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Stress Echocardiography and Risk Stratification in Patients with Suspected Ischemic Heart Disease: Review Article

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ABSTRACT

Background: In addition to atherosclerosis, non-atherosclerotic occlusive disease and vasospasms all contribute to coronary artery disease (CAD). The leading cause of CAD, atherosclerosis, continues to be a leading contributor to mortality as well as disability globally. Several possible indicators and imaging techniques exist with the potential to enhance diagnosis accuracy in stable CAD. Stress echocardiography and computed tomography coronary angiogram are two of the most prominent imaging techniques.

Objective: Review of literature about Stress echocardiography and Risk stratification in patients with suspected ischemic heart disease.

Methods: Ischemic heart disease and Stress Echocardiography were searched for on Science Direct, Google Scholar, and PubMed. The authors also reviewed the relevant literature, Nonetheless, only the most recent or exhaustive analysis was included, covering the time span from January 1997 to August 2021.There are no translation resources available, thus non-English documents are out. Unpublished articles, oral presentations, conference abstracts, and dissertations were not included because they were not considered to be part of major scientific projects.

Conclusion: The use of stress echocardiography has expanded greatly in recent years as a diagnostic and prognostic tool for patients suspected of having coronary artery disease (CAD).

Keywords: Ischemic heart disease, Coronary artery disease, Stress echocardiography.

INTRODUCTION

In addition to atherosclerosis, non-atherosclerotic occlusive disease and vasospasms all contribute to coronary artery disease (CAD). Risk factor reduction, screening and early identification, and early and effective treatment are just some of the methods available for reducing the incidence of atherosclerosis and the deaths it causes. The diagnosis of vasospasm typically involves ruling out obstructive coronary artery disease because it is so common [(1)].

When it comes to people who are at a high absolute risk of developing CAD, aggressive therapy typically renders extra non-invasive testing unnecessary. Similarly, additional non-invasive testing is unnecessary in low-risk patients. Many people, however, fall somewhere in the middle and could benefit from further non-invasive risk stratification in order to "subclassify" risk/prognosis and guide future therapy [(2)].

Therefore, the preferred modality would be one that is easily accessible, has sufficient knowledge, is cost-effective, uses a low dose of radiation, and accurately diagnoses and predicts outcomes. The aforementioned requirements can be satisfied through stress echocardiography. However, CT angiography is recommended as a primary investigation according to the NICE guidelines. CT angiography's limited specificity and lack of ability to diagnose ischemia result in more frequent follow-up exams, although the findings of the most recent SCOT-Heart study may help to justify this choice [(3, 4)].

Stress echocardiography:

Stress can come in the form of either exercise or medication. Exercise equipment (Treadmill vs. bicycle) is now a question of personal preference and lab protocol. When working out on a treadmill, the only option for imaging is after the fact. This raises the prospect of a false-negative study due to the quick resolution of WMA. This is especially true in mild or single-vessel stenosis. The heart can be imaged at peak exercise intensity when cycling. Theoretically, this could lead to a higher degree of sensitivity, allowing for earlier identification of ischemia. To prevent the resolution of stress-induced WMA, imaging after the treadmill must be conducted within 45 to 60 seconds [(5)].

For patients who are unable to participate in sufficient physical activity, pharmacologic stress may be an alternative. The most common medications are dobutamine and dipyridamole (or adenosine). Due to its low cost and wide availability, dobutamine has become the drug of choice in the United States. Myocardial oxygen demand and flow disparity are both raised when dobutamine and dipyridamole are administered together. Heart arrhythmias can be treated in non-exercise ways, such as with stress pacing by transvenous catheter, permanent pacemaker, or transesophageal atrial pacing. When evaluating dyspnoea and tiredness, as well as the presence or absence of coronary artery disease in exercise-capable patients, exercise is preferred over pharmacologic testing. Although the tricuspid regurgitation jet has been shown to accurately reflect the response of the pulmonary artery pressure to exercise, this does not hold true when pharmacologic stress is applied [(4)].

Stress echocardiograms Analysis:

Stress echocardiogram analysis is a complex part of echocardiography, and only individuals with the appropriate knowledge and experience should attempt it. Multiple scales are available for analysing wall motion. The basic qualitative assessment of normal versus pathological regional wall motion using adjectives like

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"normal," "hypokinetic," "akinetic," and "dyskinetic" is a quantitative method. Other quantitative methods include measuring ventricular sizes, ejection fractions, chordal and area shrinkage. After describing segments as "normal," "hypokinetic," "akinetic," or "dyskinetic," a wall motion score is sometimes generated [6].

The intensity and spread of WMA can be quantified by a unitless quantity called a wall motion score index. Each segment of the left ventricle (LV) is assigned a value between one and four that is used in the calculation (normal, hypokinetic, akinetic, or dyskinetic, respectively). Total segment scores are averaged and then divided by the total number of segments to determine the wall motion score. Stress echocardiograms can be evaluated with more than just the typical image analysis technologies. Doppler tissue imaging has lately been used for quantitative assessment of resting and stressed heart mechanics, and most investigations show that it is more sensitive than visual examination alone. It is possible to use Doppler methods to determine strain or strain rate. Myocardial ischemia can be detected with greater sensitivity using strain rate imaging than either Doppler tissue velocity or displacement, according to preliminary research. However, standard clinical laboratories have not yet adopted these methods [6].

The hemodynamic response to vasodilator stress is not a reliable indicator of diagnosis or prognosis. Some patients experience a paradoxical drop in blood pressure during dobutamine stress echocardiography (DSE). Hypotension during DSE does not always indicate serious ischemia, unlike during exercise [7].

Evaluation of myocardial thickening and endocardial motion is crucial to the reliability of stress echocardiography, hence it's important that all myocardial segments may be clearly seen. Tissue harmonic imaging has substantially improved the capacity to detect and examine different layers of wall. Intravenous contrast for LV cavity opacification improves delineation of the endocardial border and may save a flawed study [4].

Role of stress echocardiography in CAD:

Stress echocardiography is typically utilised in the CAD diagnostic process and prognostic evaluations. Diagnosing CAD requires the detection of a WMA, either at rest or during induction. Abnormalities in wall motion while at rest are indicative of infarction or of sufficient resting ischemia to induce systolic dysfunction. The existence of obstructive CAD is indicated if WMA is triggered at times of stress. In most cases, a qualitative evaluation is all that is needed to make the diagnosis of CAD. Myocardial infarction risk assessment, prognosis, and risk stratification may all benefit from the semiquantitative aspect of wall motion score calculation [8].

Studies claiming the highest sensitivity had a specificity of 64%, while studies reporting the lowest sensitivity had a specificity of 90%, as expected, when the WMA threshold level for a positive study was dropped. Single-vessel disease detection sensitivity has historically been lower (59% to 94%) than multi-vessel disease detection sensitivity across all imaging modalities (85 to 100%). Despite the great sensitivity, it is common to underestimate the number of damaged vessels when trying to diagnose patients with multivessel disease. When an ST-segment depression or angina cause a test to be terminated, this phenomena occurs. This means that less severe stenoses may go unreported because the investigation will be stopped when the most important lesion becomes revealed. Overall accuracy has remained rather high despite a decline in sensitivity due to greater specificity (69 to 92%). DSE has been observed to have a similar degree of accuracy with many of the same limitations [9].

Determining what constitutes a "substantial" degree of stenosis is a challenge for sensitivity analysis. As with all other diagnostic imaging modalities, sensitivity improves when considering severe stenosis to be a threshold of 70% diameter narrowing, whereas it declines when the threshold is decreased to 50% diameter narrowing. When compared to an angiographic gold standard, stress echocardiography can be inaccurate in a few different scenarios. The latter scenario results in less wall stress and an increased possibility of a false-negative finding. Several studies have compared how well the LAD and the posterior circulation detect coronary lesions (right and circumflex coronary arteries). Patients with coronary disease can be identified with about the same precision using either approach, however blockages can be identified with greater precision with the LAD. This is likely due to the fact that the anterior circulation supplies blood to a larger portion of the heart and that the LAD territory is easier to image than the posterior endocardium. It's not easy to tell the right coronary artery from the circumflex coronary artery because their territories overlap [10].

Any technical complication that slows down the imaging process, as well as inadequate image quality, might have a negative effect on accuracy. As is the case with other types of stress testing, the sensitivity for identifying CAD will decrease if the level of physical stress is modest, resulting to a light cardiovascular workload. The effect of a slow heart rate on the reliability of pharmacologic stress testing is less well understood. Traditional measures of cardiovascular workload may not be applicable when dealing with vasodilator stress because it does not depend on increasing cardiovascular activity. Dobutamine increases myocardial oxygen demand in a manner analogous to that of exercise by increasing heart rate and blood pressure through effects primarily on contractility. As a result, in the context of a hyperdynamic reaction, a "suboptimal" heart rate response to dobutamine could not lead to as much of a fall in accuracy as a similar decline in heart rate with physical stress. Atropine, administered either at the peak dose of dobutamine or frequently during intermediate phases (usually 20 g/kg/min), can increase heart rate if desired [4].

Stress echocardiography's diagnostic efficacy has been compared to that of alternative methods. The accuracy of stress echocardiography and radionuclide scintigraphy are roughly equal when compared head-to-head in similarly equipped laboratories. Stress

echocardiography was found to have a higher specificity than radionuclide imaging in a meta-analysis, although having similar sensitivity to radionuclide imaging. Radionuclide scintigraphy has certain advantages over other imaging modalities since the data can be easily measured and used in longitudinal research. Stress echocardiography is advantageous in comparison to other diagnostic methods because of its adaptability and capacity to assess multiple types of heart illness at once [(11)].

Similarly to other methods, stress echocardiography validation studies are vulnerable to referral and test verification bias. Overestimating sensitivity is common in preliminary research due to referral and verification bias. Sensitivities are often lower and specificities are typically greater in the unselected general population after adjusting for referral and verification bias [(12)].

Cardiac risk stratification Using stress echocardiography:

Diagnostic and prognostic features:

The results of a stress echocardiogram are given using a classification system that categorises wall motion as either normal, ischemic, viable, or damaged myocardium. At rest, parts of normal myocardium move normally, and following stress, all segments move normally or hyperkinesially, leading to an increase in ejection fraction. Positive test results require a change from normal to hypokinetic, akinetic, or dyskinetic contractile activity following stress in at least two consecutive segments of ischemic myocardium. Resting dysfunction (hypokinesis or akinesis) is permanent in myocardial with scarring (from a previous MI). When segments with resting hypokinesis improve with stress and continue to improve after stress is applied (indicating the presence of "stunning"), or when segments with resting hypokinesis improve during the early stress phase and then deteriorate at peak (i.e., biphasic response), the myocardium is considered viable and may benefit from revascularization [(13)].

In comparison to stress ECG alone, stress echocardiography has higher diagnostic accuracy, and it does so without exposing the patient to harmful levels of radiation. This makes it a go-to screening method for women in their mid-30 s who are showing symptoms and have a moderate risk of cardiovascular disease. Patients experiencing dyspnea may also benefit from this, as additional hemodynamic examination can be performed during the same procedure. There is prognostic value in stress echocardiography. A cardiac event rate of less than 1% per year is associated with a normal test showing no regional wall-motion anomalies. Increasing frequency of clinical events are correlated with more severe regional wall-motion anomalies following peak stress [(14)].

Limitations:

Stress echocardiography interpretation might be subjective like any other imaging modality. Therefore, it is critical to have reliable imaging techniques, high-quality acquisitions, and skilled professionals to evaluate the results. Mild ischemia caused by tiny, distant, or branch-vessel illness may go undetected by stress echocardiography, and the technique is generally regarded as less sensitive than nuclear imaging. Poor acoustic windows, which can lead to less-than-ideal images in patients with obesity or emphysema [(14)].

Patients with known or suspected CAD:

Clinical factors, exercise duration, ECG alterations, and resting ventricular function all play a role in predicting cardiac events, but the information acquired from regional and global ventricular function at peak exercise is particularly useful. Regardless of age or gender, this predictive value has been demonstrated in a variety of clinical subgroups, including hypertension and diabetes mellitus. If your exercise wall motion score index is greater than 1.4 or your ejection fraction is less than 50%, your outlook is not looking good. This cutoff for prognosis is comparable to that of a radionuclide perfusion deficit of >15%. The Duke Treadmill score and exercise echocardiography data have been integrated to better stratify cardiac risk [(15)].

Although ventricular function at peak exertion is the strongest independent predictor of prognosis, other strong prognostic indications include ischemic ST-segment depression and exercise duration. Recently, a risk index incorporating echocardiographic and exercise features has been used to verify and improve the negative predictive value of exercise echocardiography for cardiac events (Figure 1). The annual rate of spontaneous cardiac events is less than one percent in those with high exercise tolerance and normal exercise echocardiography. Costs associated with diagnosing and treating patients with known or suspected CAD can be reduced by using exercise echocardiography instead of exercise electrocardiography. It has been shown

that pharmacologic stress with dobutamine or dipyridamole, like exercise echocardiography, has significant predictive power. A bad prognosis is indicated by the presence of more severe WMA, left ventricular (LV) dilatation at peak stress, and early start of ischemia. The risk of spontaneous cardiovascular events is normally just 1.5% per year, but it can be as high as 8% in those with a normal dobutamine stress echocardiogram. Changes in population and health are two possible explanations [(16)].

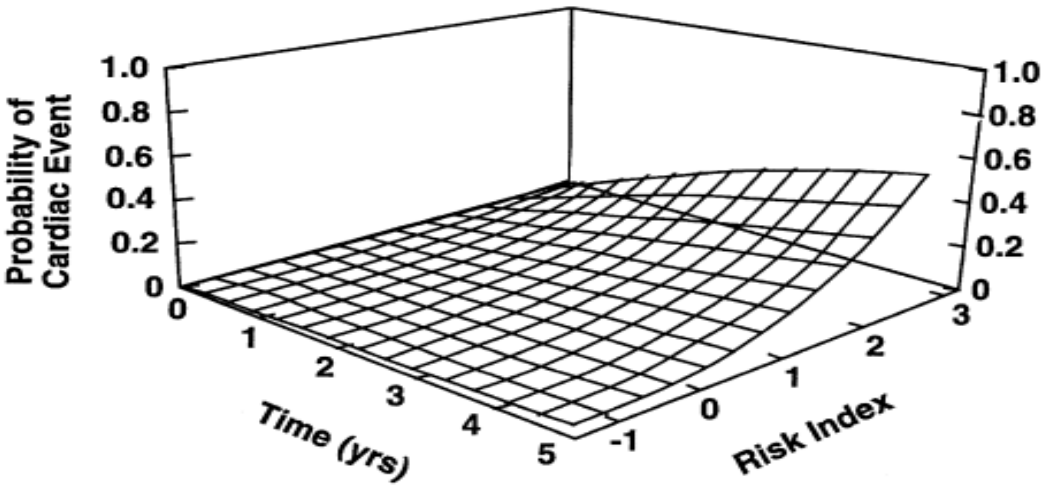

Figure (1): Exercise echocardiography and the risk of cardiac events in the subsequent five years: a probabilistic hazard model [(16)].

Post-acute myocardial infarction prognosis:

Patients at high risk after an acute myocardial infarction can be identified with the help of clinical signs such recurring post-infarction angina, old age, heart failure, and cardiogenic shock. However, the absence of these clinical characteristics is insufficient to infer a benign course. Ejection fraction of the left ventricle (LV), ventricular dysrhythmias, and the presence of residual or remote myocardial ischemia are all factors that improve risk categorization. Stress echocardiography is able to detect stress-induced WMA, which is the result of residual or distal ischemia. A deteriorating prognosis is associated with stress-induced ventricular dysfunction following infarction. Most previous research has relied on the use of pharmaceutical stress [(17)].

Preoperative risk assessment:

Determining the patient's cardiac risk prior to major noncardiac surgery is an important clinical challenge. In terms of clinical predictions, myocardial infarction and cardiac death are most strongly associated with a history of infarction, angina, heart failure, and diabetes mellitus. Patients with more than one of these risk factors require more thorough evaluation. Since most patients undergoing preoperative evaluations for major surgical procedures, especially vascular procedures, cannot exercise to the necessary levels, pharmacologic stress testing is preferable. Dobutamine stress testing improves risk classification for patients undergoing vascular or nonvascular surgery [(18)].

The best predictor of cardiac events is a low ischemia threshold during stress testing, defined as a heart rate 70% of the age-predicted maximal heart rate. Recent meta-analyses have shown that stress echocardiography has predictive power that is comparable to, if not greater than, that seen with radionuclide testing. Patients having major noncardiac surgery benefit from beta-blocker therapy because it reduces the risk of cardiac events during the perioperative period. Beta-blocker patients, in particular those with three or more clinical risk factors, benefited from DSE for additional risk stratification [(18)].

Myocardial viability and the role of stress echocardiography:

Myocardial damage may be reversible in cases of chronic systolic ventricular failure. Intact myocardial perfusion and metabolism, in addition to contractile reserve to inotropic stimulation, have all been used as indicators of myocardial vitality. DSE has been demonstrated to be useful in assessing myocardial viability in a number of research studies. Dobutamine infusion at increasing doses improves regional function in malfunctioning segments, which is a good predictor of post-revascularization function restoration. Differences in contractile reserve are shown by administering high- and low-dose dobutamine, which has major ramifications for prognosis and the rate of function recovery following revascularization [(19)]. Regaining function following revascularization is most reliably predicted by a two-stage response. DSE's sensitivity for forecasting functional recovery is improved by including other types of dobutamine responses (such as any contractile reserve) but at the expense of specificity. Investigations comparing DSE to radionuclide studies for viability determination have found that the latter have slightly higher sensitivity but lower specificity [(19)].

One additional measure of cardiac health is wall thickness. Very little hope of survival and function restoration following revascularization exists in myocardium that is thin (6 mm) (negative predictive value of 93%). For echocardiography to be most accurate in predicting functional recovery. Predicting future ischemia episodes and increased overall mortality is defective, viable myocardium that has not been revascularized, according to observational research. Individuals with decreased ventricular function and no indication of myocardial viability, as shown by recent DSE investigations, have a very dismal prognosis regardless of whether or not they undergo revascularization. Myocardial viability patients who do not get revascularization have a similarly dismal outlook. Patients with radiological or PET indications of myocardial viability who underwent revascularization had the greatest long-term outcomes [(20)].

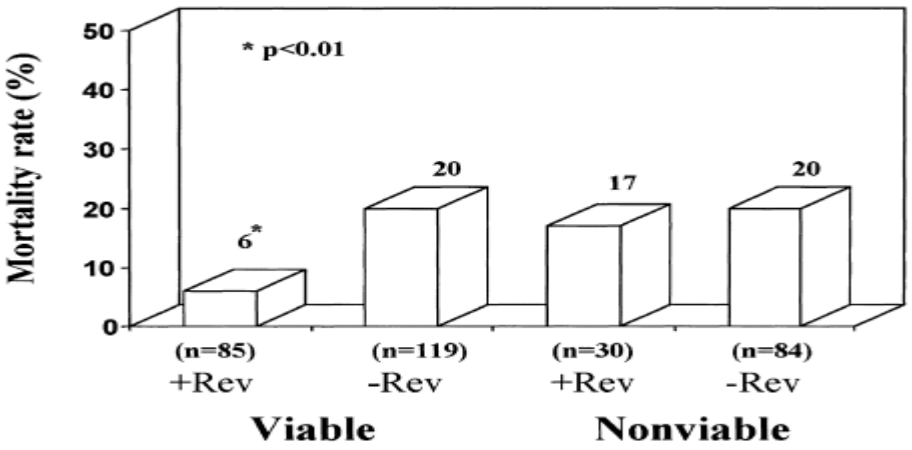

Figure (2): The effect of dobutamine stress echocardiography (DSE) on mortality in patients with ischemic left ventricular (LV) failure [(20)].

Recent advances in stress echocardiography:
Real-time three-dimensional (3D) imaging:

Recent developments in transducer and computer technology have made real-time 3D echocardiography possible for the first time. Within one to four cardiac cycles, a 3D volume set can be acquired in real-time.

Foreshortening of the ventricle can be avoided and accuracy may be improved with several off-line tomographic interrogations made possible by the subsequent analysis. In the same way that two-dimensional echocardiography can improve endocardial border definition and perhaps myocardial perfusion, contrast echocardiography can do the same. Early research on the use of 3D echocardiography to monitor the heart's response to pharmacological stress is promising [(21)].

Evaluation of simultaneous myocardial perfusion with contrast echocardiography:

Myocardial contrast echocardiography has come a long way in the past decade thanks to the discovery of microbubbles that can traverse the pulmonary circulation, enhance LV border delineation, and evaluate myocardial perfusion. Due to the instability of microbubbles when exposed to ultrasonic radiation, imaging them needs either low-power or intermittent imaging. Using these methods in conjunction with vasodilator stress, DSE, or exercise to image myocardial perfusion has been shown to be feasible in preliminary trials. Attenuation at the heart base and variability in regional perfusion parameters are two current drawbacks of the approach. Stress myocardial contrast echocardiography is now being tested in large-scale clinical trials to determine its efficacy in comparison with radioactive perfusion methods and angiography [(22)].

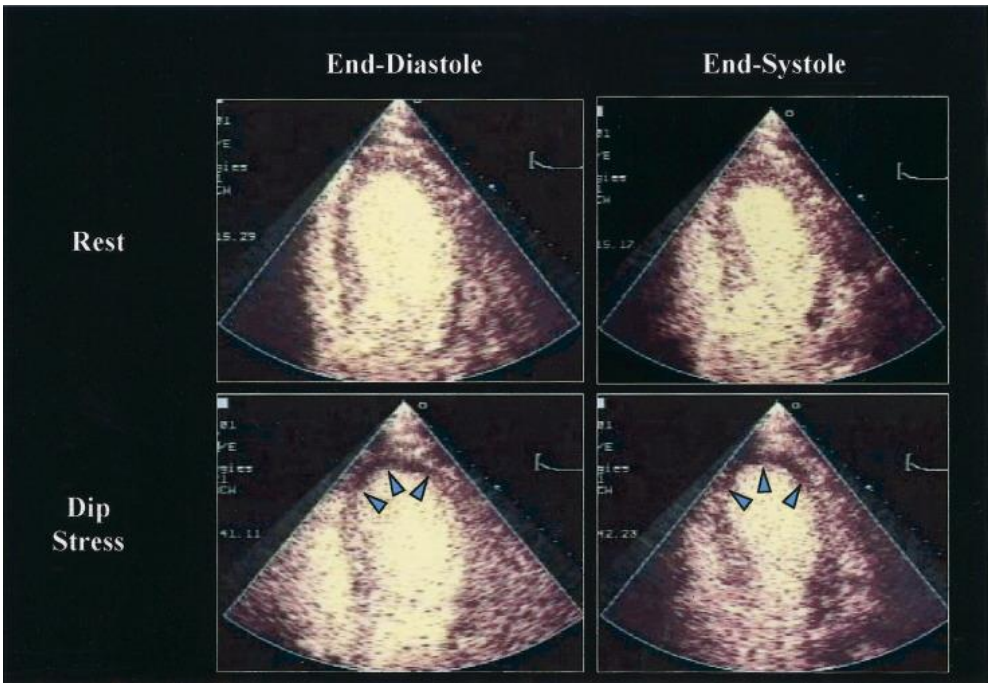

Figure (3): Pictures of a patient's heart taken during a dipyridamole (Dip) stress contrast echocardiogram reveal significant stenosis of the left anterior descending coronary artery [(23)].

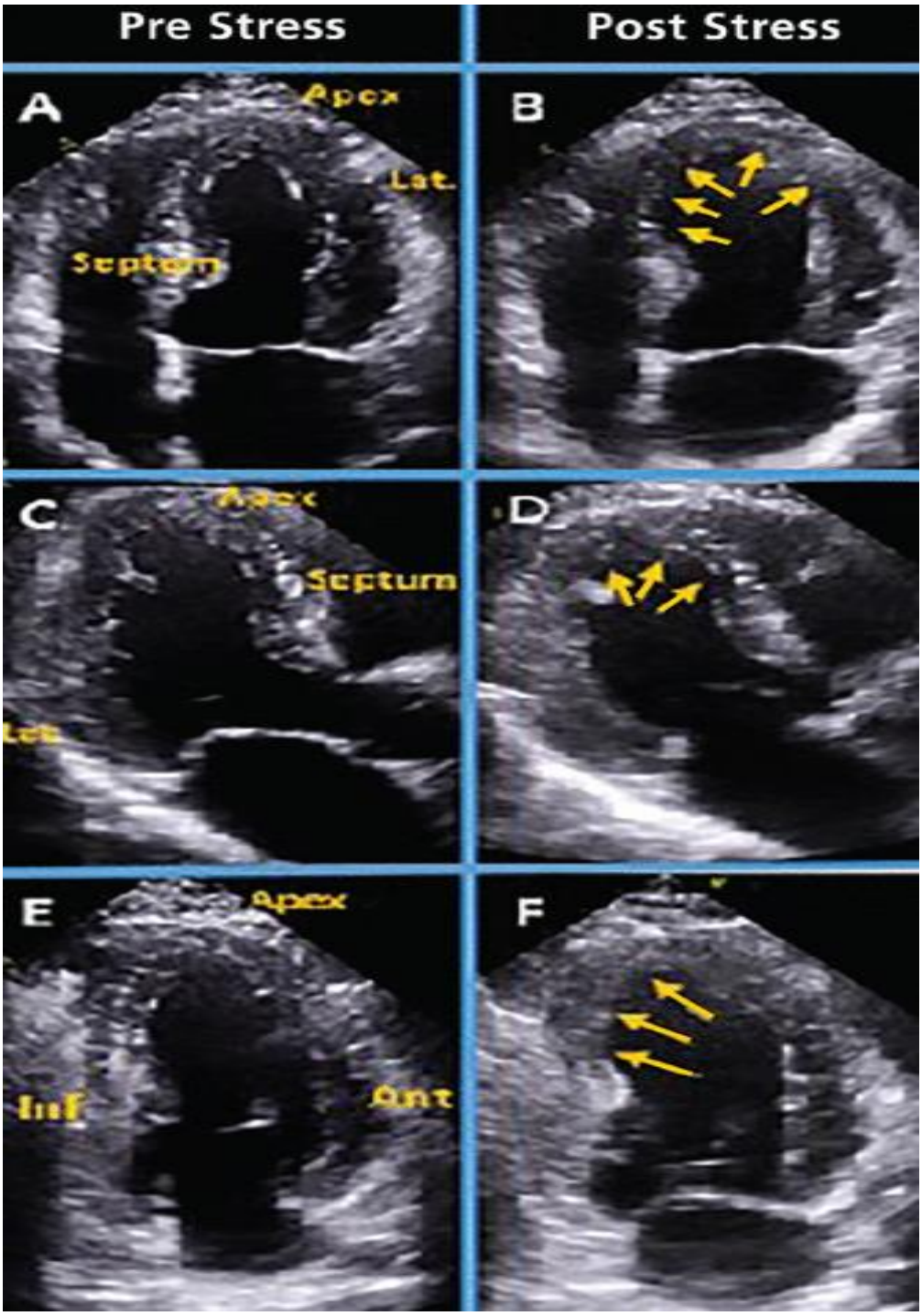

Figure (4): A stress echocardiogram performed on a 54-years-old woman with chest discomfort revealed ischaemia in the left anterior descending artery and right coronary artery areas. The 4-chamber view (A and B panels) is shown both before and after the stress test. Hypokinesis is indicated by arrows at the apex and distal septum in the post-stress image (B), and severe ischemia is indicated by the enlargement of the left ventricular chamber. Hypo-kinesis at the apex and distal septum is indicated by the arrows in the long-axis views (C, D). Arrows in E and F indicate hypokinesis in the middle and top of the inferior wall in the 2-chamber view. [(24)].

Future advancements in stress echocardiography will centre on honing the methodology and quantitative tools in order to further improve accuracy, reduce subjectivity, and boost reproducibility of interpretation. Contrast echocardiography, 3D imaging, myocardial strain and strain rate imaging, tissue Doppler, and strain imaging are all methods that could be used to enhance current diagnostic capabilities. Myocardial contrast echocardiography is getting closer to its ultimate aim of non-invasive physiologic evaluation of CAD by allowing simultaneous monitoring of myocardial regional function and perfusion [(24)].

CONCLUSION

The use of stress echocardiography has expanded greatly in recent years as a diagnostic and prognostic tool for patients suspected of having coronary artery disease (CAD).

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