

Echocardiographic assessment of myocardial ischemia

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Abstract: Over the last 60 years, echocardiography has emerged as a dominant and indispensable technique for the detection and assessment of coronary heart disease (CHD). In this review, we will describe and discuss this powerful tool of cardiology, especially in the hands of an experienced user, with a focus on myocardial ischemia. Technical development is still on-going, and various new ultrasound techniques have been established in the field of echocardiography in the last several years, including tissue Doppler imaging (TDI), contrast echocardiography, three-dimensional echocardiography (3DE), and speckle tracking echocardiography (i.e., strain/strain rate-echocardiography). High-end equipment with harmonic imaging, high frame rates and the opportunity to adjust mechanical indices has improved imaging quality. Like all new techniques, these techniques must first be subjected to comprehensive scientific assessment, and appropriate training that accounts for physical and physiological limits should be provided. These limits will constantly be redefined as echocardiographic techniques continue to change, which will present new challenges for the further development of ultrasound technology.

Keywords: Echocardiography; coronary heart disease (CHD); myocardial infarction; stress echocardiography (SE)

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Introduction

Since the introduction of “ultrasound cardiography” (echocardiography) by Edler and Hertz (1-3) and the first trial involving the investigation of cardiac wall abnormalities, echocardiography (3) has become the most important and most used tool in cardiology besides electrocardiography (ECG). The first milestones were the detection of abnormal wall motion during angina pectoris (4) and acute myocardial infarction (AMI) (5). The introductions of two-dimensional echocardiography (2DE), pulsed wave (PW)/continuous wave (CW) Doppler techniques, Echo-Contrast (6-8), Trans-esophageal echocardiography (TEE) (9), tissue Doppler imaging (TDI) (10), three-dimensional echocardiography (3DE) (11), and strain echocardiography (strain) (SE) (12) have

provided numerous tools with which to manage all conditions related to coronary heart disease (CHD). Additional analyses of diastolic function (13) and myocardial architecture using all possible sonographic technologies (14-16) allow for full functional evaluations of cardiac function.

In the hands of an experienced user, echocardiography can be sufficiently reliable to assess all stages of cardiovascular disease. Further substantiation can be provided by the use of the trans-esophageal approach (17-19). It can be postulated that an experienced cardiologist who is very familiar with echocardiography does not need apply additional techniques, with the exception of supplementation with a Troponin test, in the clinical management of patients with chronic cardiovascular disease (20). Although it sounds quite provocative, this hypothesis is

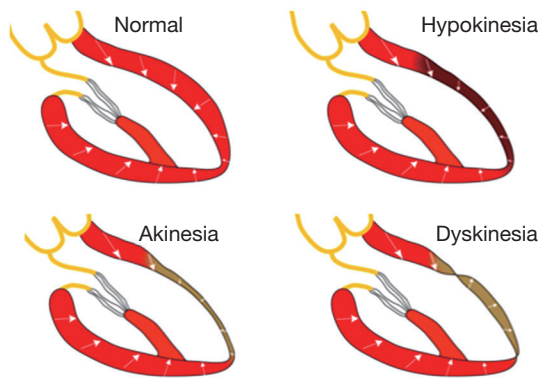


Figure 1 Each myocardial segment [see Lang *et al.* (28)] can be evaluated according to wall thickening and wall motion assessments.

tenable. Cardiovascular magnetic resonance (CMR) (21) and computed tomography (cardio-CT) (22,23) are important tools for ischemic (24) heart disease, but the depth of modern echocardiography (13-15,25-30) and the technical possibilities of advanced echocardiography with the corresponding experience provides many of the answers we need. The use of echocardiography can differ between the USA and Europe. For example, in Germany, cardiologists perform 99% of all examinations themselves. The associated broad clinical expertise provides more options compared with scenarios in which echocardiography is performed by a technician and is based solely on visual expertise. Discussion about the quality improvement process is on-going (31,32).

Echocardiography in the chronic and acute stages of CHD

The physiological response of the myocardial wall to coronary occlusion is the basis for echocardiographic examinations. Tennant and Wiggers were the first to report a reduction in contractility during coronary occlusion (33). This finding was further investigated by Prinzmetal *et al.* (34). Visualization of a regional decrease in the systolic movement of the endocardium and a decrease in myocardial thickening are the main principles for the diagnosis of myocardial damage (*Figure 1*). In recent years, an ischemic cascade was suggested (*Figure 2*) [in the clinical setting, a test for coronary ischemia is not evident in any case what is caused by the different localization of collaterals (35-38)].

2DE provides assessments of the locations and the extent of the acute/chronic stages of CHD (*Figure 3*) (39) and was introduced as “cross-sectional echocardiography”

in 1976 by Feigenbaum *et al.* (40). The main advantage of this technique is the direct clinical use of this method, for example, as a bedside method in the emergency room and in hospital stations and clinical practice. In patients with thoracic pain, we are able to localize regional wall motion abnormalities using wall motion scores (28) (*Figure 1*) at rest and diagnose diseases other than CHD (e.g., pericardial effusion, endocarditis, aortic dissection, and valvular disease). In chest pain units, we can evaluate chest pain patients using SE and thus recognize exercise-induced ischemia and evaluate the need for invasive diagnostics. In experienced hands, this technique is a safe and valuable tool (20).

AMI

The first description of the use of echocardiography involved the use of M-mode technology during acute infarction (5). Fogelman *et al.* described wall motion abnormalities during angina pectoris (4). The extent of myocardial ischemia during myocardial infarction should be evaluated by 2DE according to the ASE criteria (28). Additionally, techniques such as PW-Doppler, TDI, strain and 3DE (11) extend the possibilities and supply additional functional or geometrical (11) information, but in the acute phase of infarction, analyses of wall abnormalities or wall structure and valve function via color Doppler provide sufficient clinical information and enables the identification of addition complications of extended infarction, such as inter-ventricular shunts caused by infarction (*Figures 4,5*), papillary muscle dysfunction and perimyocardial effusion. One of the simplest types of information is that provided by acute measurements of wall motion scores or ejection fractions and analyses of the extent of hypokinesia or akinesia (*Figure 1*) in terms of the myocardial wall segments. Myocardial contrast echocardiography in AMI (given that the infarction is intracoronary) delineates the area that is at risk for necrosis and the extent of collateral blood flow (41) and aids the evaluation of the microvasculature for “no-reflow” areas. Serial intravenous myocardial contrast echocardiography has the potential to identify patients who are likely to exhibit improved left ventricular function after AMI and can be used to define perfusion defects (42).

Chronic stages of ischemic coronary disease

Ventricular remodeling after myocardial infarction is a primary issue in echocardiography (43). The management of patients in the chronic stages of ischemic heart disease

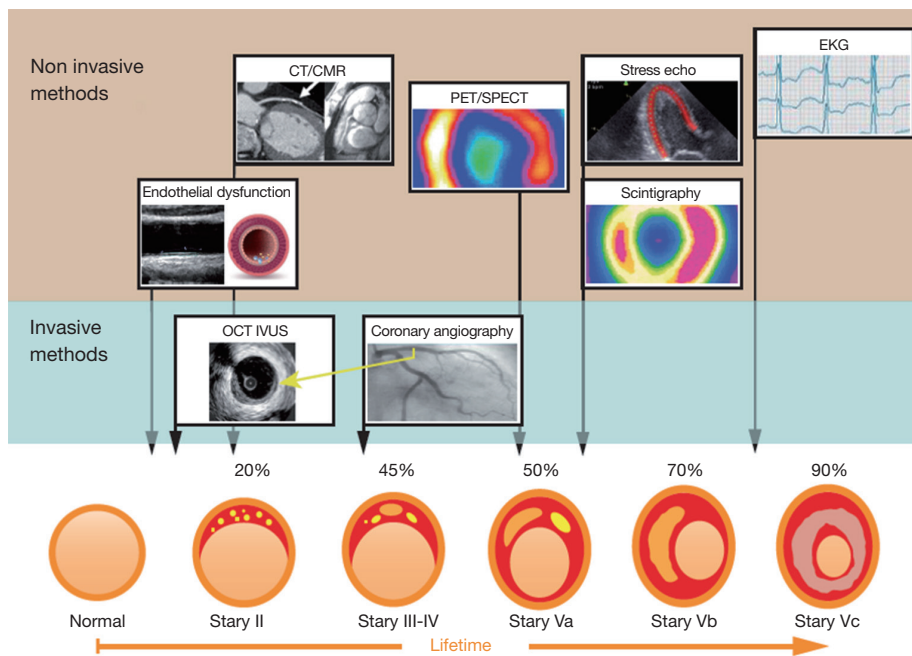


Figure 2 Ischemic cascade.

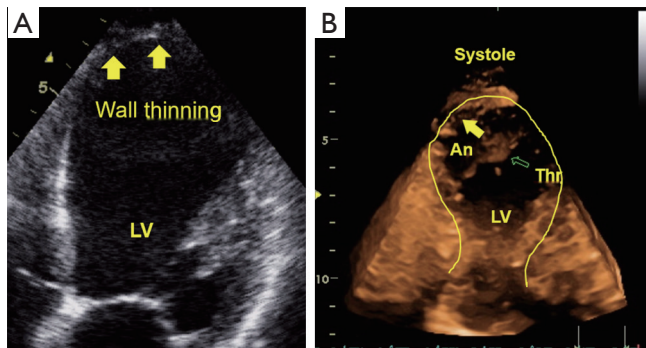


Figure 3 Two-dimensional echocardiography elucidates wall thinning in cases of anterior wall infarction (A). In (B), a left ventricular aneurysm (An) and an apical thrombus are visualized (3DE).

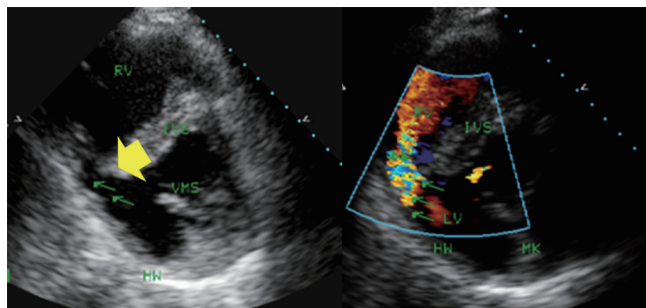


Figure 4 Inter-ventricular septum defect (VSD) after acute myocardial infarction (arrows) with shunt (color Doppler).

requires the following important information: (I) global and regional contractile function of the heart at rest; (II) valvular function; and (III) local complications, such as mural thrombi, myocardial scars and ventricular septal defects. Information concerning these three points can be provided by basic 2DE. Using additional techniques, such as PW Doppler, color Doppler or TDI/strain or 3DE, we are able to perform full conservative assessments of cardiac function, including right ventricle (RV) and left ventricle (LV) function, to manage the patient without the complications of an infarction and manage patients with heart failure in all stages of the disease. After an acute infarction, it may be important to know whether the patient develops an apical LV aneurysm (Figure 3, which usually occurs after anterior myocardial infarction). This type of aneurysm exhibits greater hemodynamically effects than inferior/posterior aneurysms. Early reperfusion strategies in many countries with 24-h PCI-attendance reduce the development of LV aneurysms. Using all views (including the subcostal echo window) and all lying positions of the patient, it is possible to obtain echocardiograms that enable sufficient visual evaluation and clinical management that reaches 100%. Under these conditions and managements, obese patients can also be examined echocardiographically. Indeed, we have experienced greater difficulties with patients with severe chronic pulmonary disease.

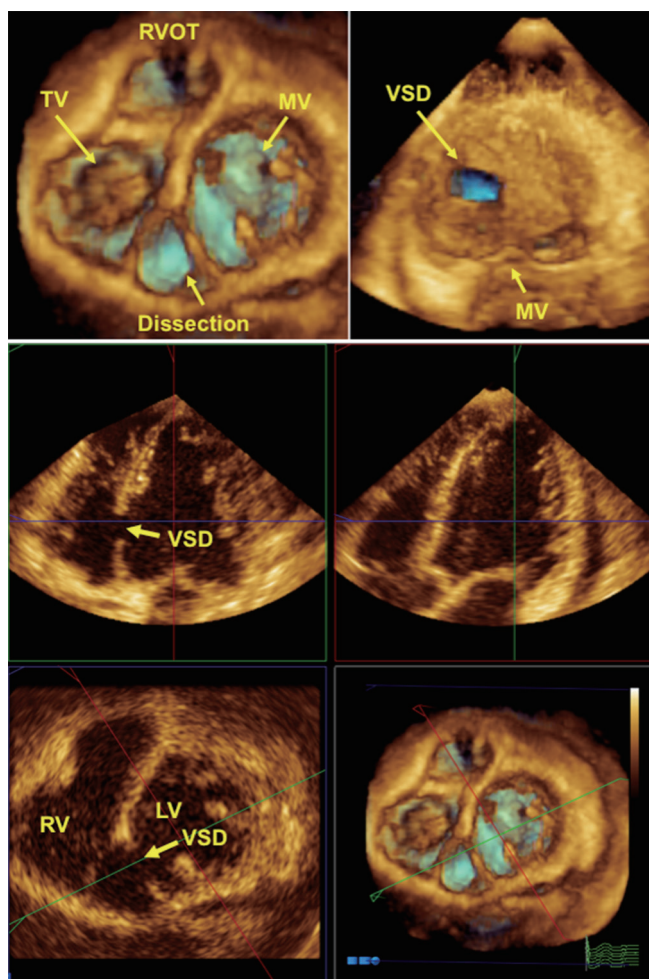


Figure 5 Inter-ventricular septum defect (VSD) and dissection of the interventricular septum after anterior myocardial infarction (from Buck, Franke, Monaghan, eds. *Three-dimensional Echocardiography*, Springer, 2015).



Figure 6 Stress echocardiography during exercise illustrating apical ischemia.

SE

In the last 35 years, since one of the first descriptions of two-dimensional stress echocardiography (2D-SE) by Wann

et al. (44), 2D-SE has considerably developed. This method is cost effective, safe and free of non-ionizing radiation (32). SE is one of the most important tools for assessing myocardial ischemia (20,29,45) and viable myocardia (46,47), in addition being easy to use at the bedside (45,48). Developments in digital hardware and software and improvements in ultrasound techniques have yielded excellent results from SE regarding scanning for ischemia (Figure 6) and risk assessment (45,49-52), screening after PTCA (53) and testing for anti-ischemic drug effects (54). Recent studies have demonstrated the advantages of exercise echocardiography from the prognostic perspective in patients with known and unknown CHD (20) and left bundle branch block (55). In patients who have undergone non-surgical revascularization (56), studies have demonstrated that analyses of quantitative parameters determined by exercise echocardiography increase the sensitivity of the diagnosis of restenosis (57).

SE can be performed using physical exercise (e.g., bicycles and treadmills), atrial pacing, and various drugs, such as dobutamine, dipyridamole and adenosine. The sensitivity of catecholamine SE is lower than that of peak exercise echocardiography, but dobutamine SE is technically simpler and can be performed in patients who are unable to exercise. The limitations of pharmacological stress are adverse side effects and the more time-consuming stress procedure. In assessments of patients with CHD, SE has been demonstrated to be valuable for diagnosis and prognosis (20). Furthermore, there are different stress modalities (in particular, low-dose dobutamine stress) for the detection of viable myocardium (46). Despite the high reported accuracy of exercise echocardiography in the diagnosis of CHD, the sensitivity and specificity can be affected by multiple factors (58,59). In most cases, decreased accuracy is caused by suboptimal image quality and decreased detection of the endocardial border. The diagnostic accuracy of SE depends on the type of stress procedure utilized, the digital processing technique and the experience of the investigator (59). The inter-institutional observer variance in the interpretation of SE varies from agreements of 100% to 43% in the lowest image quality stress echocardiograms (58). Presently, we have to decide which technique we should select as the gatekeeper to cardiac catheterization (60). It can be suggested that in each clinical situation, we need to select the technique and stress method for which we have the optimal personal/individual expertise (59), and we have to consider the economic and biological costs of all cardiac imaging techniques (61).

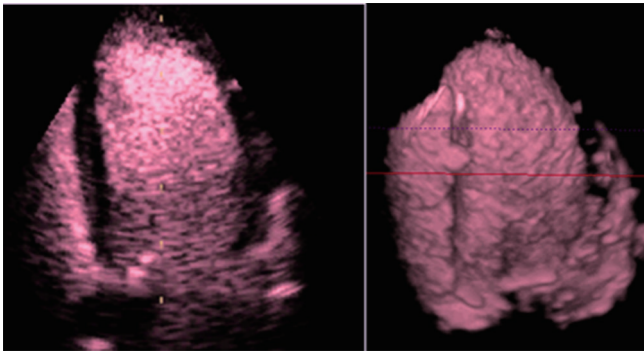


Figure 7 Intravenous Contrast Echocardiography delineates the left ventricular border and illustrates the plasticity of the left ventricle volume in three-dimensional echocardiography (3DE).

Novel techniques and screening for ischemia

In recent years, ultrasound technology has developed rapidly with continuous improvements in image quality and the use of new approaches (e.g., TDI, strain, contrast echocardiography, and 3DE). Thus, new ischemic indicators need to be identified (12,29,62-65). TDI has provided new insight into the analysis of myocardial mechanics in patients with coronary disease (10,62,66). The clinical utility of the TDI technology has offered new insight into the analysis of LV dyssynchrony (67,68), and among the most frequently used applications are the evaluation of diastolic function (13,69,70) and the appraisal of LV end-diastolic pressure (71) (E/e' ratio) (72). The last issue remains controversial (73).

Contrast echocardiography (Figure 7) has been well introduced to the clinical and scientific settings (6,74,75) and has a safe place regarding volume diagnostics and improvements in endocardial border visualization (76-78). The technique can be recommended for patients with poor acoustic windows and is applicable when CMR cannot be performed (79).

Strain-technology (speckle tracking imaging) was introduced in 1998 by Heimdal *et al.* (12) to determine the deformation or strain of the myocardial tissue. The rate of this deformation, i.e., the strain rate, is equivalent to the myocardial velocity gradient. The strain rate has been described as equivalent to the shortening velocity per fiber length (12). It's postulated that it can also be used to evaluate the function of the ventricular fiber architecture (80,81) and to measure dynamic changes in the geometry and fibrous structure of the heart (82). Acute systolic and diastolic changes during angioplasty could potentially be

evaluated using strain and strain rate measurements (83) as well as early changes in myocardial function in hypertensive patients could be detected (30). The first announcements about the use of strain-technology in CHD were published by Voigt *et al.* (84,85). The first clinical use was suggested as early as 2003 (86), and today, further standards for the analyses of left myocardial function are being proposed (65). The use of apical views for the evaluation of cardiac deformation seems to be clinically useful (87), and apical views result in the best reproducibility (88). Analyses of systolic regional deformations (Figure 8), the diastolic properties in CHD, estimations of LV filling and left atrial function (73) are further advantages of this technology. The value of myocardial deformation imaging using speckle tracking echocardiography (strain) has been suggested to be comparable with that of CMR (89). We are looking forward to new comprehensive research with new technologies and equipment with better resolution to achieve reliable and safe diagnoses in myocardial ischemia using echocardiography.

Pitfalls and limitations of diagnosing ischemia via echocardiography

Basically, the diagnosis of ischemia using echocardiography is safe and has a secure place in the management of stable angina pectoris (90). However, one constant problem is reproducibility (58,77,88). Additional second problem is the "low volume" of SE examinations by a single operator in clinical practice (32). In the UK, only 28.2% of operators performed >500 procedures/year. At the frame rates of 3DE and SE, spatial and temporal resolution are problems. In general, when 3DE is used for stress examination, if the heart rate is >110 beats/min [we need >130 beats/min from the prognostic perspective (20)], the acquisition of a sufficient number of volumes per heart cycle becomes a problem. An additional problem can be the acoustic window for echocardiography when a safe answer for decision making regarding interventional procedures is needed (91,92). In these cases, an additional imaging technology, such as CMR or single-photon emission computed tomography (SPECT), is needed. It seems that echo contrast improves endocardial border detection and can improve the reproducibility of LV volume estimation (77). The intravenous injection of contrast agent improves the opacification of the myocardial border, but the analysis of myocardial perfusion remains problematic (78). Even after 20 years of research, echocardiographic perfusion analysis is not sufficiently reliable (and perhaps too expensive) and

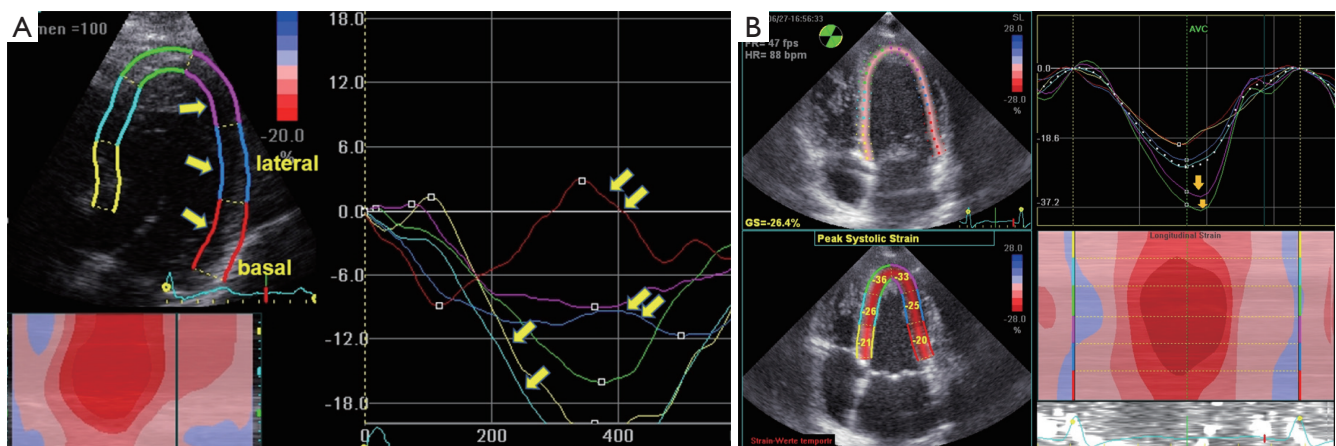


Figure 8 (A) Longitudinal strain: Preserved strains septally (single arrows) and considerably impaired strain values basally and laterally after posterior-lateral infarction (double arrows); (B) normal strain values with “hyper-performance” of the apical segments (arrows).

has failed to be implemented in daily routines despite some reports have demonstrated opposite results (6,74,91,93). Myocardial perfusion analysis using CMR and SPECT seems to be more reliable and safer (24,90,91).

Conclusions and insights for the future

When using echocardiography to assess ischemia, the results obtained at rest *vs.* those obtained during exercise need to be differentiated. We suggest that, regarding resting assessments, echocardiography combined with all of the new developments (e.g., 3DE, harmonic imaging, TDI, strain, and contrast echocardiography) offers at least as many advantages (and can be nearly as reliable) as CMR when conducted by experienced operators, given that it is possible to obtain individual acoustic windows and a regional evaluation of the myocardium. For exercise assessments, there is a resolution limitation that is caused by non-sufficient scanning conditions in nearly 5% of patients, and for these patients, additional imaging techniques should be recommended. When using echocardiography to evaluate cardiovascular disease, we need to consider the following issues:

- (I) Daily clinical use;
- (II) Institutional/personal availability (in terms of costs, education, and equipment);
- (III) Principal technical opportunities;
- (IV) Research situations and the “pressure to publish”.

Referring to (I): for daily use, we need and have a simple, reliable, safe situation for the use of 2DE (a high-end machine) in combination with Doppler/TDI/strain/3DE

and contrast echocardiography for use in clinical decision-making.

Referring to (II): it is necessary to become an expert and to strive for improvement even after 30 years of experience. Additionally, there is a need for high-quality equipment and intensive training of the operator with continuous updates regarding new developments in the field.

Referring to (III): the technical opportunities for high-end sonographic devices are great, and these opportunities combined with workstations are rarely ever fully exploited in daily routines or even in research. This issue must be considered by cardiologists in their daily work. Otherwise, there is a risk of becoming frustrated due to failure in reaching the goals presented in presentations and publications.

Referring to (IV): work on new developments and with new equipment is always exciting and stimulating. Only due to this enthusiasm were all of the following new technologies introduced into daily practice: 2DE, color Doppler, SE, TDI, 3DE, and Strain. This enthusiasm persisted despite all of the initial attempts to use the new technologies being called “crazy”. Echocardiography is an excellent tool for the diagnosis of acute, chronic and exercise-induced ischemia. The critical use of echocardiography is recommended (94). In brief, it is necessary to use echocardiography in the assessment of CHD, and it is important to gain solid expertise with the related techniques (59).

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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