Review Article

Stress Echo 2030 Study: A Flagship Project of the Italian Society of Echocardiography and Cardiovascular Imaging

Eugenio Picano, Quirino Ciampi[1], Rosina Arbucci[2], Angela Zagatina[3], Elena Kalinina[3], Ratnasari Padang[4], Garvan C. Kane[4], Hector R. Villarraga[4], Adelaide M. Arruda-Olson[4], Jesus Peteiro Vazquez[5], Alla Boshchenko[6], Olga Zhuravleva[6], Tamara Ryabova[6], Natalia Sviazova[6], Jelena Celutkiené[7], Laura Balkevičienė[7], Ariel Saad[8], Francesca Bursi[9], Ana Djordjevic-Dikic, Sergio Kobal[10], Matteo Lisi[11], Elisa Merli[11], Fiore Manganelli[12], Clarissa Borguezan-Daros[13], Hugo Rodriguez-Zanella[14], Maria Grazia D'Alfonso[15], Fabio Mori[15], Nicola Gaibazzi[16], Jaroslaw D. Kasprzak[17], Ayten Safarova[18], Tatiana Timofeeva[18], Hugo Mosto[19], Karina Wierzbowska-Drabik[20], Nithima Chaowalit Ratanasit[21], Marco Fabio Costantino[22], Paolo Colonna[23], Tamara Kovačević Preradović[24], Miodrag Ostojic[24], Lauro Cortigiani[25], Albert Varga[26], Aleksandra Nikolic[27], Rosangela Cocchia[28], Attila Palinkas[29], Eszter Dalma Palinkas[29], Fausto Rigo[30], Giovanni Benfari[31], Filipa Xavier Valente[32], Dimitrios Soulis[33], Yi Wang[34], Lixue Yin[34], Caroline M. Van de Heyning[35], Alberto Mazzi[36], Jorge Lowenstein[2], Diego M. Lowenstein Haber[2], Sofia Marconi[2], Andrea Barbieri[37], Francesca Mantovani[38], Giovanni L. Tripepi[39], Michele De Nes[39], Ylenia Bartolacelli[40], Bruno Villari[1], Mauro Pepi[41], Scipione Carerj[42], Patricia A. Pellikka[4]

Cardiology Clinic, University Clinical Center of Serbia, Medical School, University of Belgrade, [27]Department of Noninvasive Cardiology, Institute for Cardiovascular Diseases, School of Medicine, Belgrade, Serbia, [1]Division of Cardiology, Fatebenefratelli Hospital, Benevento, [9]Department of Health Sciences, University of Milan, Cardiology Division, ASST Santi Paolo e Carlo, [41]Centro Cardiologico Monzino, IRCCS, Milan, [11]Cardiology Unit, Ospedale per gli Infermi, Faenza, [12]Cardiology Division, Moscati Hospital, Avellino, [15]Department of Cardiology, Careggi University Hospital, Florence, [16]Department of Cardiology, University of Parma, Parma, [22]Cardiology Division, San Carlo Hospital, Potenza, [23] Department of Cardiology, Policlinico University Hospital of Bari, Bari, [25]Department of Cardiology, San Luca Hospital, Lucca, [28]Department of Cardiology, Cardarelli Hospital, Naples, [30]Division of Cardiology, Villa Salus Foundation/IRCCS San Camillo Hospital, Venice, [31]Department of Cardiology, University of Verona, Verona, [36]Department of Cardiology, Oglio Po Hospital, Cremona, [37]CNR, Institute of Clinical Physiology, Reggio Calabria, [38]Department of Biomedical, Metabolic and Neural Sciences, Cardiology Division, University of Modena and Reggio Emilia, Policlinico di Modena, Modena, [39]Cardiology Division, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, [40]Department of Cardio Thoracic and Vascular Medicine, Paediatric Cardiology and Adult Congenital Heart Disease Program, S. Orsola-Malpighi Hospital, Bologna, [42]Cardiology Division, University Hospital G. Martino, University of Messina, Messina, Italy, [2]Cardiodiagnosticos, Investigaciones Medicas, and Bioimagenes Medical Center, [8]División de Cardiología, Hospital de Clínicas José de San Martín, [19]Echocardiography Laboratory Division, Ramos Mejia Hospital, Buenos Aires, Argentina, [3]Department of Cardiosurgery, St. Petersburg State University Hospital, St. Petersburg, [6]Department of Cardiology, Cardiology Research Institute, Tomsk National Research Medical Centre of the Russian Academy of Sciences, Tomsk, [18]Department of Internal Medicine with a Course in Cardiology and Functional Diagnostics at the Medical Institute of the Peoples' Friendship University of Russia, Moscow, Russia, [4]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota, USA, [5]CHUAC-Complexo Hospitalario Universitario A Coruna-University of A Coruna, La Coruna, [32]Department of Cardiology University Hospital Vall d'Hebron, Barcelona University. Barcelona, Spain, [7]Centre of Cardiology and Angiology, Clinic of Cardiac and Vascular Diseases, Faculty of Medicine, Institute of Clinical Medicine, Vilnius University, State Research Institute Center for Innovative Medicine, Vilnius, Lithuania, [10]Echocardiography Division, Soroka University Medical Center, Beer Sheva, Israel, [13]Cardiology Division, San José Hospital, Criciuma, Brazil, [14]National Institute of Cardiology Ignacio Chavez, Mexico City, Mexico, [17]I Department of Cardiology, Bieganski Hospital, Medical University of Lodz, [20]Department of Internal Diseases and Clinical Pharmacology, Medical University, Lodz, Poland, [21]Department of Medicine, Division of Cardiology, Siriraj Hospital, Mahidol University, Bangkok, Thailand, [24]Clinic of Cardiovascular Diseases, University of Banja Luka, University Clinical Centre of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina, [26]Department of Family Medicine, University of Szeged, Szeged, [29]Department of Internal Medicine, Elisabeth Hospital, Hódmezővásárhely, Hungary, [33]Kosmoiatriki Medical Center, Athens, Greece, [34]Department of Cardiovascular Ultrasound and Non-Invasive Cardiology, Sichuan Provincial People's Hospital, Chengdu, China, [35]Department of Cardiology, Antwerp University Hospital, Edegem, Belgium

Abstract

Over the past decade, stress echocardiography has evolved from a test for assessing epicardial artery stenosis to a comprehensive functional test, targeting multiple cardiovascular parameters. The new approach includes several structured steps: (a) evaluating regional wall motion abnormalities to detect epicardial artery stenosis or vasospasm; (b) assessing pulmonary congestion and diastolic function via B-lines with lung ultrasound; (c) gauging preload and contractile reserve with volumetric echocardiography; (d) measuring coronary microvascular reserve using Doppler-based coronary flow velocity in the middistal left anterior descending artery; and (e) determining cardiac sympathetic reserve by tracking heart rate reserve on an ECG. This evolution was supported extensively by the Italian Society of Echocardiography and Cardiovascular Imaging (SIECVI), which

Address for correspondence: Prof. Quirino Ciampi, Division of Cardiology, Fatebenefratelli Hospital, Principe di Napoli Street, Benevento, I-82100, Italy.
E-mail: qciampi@gmail.com

Access this article online

Quick Response Code:

Website:
https://journals.lww.com/JCEG

DOI:
10.4103/jcecho.jcecho_2_25

Submitted: 07-Jan-2025 **Revised:** 20-Jan-2025
Accepted: 27-Jan-2025 **Published:** 30-Apr-2025

How to cite this article: Picano E, Ciampi Q, Arbucci R, Zagatina A, Kalinina E, Padang R, *et al*. Stress echo 2030 study: A flagship project of the Italian Society of Echocardiography and Cardiovascular Imaging. J Cardiovasc Echography 2025;35:1-7.

played a key role in five areas: (1) developing the initial, curiosity-driven project; (2) disseminating protocols and results at national and international conferences, supporting logistic infrastructure and publication expenses; (3) establishing a digital platform (customized Redcap) for data entry and storage; (4) facilitating patient recruitment across 19 Italian centers; and (5) offering formal endorsement through six presidencies, adding credibility and reach beyond any single institution. The protocol quickly advanced from concept to high-impact publications, earning inclusion in 2024 specialty guidelines. Initially Italian-led, the study now includes 50 centers across 20 countries (e.g. USA and China). Beyond the 50 peer-reviewed papers published in 2016–2024, this study offers a novel, sustainable approach to cardiac stress testing, providing more information at lower costs, with zero radiation and minimal environmental impact. SIECVI's endorsement was instrumental in amplifying the study's rigor and outreach.

Keywords: Chronotropic reserve, coronary flow reserve, echocardiography, lung water, stress echocardiography, stress testing

The Historical Roots of the ABCDE Stress Echo: Legacy of a Master

The Golden Age of the Institute of Clinical Physiology in Pisa, Italy, located in Via Savi ("the Street of Wise Men"), began in 1975–1980, under the guidance of the late Professor Attilio Maseri, a towering figure in medicine and mentor to multiple generations of cardiologists.[1] With a view from the "Place of Miracles," the Institute witnessed scientific breakthroughs during those years, the influence of which persists today.[2] Maseri fostered a cohort of pioneering cardiologists, later called the "Via Savi boys," a nod to the celebrated physicists of Rome's Via Panisperna, gathered around Enrico Fermi 50 years earlier. Maseri's intellectual legacy catalyzed the careers of many brilliant young researchers, planting seeds that continue to thrive in cardiology today, notably through the ABCDE protocol.

Step A: Foundations of stress echocardiography

Step A is foundational to stress echocardiography. Its importance stems from the pioneering work of Professor Alessandro Distante, who, using M-mode and two-dimensional (2D) techniques, studied vasospastic ischemia.[3,4] This research established that regional wall motion abnormalities serve as an early, sensitive, and bedside marker of myocardial ischemia, a discovery that has since become integral to Step A.

Step B: Pulmonary congestion and lung water assessment

Step B originates from Professor Carlo Giuntini's work on extravascular lung water as a biomarker for pulmonary congestion and elevated left ventricular filling pressures, which can be managed through diuretics and dialysis. Giuntini *et al*. explored lung water scoring using chest X-rays and nuclear medicine or invasive methods, though these approaches were limited by complexity.[5] Decades later, moving the ultrasound transducer from the apical window upward led to the use of lung ultrasound. A new generation of cardiologists used B-lines as the new standard for assessing extravascular lung water in the echocardiography and stress echo lab. Ultrasound B-lines became the shape of lung water.[6,7]

Step C: Insights into global left ventricular function

Step C focuses on global left ventricular function, acknowledging that it provides more comprehensive information than regional wall motion abnormalities alone. Professor Mario Marzilli's early work in Detroit demonstrated that global left ventricular dysfunction could exist even when regional wall thickening appears normal.[8] This understanding evolved further at Pisa through studies on pressure-volume loops. Dr. Bombardini later refined and simplified the seminal concept of Suga and Sagawa into a clinically practical tool assessing preload and contractile reserve, insights invaluable to clinicians.[9] LV force, also known as elastance, entered the echocardiography and stress-testing laboratory as a load-independent measure of contractility through the simple combination of systolic blood pressure obtained with cuff sphygmomanometer and end-systolic volume with volumetric echocardiography.[10]

Step D: Uncovering coronary microvascular dysfunction

Step D addresses coronary microvascular dysfunction, a phenomenon identified by Mario Marzilli and Professor Antonio L'Abbate.[11] Dr. Danilo Neglia's studies with positron emission tomography underscored the prognostic significance of coronary microvascular dysfunction.[12] The feasibility of transthoracic echocardiography in assessing microvascular function was proven by the pioneer Rigo *et al*. from Venice, enabling noninvasive assessment of coronary flow reserve alongside Step A.[13] This breakthrough enables clinicians to detect and understand microvascular dysfunction's implications in chronic coronary syndromes and beyond, extending to valvular heart disease, heart failure, hypertrophic cardiomyopathy, and heart transplant rejection.

Step E: Cardiac autonomic function's role

Step E completes the protocol by incorporating cardiac autonomic function, a significant factor in ischemia as emphasized by the physiologist Malliani and Lombardi.[14] Although this aspect was previously neglected in imaging, Dr. Clara Carpeggiani's work introduced heart rate reserve as an essential metric for understanding cardiac stress responses.[15] In recent years, her research with Dr. Lauro Cortigiani has further illuminated the "physiologic scotoma" of traditional cardiac imaging, underscoring the importance of autonomic function.[16] Finally, with the inclusion of Step E, the ABCDE protocol was ready for real-world application, successfully providing clinicians with a multi-marker approach to stratifying risk and diagnosing coronary artery disease.

Each marker in the ABCDE protocol has demonstrated incremental diagnostic and prognostic value beyond Step A alone,[17] revealing actionable therapeutic targets and advancing the understanding of myocardial ischemia's complexities.[18-20]

While the ischemic cascade model served the field well for four decades, it falls short of capturing myocardial ischemia's full spectrum.[21] Employing the multi-marker approach of the ABCDE protocol offers a comprehensive view, capturing the diverse phenotypes of ischemia, even in patients with normal coronary arteries, chest pain, ST-segment depression, and reduced coronary flow reserve under stress.[22] This prism approach illuminates the many colors of myocardial ischemia, empowering clinicians with nuanced diagnostic and therapeutic insights [Table 1].

At the core of this methodological shift is Professor Maseri's pioneering concept that organic epicardial coronary artery stenosis is not the sole, and perhaps not even the primary, cause of chronic coronary syndromes. While a good cardiologist diagnoses (and treats) coronary artery stenosis, the best cardiologist diagnoses (and manages) the vulnerable patient.[1]

ABCDE+: to Each Patient the Right Test

Beyond the core ABCDE protocol, stress echocardiography offers unmatched flexibility and adaptability for evaluating patients with conditions beyond coronary artery disease. Stress echocardiography allows clinicians to tailor testing to each patient, optimizing the choice of test, timing, and focus. During stress imaging, time is limited, and clinicians must prioritize elements within the imaging sequence. The ABCDE protocol can be extended as needed with additional steps: step G for gradients, Step F for regurgitant flows, Step L for left atrial volume and function, Step P for pulmonary artery systolic pressure with E/e' as a surrogate for left ventricular filling pressure, and Step R for the right ventricular function. Each added step provides targeted information for specific conditions.

For example, in hypertrophic cardiomyopathy, all ABCDE protocol steps are useful, but assessing the left ventricular outflow tract peak gradient at peak exercise is essential, particularly in symptomatic patients with a resting peak gradient below 50 mmHg. This individualized approach maximizes stress echo's versatility, enabling precise, patient-specific testing based on individual vulnerabilities.[23,24]

From Stress Echo 2020 to Stress Echo 2030: a 10-Year Long Journey

The ongoing Stress Echo 2030 project explores stress echo applications in various contexts. Although the ABCDE protocol provides a foundational framework across these applications, specific steps are often added to address unique vulnerabilities in individual patients.[25] The recruitment phase for the study spans from July 2016 to December 2025, with significant updates introduced during the COVID-19 pandemic. The pandemic-imposed pause from 2020 to 2021 slowed recruitment considerably, allowing time for the study framework to be revised and expanded, evolving from Stress Echo 2020 to Stress Echo 2030. During this period, the database was migrated to REDCap, managed by the scientific society Italian Society of Echocardiography and Cardiovascular Imaging (SIECVI). In addition, the project scope was broadened to include new international sites, such as those in the USA and China, and data collection methods were enhanced to integrate additional clinical, echocardiographic, and follow-up data points. The primary endpoint of the final analysis will assess all-cause mortality after recruiting 10,000 patients by December 2025, followed by a 5-year follow-up through 2030, as outlined in the prespecified study protocol. All participating centers successfully passed quality control and are now required to contribute a minimum of 100 enrolled patients to ensure high data quality, as limited or irregular data submissions were associated with reduced reliability and often reflected low laboratory volume or limited engagement in the study.

The Need to Go Beyond Step A

As always, with innovation, responses to adopting the new ABCDE+ protocol vary. We see innovators, early adopters, late adopters, and laggards (innovation-resistant laboratories) within the echo community.

Differences in adoption rates also are not solely explained by age, though younger colleagues may generally be quicker to embrace change than their senior counterparts, who might view any shift from routine cautiously. After all, laggards argue, with some truth, that "Step A alone served us well for 50 years," and the simplicity of conventional (Step A-only) stress echo is appealing. However, Step A is no longer sufficient. In modern populations with atypical symptoms and multiple treatments, the positivity rate for regional wall motion abnormalities has dropped below 10% (from over 70% in the 1980s when the technique first appeared), and its negative predictive value has also decreased.[26] Back in the 1980s, a negative test for regional

Table 1: Imaging and nonimaging parameters for ABCDE SE protocol

	RWMA	B-lines	LVCR	CFVR	HRR
Step	A	B	C	D	E
IFC roots	Distante	Giuntini	Marzilli	L'Abbate	Carpeggiani
Reserve	Epicardial	Diastolic	Contractile	Small vessel	Sympathetic
Imaging time	Minutes	Seconds	Seconds	Minutes	None
Analysis time	Seconds	Seconds	Minutes	Seconds	Seconds
Feasibility (%)	>95	100	>95	>80	100

CFVR=Coronary flow velocity reserve, HRR=Heart rate reserve, IFC=Institute of Clinical Physiology, LVCR=Left ventricular contractile reserve, LUS=Lung ultrasound, PWD=Pulsed-wave Doppler, RWMA=Regional wall motion abnormality wall motion corresponded to a <1% annual event rate; now, a negative test is associated with an all-cause mortality rate closer to 2%, indicating that even "low-risk" patients may not be as low-risk as once thought.[27]

Additional markers are necessary to address these limitations, but incorporating steps A, B, and C (ACE) into the core protocol requires minimal effort. Practitioners simply need to analyze the same 2D image, adding left ventricular volumes, a task made straightforward and operator-independent by artificial intelligence systems now included in most high-end instruments. End-diastolic volume changes reflect preload reserve and diastolic function, while end-systolic volume changes, when combined with systolic blood pressure, indicate a relatively load-independent measure of left ventricular contractility such as force. Practically speaking, patients with no regional wall motion abnormalities and normal left ventricular contractile reserve experience a reduction in yearly death rate from 2% to 1.5%. Adding an evaluation of heart rate reserve can further lower this risk. Although cut-off values vary based on stress type (higher for intense inotropic and chronotropic stresses like exercise and dobutamine, lower for milder ones like vasodilators), the clinical implications remain strong: a normal heart rate reserve further lowers mortality, and with triple negativity (Steps A, C, and E), the all-cause yearly mortality rate drops below 1%, truly defining a low-risk group.

Some may question how vasodilators can assess cardiac sympathetic reserve, mistakenly attributing the heart rate increase during dipyridamole administration to a reflexive sympathetic response. However, this heart rate rise results from elevated circulating norepinephrine, unrelated to blood pressure changes or induced ischemia.[28] Furthermore, denervated hearts show no heart rate increase following vasodilator stress,[29] affirming that the response is due to endogenous adenosine's stimulation of A2a receptors in carotid body chemoreceptors, which through efferent sympathetic pathways activate adrenergic beta-1 receptors in sinus node cells. This mechanism, first identified by nuclear cardiologists,[30] clarifies the pathophysiology behind the heart rate response to vasodilators.

Heart rate reserve thus serves as a reliable indicator of cardiac sympathetic reserve,[31] offering prognostic insight alongside regional wall motion abnormalities induced by exercise, dobutamine, or vasodilators.[16,32-34] Heart rate is read automatically on echo monitors and has been included in stress echo's minimum data set for decades, providing substantial value with minimal effort. The ACE protocol, built into the standard image acquisition processes, is ready for clinical application.

Today, many laboratories have also adopted Step B, although initial acceptance was low (~30%) in those entering Stress Echo 2020, which started in 2016. This reluctance stemmed from the time required for the original 28-site scan, which added 3 min at rest and another 3 min poststress. However, the network's clinical validation ultimately affirmed the innovation's value. B-line detection is straightforward, the "kindergarten" of echocardiography, and is now conducted with the simplified 4-site scan. After a thorough comparison of different scanning approaches (28, 16, 8, 4, and 1 site), a simplified 4-site scan emerged as effective, as wet sites were primarily located in the third intercostal space symmetrically in the right and left hemithorax, from midaxillary to the anterior axillary line, and from anterior axillary to the midclavicular line.[35,36] With this simplified scan, Step B acceptance rates surged to nearly 100% in Stress Echo 2030 (started in September 2021). Moreover, centers have observed that pulmonary congestion, indicated by stress-induced B-lines, is linked not only to ischemia but also to diastolic dysfunction, even in the absence of coronary artery disease. Vasodilation is an effective diastolic stress independent of underlying coronary artery disease.[37,38] B-line accumulation during exercise, dobutamine, or vasodilator stress carries a significant prognostic impact.[18]

Coronary flow velocity reserve presents a higher technical challenge, particularly with exercise or dobutamine. However, with vasodilators, the coronary flow velocity signal becomes stronger and easier to capture, as heart rate and left ventricular contractility increase only slightly but flow increases 4-fold. The prognostic power of a reduced coronary flow velocity reserve, with a relative risk of 4 for predicting all-cause death, is well-documented in meta-analyses.[39] Although myocardial perfusion contrast echocardiography is an alternative, it is more complex, costly, and prone to artifacts. Coronary flow velocity reserve, while limited to the middistal left anterior descending artery, is sufficient for assessing coronary microvascular function in noncoronary artery disease conditions,[40,41] akin to blood pressure measurement in the brachial artery. There are variations in blood pressure in different arterial districts, but what we measure in the brachial artery is a good indicator of the global blood pressure burden. Similarly, there may be variations in coronary microvascular conditions in the other major coronary arteries, but in the absence of epicardial artery stenosis, what we measure in the middistal left anterior descending artery is indicative of the conditions of the entire coronary artery tree.

Stress echo laboratories can now follow a "starry guide" code [Figure 1] based on the number of steps included in their routine: 1-star protocols (Step A only, or "vintage"), 2-star protocols (usually Steps A and B, focusing on heart failure and valvular disease),[42] 3-star laboratories with the ACE protocol, 4-star laboratories with the ABCE protocol, and 5-star laboratories with the complete ABCDE protocol. The roadmap to 5-star stress echo is now clear, with recent 2024 European Society of Cardiology guidelines already endorsing the inclusion of left ventricular volumes (Step C) and Doppler assessment of coronary flow velocity alongside Step A for patients with and without coronary artery disease.[43] Step B and Step E are already present in Stress Echo 2017 specialty recommendations in nonischemic ischemic heart disease,[24] and the full ABCDE protocol is now recommended as the new standard of functional cardiac stress testing by the European Association of Cardiovascular Imaging 2024.[25]

Economic, Ethical, and Environmental Sustainability

All five primary cardiac imaging techniques, stress echocardiography, coronary computed tomography angiography, stress-cardiac magnetic resonance imaging, stress-single photon emission computed tomography, and stress-positron emission tomography, hold comparable recommendation levels in recent European Society of Cardiology 2024 guidelines. The choice of modality is typically determined by "local availability and physician preference."[43] However, recent developments in healthcare demand a reconsideration of imaging selection, influenced by three major trends changing the landscape outside the cardiac imaging laboratory: (1) financial constraints in the postpandemic era, (2) rising cancer rates with evidence that the cumulative effects of diagnostic medical imaging exposure contribute significantly to low-dose radiation risks, now established as a major environmental cause of cancer,[44,45] and (3) the climate emergency, which necessitates attention to the environmental impact of medical choices.

Physicians should, therefore, weigh not only diagnostic accuracy but also economic, radiologic, and environmental sustainability.[46] Different costs can be evaluated as monetary costs (in euros or dollars), radiologic costs (in chest X-ray equivalents), and carbon costs (carbon dioxide emissions equivalents). When considering a composite sustainability index, health outcomes per dollar spent, radiation dose, and carbon emissions, stress echocardiography demonstrates clear advantages over other techniques.[47]

Stress Echo 2030 Beyond 2030

The comprehensive protocol developed in the Stress Echo 2020 study laid the foundation for Stress Echo 2030. This new initiative is based on the expanded ABCDE+ protocol, encompassing 12 projects addressing a broad range of conditions, from chronic coronary syndromes and coronary vasospasm to hypertrophic cardiomyopathy and heart failure with preserved ejection fraction; from chest radiotherapy effects to COVID-19 sequelae; from valvular and congenital heart disease to the impact of air pollution on stress echo outcomes and the influence of cumulative medical imaging radiation load on long-term health. As of November 10, 2024, the network has accumulated >10,000 studies, half of which include the complete ABCDE protocol, complemented by >5000 studies from the Stress Echo 2020 project, totaling approximately >15000 studies [Figure 2].

Despite substantial progress, much remains to be addressed. By posing clinically relevant questions, the SIECVI community continues to drive forward.[48] The current focus is expanding to resting transthoracic echocardiography for detecting high-risk markers, such as excessive resting force as the hallmark of the left ventricular hypercontractile phenotype,[49-51] or elevated

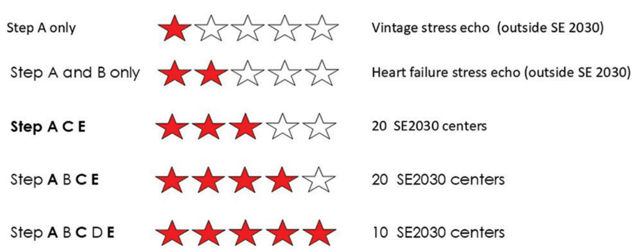

Figure 1: Stress Echo 2030. The guide to stress echo laboratory scoring in the ABCDE era

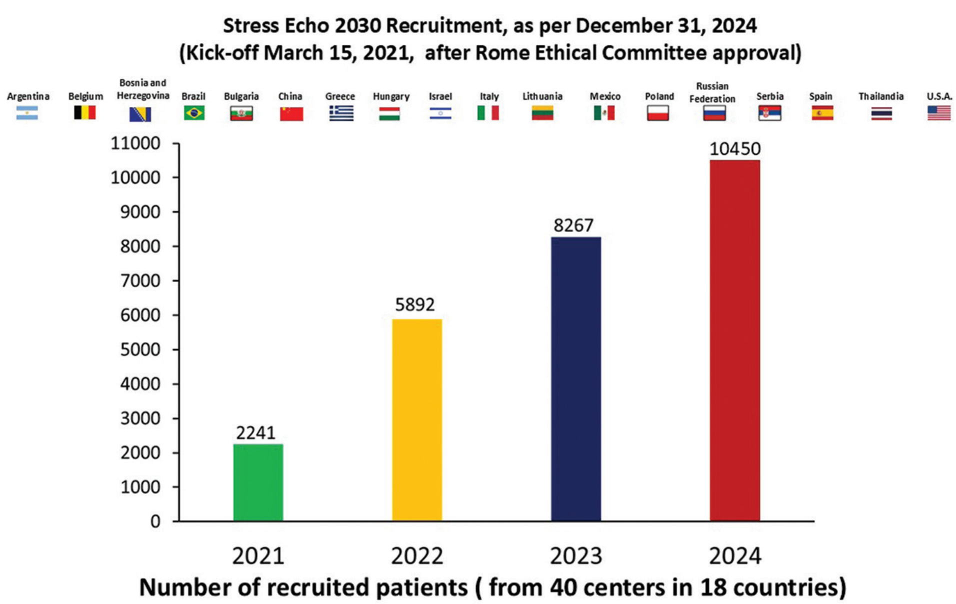

Figure 2: Stress Echo 2030. The state of recruitment of Stress Echo 2030 as of November 10, 2024

resting coronary flow velocity as a biomarker of the coronary hyperperfusion phenotype.[52]

Technological advancements are shifting the methodology from expert cardiologist interpretation toward fully automated, artificial intelligence-assisted analyses of left ventricular volumes, wall motion, B-lines, and coronary flow velocity profiles.[53] Stress echocardiography is on track to become a sustainable, fully operator-independent modality. The goal is clear: to achieve more (information) with less (economic, radiologic, and environmental costs).[54]

Ethical statement

The study was approved by the institutional Ethical committee of Lazio 1, Approval Number: 295 of march 8th, 2021.

Acknowledgments

We extend our heartfelt gratitude to the six SIECVI Presidents who proactively supported the Stress Echo 2020 and 2030 project: Paolo Colonna, 2016–2018; Frank Benedetto, 2018–2020; Francesco Antonini-Canterin, 2020–2022; Mauro Pepi, 2022–2024; Scipione Nino Carerj, 2024–2026, Giovanni Di Salvo, 2026–2028. A special thank to all the participants who contributed enthusiastically to the project. In loving memory of the dear friends we lost during this 10-year journey, brilliant colleagues, generous scientists, and cherished friends: Nadezhda Zhuravaskaya, Maurizio Galderisi, and Antonio Tota.

Financial support and sponsorship

The study was financially supported by the Italian Society of Echocardiography and Cardiovascular Imaging.

Conflicts of interest

There are no conflicts of interest.

References

1. Crea F, Liuzzo G. Attilio Maseri: Scientist, clinician, mentor, and gentleman. Cardiovasc Res 2022;118:e57-8.
2. Picano E. Italy's institute of clinical physiology. Eur Heart J 2014;35:879-81.
3. Distante A, Rovai D, Picano E, Moscarelli E, Palombo C, Morales MA, *et al.* Transient changes in left ventricular mechanics during attacks of Prinzmetal's angina: An M-mode echocardiographic study. Am Heart J 1984;107:465-74.
4. Distante A, Rovai D, Picano E, Moscarelli E, Morales MA, Palombo C, *et al.* Transient changes in left ventricular mechanics during attacks of Prinzmetal angina: A two-dimensional echocardiographic study. Am Heart J 1984;108:440-6.
5. Giuntini C, Pistolesi M, Miniati M, Fazio F. Theoretical and practical considerations of measuring extravascular lung water. J Thorac Imaging 1988;3:36-43.
6. Picano E, Frassi F, Agricola E, Gligorova S, Gargani L, Mottola G. Ultrasound lung comets: A clinically useful sign of extravascular lung water. J Am Soc Echocardiogr 2006;19:356-63. [doi: 10.1016/j.echo.2005.05.019].
7. Picano E, Pellikka PA. Ultrasound of extravascular lung water: A new standard for pulmonary congestion. Eur Heart J 2016;37:2097-104.
8. Stein PD, Marzilli M, Sabbah HN, Lee T. Systolic and diastolic pressure gradients within the left ventricular wall. Am J Physiol 1980;238:H625-30.
9. Bombardini T, Correia MJ, Cicerone C, Agricola E, Ripoli A, Picano E. Force-frequency relationship in the echocardiography laboratory: A noninvasive assessment of Bowditch treppe? J Am Soc Echocardiogr 2003;16:646-55.
10. Bombardini T, Agrusta M, Natsvlishvili N, Solimene F, Pap R, Coltorti F, *et al.* Noninvasive assessment of left ventricular contractility by pacemaker stress echocardiography. Eur J Heart Fail 2005;7:173-81.
11. Marzilli M, Sambuceti G, Fedele S, L'Abbate A. Coronary microcirculatory vasoconstriction during ischemia in patients with unstable angina. J Am Coll Cardiol 2000;35:327-34.
12. Neglia D, Michelassi C, Trivieri MG, Sambuceti G, Giorgetti A, Pratali L, *et al.* Prognostic role of myocardial blood flow impairment in idiopathic left ventricular dysfunction. Circulation 2002;105:186-93.
13. 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.
14. Malliani A, Lombardi F. Circulatory markers of nervous activation during myocardial ischemia. Can J Cardiol 1986;Suppl A: 40A-5A.
15. Carpeggiani C, Skinner JE. Coronary flow and mental stress. Experimental findings. Circulation 1991;83:I90-3.
16. Cortigiani L, Carpeggiani C, Landi P, Raciti M, Bovenzi F, Picano E. Usefulness of blunted heart rate reserve as an imaging-independent prognostic predictor during dipyridamole stress echocardiography. Am J Cardiol 2019;124:972-7.
17. Picano E, Pellikka PA, editors. The road to stress echo 2030. In: Stress Echocardiography. 7th ed., Ch. 43. New York: Springer Nature; 2023. p. 657-72.
18. Scali MC, Ciampi Q, Zagatina A, Cortigiani L, D'Andrea A, Daros CB, *et al.* On behalf of the stress echo 2020 study group of the Italian society of echocardiography and cardiovascular imaging. Lung ultrasound and pulmonary congestion during stress echocardiography. JACC Cardiov Imaging 2020;19:2085-95.
19. Ciampi Q, Zagatina A, Cortigiani L, Gaibazzi N, Borguezan Daros C, Zhuravskaya N, *et al.* Functional, anatomical, and prognostic correlates of coronary flow velocity reserve during stress echocardiography. J Am Coll Cardiol 2019;74:2278-91.
20. Ciampi Q, Zagatina A, Cortigiani L, Wierzbowska-Drabik K, Kasprzak JD, Haberka M, *et al.* Prognostic value of stress echocardiography assessed by the ABCDE protocol. Eur Heart J 2021;42:3869-78.
21. Gaibazzi N, Ciampi Q, Cortigiani L, Wierzbowska-Drabik K, Zagatina A, Djordjevic-Dikic A, *et al.* Multiple phenotypes of chronic coronary syndromes identified by ABCDE stress echocardiography. J Am Soc Echocardiogr 2024;37:477-85.
22. Picano E, Ciampi Q, Arbucci R, Cortigiani L, Zagatina A, Celutkiene J, *et al*. Stress echo 2030: The new ABCDE protocol defining the future of cardiac imaging. Eur Heart J Suppl 2023;25:C63-7.
23. Picano E, Pellikka PA. Stress echo applications beyond coronary artery disease. Eur Heart J 2014;35:1033-40.
24. 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. J Am Soc Echocardiogr 2017;30:101-38.
25. Picano E, Pierard L, Peteiro J, Djordjevic-Dikic A, Sade LE, Cortigiani L, *et al.* The clinical use of stress echocardiography in chronic coronary syndromes and beyond coronary artery disease: A clinical consensus statement from the European Association of Cardiovascular Imaging of the ESC. Eur Heart J Cardiovasc Imaging 2024;25:e65-90.
26. Cortigiani L, Urluescu ML, Coltelli M, Carpeggiani C, Bovenzi F, Picano E. Apparent declining prognostic value of a negative stress echocardiography based on regional wall motion abnormalities in patients with normal resting left ventricular function due to the changing referral profile of the population under study. Circ Cardiovasc Imaging 2019;12:e008564.
27. Smulders MW, Jaarsma C, Nelemans PJ, Bekkers SC, Bucerius J, Leiner T, *et al.* Comparison of the prognostic value of negative non-invasive cardiac investigations in patients with suspected or known coronary artery disease-a meta-analysis. Eur Heart J Cardiovasc Imaging 2017;18:980-7.
28. Lucarini AR, Picano E, Marini C, Favilla S, Salvetti A, Distante A. Activation of sympathetic tone during dipyridamole test. Chest

1992;102:444-7.

29. Picano E, De Pieri G, Salerno JA, Arbustini E, Distante A, Martinelli L, *et al.* Electrocardiographic changes suggestive of myocardial ischemia elicited by dipyridamole infusion in acute rejection early after heart transplantation. Circulation 1990;81:72-7.
30. Hage FG, Iskandrian AE. Heart rate response during vasodilator stress myocardial perfusion imaging: Mechanisms and implications. J Nucl Cardiol 2010;17:536-9.
31. Brubaker PH, Kitzman DW. Chronotropic incompetence: Causes, consequences, and management. Circulation 2011;123:1010-20.
32. Lauer MS, Mehta R, Pashkow FJ, Okin PM, Lee K, Marwick TH. Association of chronotropic incompetence with echocardiographic ischemia and prognosis. J Am Coll Cardiol 1998;32:1280-6.
33. Elhendy A, Mahoney DW, Khandheria BK, Burger K, Pellikka PA. Prognostic significance of impairment of heart rate response to exercise: Impact of left ventricular function and myocardial ischemia. J Am Coll Cardiol 2003;42:823-30.
34. Chaowalit N, McCully RB, Callahan MJ, Mookadam F, Bailey KR, Pellikka PA. Outcomes after normal dobutamine stress echocardiography and predictors of adverse events: Long-term follow-up of 3014 patients. Eur Heart J 2006;27:3039-44.
35. 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;43:2558-66.
36. Picano E, Scali MC, Ciampi Q, Lichtenstein D. Lung ultrasound for the cardiologist. JACC Cardiovasc Imaging 2018;11:1692-705.
37. Reid PG, Fraser AG, Watt AH, Henderson AH, Routledge PA. Acute haemodynamic effects of intravenous infusion of adenosine in conscious man. Eur Heart J 1990;11:1018-28.
38. Vinereanu D, Fraser AG, Robinson M, Lee A, Tweddel A. Adenosine provokes diastolic dysfunction in microvascular angina. Postgrad Med J 2002;78:40-2.
39. Kelshiker MA, Seligman H, Howard JP, Rahman H, Foley M, Nowbar AN, *et al.* Coronary flow reserve and cardiovascular outcomes: A systematic review and meta-analysis. Eur Heart J 2022;43:1582-93.
40. Tesic M, Beleslin B, Giga V, Jovanovic I, Marinkovic J, Trifunovic D, *et al.* Prognostic value of transthoracic Doppler echocardiography coronary flow velocity reserve in patients with asymmetric hypertrophic cardiomyopathy. J Am Heart Assoc 2021;10:e021936.
41. Rigo F, Gherardi S, Galderisi M, Pratali L, Cortigiani L, Sicari R, *et al.* The prognostic impact of coronary flow-reserve assessed by Doppler echocardiography in non-ischaemic dilated cardiomyopathy. Eur Heart J 2006;27:1319-23.
42. Merli E, Ciampi Q, Scali MC, Zagatina A, Merlo PM, Arbucci R, *et al.* Pulmonary congestion during exercise stress echocardiography in ischemic and heart failure patients. Circ Cardiovasc Imaging 2022;15:e013558.
43. Vrints C, Andreotti F, Koskinas KC, Rossello X, Adamo M, Ainslie J, *et al.* 2024 ESC Guidelines for the management of chronic coronary syndromes. Eur Heart J 2024;45:3415-537.
44. Picano E, Vañó E, Rehani MM, Cuocolo A, Mont L, Bodi V, *et al.* The appropriate and justified use of medical radiation in cardiovascular imaging: A position document of the ESC Associations of cardiovascular imaging, percutaneous cardiovascular interventions and electrophysiology. Eur Heart J 2014;35:665-72.
45. Picano E, Vano E, Gale RP, Serruys P. Cardiac radiation exposure and incident cancer: Challenges and opportunities. Eur Heart J Cardiovasc Imaging 2024;25:1620-6.
46. Costantino MF, Cortese F, D'Addeo G, Stolfi L. Diagnostic modalities for ischemic heart disease: Evaluating the role of stress echocardiography, cardiac CT, and myocardial perfusion scintigraphy in guiding coronary angiography. Explor Cardiol 2025;2:97-113.
47. Picano E. Economic, ethical, and environmental sustainability of cardiac imaging. Eur Heart J 2023;44:4748-51.
48. Ciampi Q, Pepi M, Antonini-Canterin F, Barbieri A, Barchitta A, Faganello G, *et al.* Stress echocardiography in Italian echocardiographic laboratories: A survey of the Italian society of echocardiography and cardiovascular imaging. J Cardiovasc Echogr 2023;33:125-32.
49. Wang Y, Ciampi Q, Cortigiani L, Zagatina A, Kasprzak JD, Wierzbowska-Drabik K, *et al.* Predictors of hypercontractile heart phenotype in patients with chronic coronary syndromes or heart failure. Int J Cardiovasc Imaging 2024. [doi: 10.1007/s10554-024-03240-6]. [Online ahead of print].
50. Wang Y, Yin L. Noninvasive identification and therapeutic implications of supernormal left ventricular contractile phenotype. Explor Cardiol 2024;2:97-113.
51. Wang Y, Ciampi Q, Cortigiani L, Zagatina A, Padang R, Kane GC, *et al.* Left ventricular elastance with resting volumetric transthoracic echocardiography identifies different phenotypes in heart failure with preserved ejection fraction: A retrospective analysis of a multicenter prospective observational study. J Am Soc Echocardiogr 2025:S0894-7317(25)00034-3. [doi: 10.1016/j.echo.2024.12.012]. [Online ahead of print].
52. Cortigiani L, Gaibazzi N, Ciampi Q, Rigo F, Rodríguez-Zanella H, Wierzbowska-Drabik K, *et al*. Stress Echo 2030 study group. High Resting Coronary Flow Velocity by Echocardiography Is Associated With Worse Survival in Patients With Chronic Coronary Syndromes. J Am Heart Assoc 2024;13:e031270. [doi: 10.1161/JAHA.123.031270].
53. Pellikka PA. Artificially intelligent interpretation of stress echocardiography: The future is now. JACC Cardiovasc Imaging 2022;15:728-30.
54. Picano E. The Ulysses syndrome of the patient with chronic coronary syndrome. Eur Heart J 2025;46:129-31.