Doppler echocardiography during dipyridamole stress. J Am Soc Echo 2003; 16:607-13. http://doi.org/d2g25c

17. Cortigiani L, Rigo F, Gherardi S, Bovenzi F, Molinaro S, Picano E, et al. Coronary flow reserve during dipyridamole stress echocardiography predicts mortality. JACC Cardiovasc Imaging 2012;5:1079-85. http://doi.org/bkgh

18. Lowenstein JA, Caniggia C, Rousse G, Amor M, Sánchez ME, Alasia D, et al. Coronary flow velocity reserve during pharmacologic stress echocardiography with normal contractility adds important prognostic value in diabetic and nondiabetic patients. J Am Soc Echocardiogr 2014;27:1113-9. http://doi.org/bkgj

19. Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, et al. 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 2016;17:1191-229. http://doi.org/chnn

20. Rudski LG, Gargani L, Armstrong WF, Lancellotti P, Lester SJ, Grünig E, et al. Stressing the cardiopulmonary vascular system: the role of Echocardiography. J Am Soc Echocardiogr 2018;31:527-50. http://doi.org/gdj86r

21. Picano E, Ciampi Q, Citro R, D'Andrea A, Scali MC, Cortigiani L, et al. Stress echo 2020: The international Stress Echo study in ischemic and non-ischemic heart disease. Cardiovasc Ultrasound 2017;15-3. http://doi.org/f9sst5

22. Ciampi Q, Picano E, Paterni M, Daros CB, Simova I, de Castro, et al; on behalf of Stress Echo 2020. Quality control of regional wall motion analysis in Stress Echo 2020. Int J Cardiol 2017;249:479-85. http://doi.org/gckch9

23. Scali MC, Ciampi Q, Picano E, Bossone E, Ferrara F, Citro R, et al; Stress Echo 2020 study group of the Italian Society of Echocardiography and Cardiovascular Imaging (SIECVI). Quality control of B-lines analysis in Stress Echo 2020. Cardiovasc Ultrasound 2018;16-20.

24. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantitation by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1-39. http://doi.org/bhj5

25. Kataoka A, Scherrer-Crosbie M, Senior R, Gosselin G, Phaneuf D, Guzman G, et al. The value of core lab stress echocardiography interpretation: observations from the ISCHEMIA trial. Cardiovasc Ultrasound 2015;18;13:47

26. Crowley AL, Yow E, Barnhart HX, Daubert MA, Bigelow R, Sullivan DC. Critical review of current approaches for echocardiographic reproducibility and reliability assessment in clinical research. J Am Soc Echocardiogr 2016;29:1144-54. http://doi.org/f9g52m

27. Gottdiener JS, Bednarz J, Devereux R, Gardin J, Klein A, Manning WJ, et al; American Society of Echocardiography. American Society of Echocardiography recommendations for use of echocardiography in clinical trials. J Am Soc Echocardiogr 2004;17:1086-119. http://doi.org/b2b34m

28. Galderisi M, Henein MY, D' hooge J, Sicari R, Badano LP, Zamorano JL, et al. Recommendations of the European Association of Echocardiography. How to use echo-Doppler in clinical trials: different modalities for different purposes. Eur J Echocardiogr 2011;12:339-53. http://doi.org/fq4957

29. Scali MC, Zagatina A, Simova I, Zhuravskaya N, Ciampi Q, Paterni M, et al. B-lines with Lung Ultrasound: the optimal scan technique at rest and during stress Ultrasound Med Biol 2017;43:2558-63. http://doi.org/gck4z8

30. Varga A, Picano E, Dodi C, Barbieri A, Pratali L, Gaddi O. Madness and method in stress echo reading. 1999;20: 1271-5.

31. Picano E, Lattanzi A, Orlandini A, Marini C, L'Abbate A. Stress echocardiography and the human factor: the importance of being expert. J Am Coll Cardiol 1991;17:666-9. http://doi.org/b67k5n