Electrocardiography for early diagnosis and prevention of cardiovascular disease in asymptomatic patients

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Abstract

Echocardiography (EchoCG) is a key non-invasive method in the early detection of cardiovascular diseases (CVD) in patients without overt symptoms. In this review, echocardiographic markers that might predict CVD are discussed and EchoCG screening's effectiveness is thoroughly investigated. These markers include systolic and diastolic function analysis and also hypertrophy and dilation of structures of the heart. In this article, different screening strategies, their clinical significance and possible consequences for asymptomatic patients are compared, accentuating the necessity of personalized screening approach, with respect to individual risk of CVD. Studies show that EchoCG may significantly facilitate heart anomalies early diagnosis and potentially lead to well-timed intervention, improving patient outcomes, thus stating the importance of integration of EchoCG into standard screening guidelines for early CVD diagnosis and prevention optimization.

Keywords: echocardiography, cardiovascular disease, left ventricular function, risk factors, screening.

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Introduction

Cardiovascular disease (CVD), including coronary heart disease (CHD) and stroke are the most common cause of death and disability worldwide with their distribution continuously and significantly growing, from 271 million cases and 12.1 million deaths per year in 1990 to 523 million cases and 18.6 million deaths per year in 2019 [1]. While smoking, unhealthy diet, lack of physical activity, arterial hypertension (AH), and diabetes mellitus (DM) still remain being the most influential CVD risk factors, combating them must be prioritized by the public health strategies [2]. Judging from an economic perspective, CVD is considered a significant burden, due to high treatment costs, productivity losses, and social protection expenditure [3]. Ominous growth of the age-standardized rate (ASR) of CVD in high-income countries and among the young indicates the necessity of novel approaches to prophylaxis and disease prevention and management [4]. Echocardiography (EchoCG) is a vital non-invasive diagnostic method, providing highly detailed heart images via ultrasound waves reflection for real-time medical analysis of its structure and function [5, 6]. EchoCG, due to its safety and effectiveness, has become the basic method of cardiac pathology diagnosis, including valvular heart disease, heart failure (HF) and myocardial disorders [7].

Accurate ejection fraction, ventricular function and volume evaluation with no need for exposing patients to invasive procedures are the key advantages that make EchoCG an irreplaceable instrument for diagnosis, disease progression monitoring, and treatment evaluation [8].

Moreover, through providing a rapid way of cardiac function evaluation, EchoCG is of great use in cases of emergency, like myocardial infarction (MI) and heart anomalies, requiring an immediate intervention [5].

Development of echocardiography began in the 1950s, when ultrasound was for the first time used for heart visualization by Swedish researchers Ingvar and Edler, providing momentum for the use of EchoCG as a non-invasive method of cardiac pathology diagnosis [8]. In the 1960s ultrasound technologies became more accessible for medical application, which allowed ultrasound cardiac assessment clinical use [9].

By the 1970s, technology was in the state of rapid development, and the first ultrasound scanners for heart assessment became available in the market. Scanning and data processing technique advancement have resulted in more clear and detailed images. During this decade, a number of technological breakthroughs have facilitated the quality of imaging and expanded the capabilities of various heart diseases diagnostics [9].

Since the 1980s, with the emergence of computer technology and digital data processing methods, EchoCG has made a significant advancement [10]. Nowadays, transthoracic, transesophageal, three-dimensional, and stress echocardiography are used for precise heart disease diagnosis and evaluation, depending on clinical conditions [11].

Based on the increasing role of echocardiography in the diagnosis and evaluation of heart disease, its potential application in predictive medicine should also be considered. By accurately visualizing and analyzing the state of the heart muscle and valves, as well as detecting EchoCG abnormalities such as left ventricular hypertrophy (LVH) and left ventricular dysfunction (LVD). EchoCG offers new opportunities for early detection of CVD risk in patients with no prior history of CVD. This is particularly relevant in light of the increasing incidence of CVD among young people and the population of high-income countries, which demands novel approaches to prevention and monitoring.

The aim of the study is to systematically analyze the literature on using echocardiography to diagnose CVD early in asymptomatic patients. The focus is on evaluating the effectiveness of echocardiographic screening in detecting early signs of CVD that are not yet clinically apparent but have the potential to progress to serious disease. The study aims to identify the most important markers and parameters to evaluate during screening and to compare different screening approaches among asymptomatic patients, in order to provide optimal clinical practice strategies.

The goal is to improve strategies for preventing CVD through early identification and intervention, which can significantly reduce the individual and socioeconomic burden of these diseases.

Methods

Literature review

The study was performed in accordance with Good Clinical Practice standards and the principles of the Declaration of Helsinki. This review article used a systematic approach to analyze the scientific literature, focusing on the identification, evaluation, and synthesis of evidence on early diagnosis of CVD among asymptomatic patients using EchoCG. Studies were selected from PubMed, Scopus, and Web of Science databases from 2015 to 2023. The search included combinations of the following keywords: "asymptomatic cardiovascular diagnostics", "early diagnosis of CVD", 'echocardiography' and "screening".

Inclusion and Exclusion Criteria

Articles describing clinical trials, observational studies, and meta-analyses evaluating the efficacy and accuracy of EchoCG in the early detection of CVD in asymptomatic patients were included. Studies involving only symptomatic patients, as well as those lacking clear information on study methodology, were excluded.

Data Analysis

Data from the selected sources were systematized to identify major themes and findings. Particular attention was paid to evaluating screening methods, the sensitivity and specificity of echocardiography, and risk predictors of CVD. The findings were then compared and analyzed to determine the most effective approaches to early diagnosis.

Ethical Considerations

For the purposes of this article, only studies that met the ethical standards for conducting clinical trials were considered. These standards include obtaining informed consent from participants, ensuring the anonymity of data, and receiving approval from the appropriate ethics committees.

Limitations

The review article is limited to English-language publications, which may have excluded relevant studies published in other languages. Additionally, the time period of the studies may not reflect the latest technological and methodological advances in echocardiography.

Echocardiographic abnormalities and their clinical significance

There are several EchoCG abnormalities: LVH, LVD, LAD, and aortic root dilation (Table 1).

Left ventricular hypertrophy

LVH refers to an increase in the thickness of the left ventricular wall, which is frequently considered an adaptive response to an elevated workload. The development of LVH is influenced by a number of significant mechanisms, including genetic factors, prolonged AH, and increased cardiac exercise. Genetic predisposition to LVH includes mutations in genes encoding sarcomeric proteins, such as myosin heavy chain (MYH7), cardiac troponin T (TNNT2), and cardiac myosin-binding protein C (MYBPC3) [12]. Genetic variations in these loci can modify sarcomere function, resulting in a reduction in myocyte contractility and an increase in myocyte size, leading to hypertrophy [13].

Hypertension has been demonstrated to induce LVH as an adaptive response intended to minimize

Table 1

Abnormality	Description and pathogenetic mechanism	Diagnosis and risk stratification
LVH	An increased left ventricular (LV) wall thickness is often an adaptive response to an increased workload. Genetic factors include mutations in the MYH7, TNNT2, and MYBPC3 genes, which alter sarcomere function. Physical exertion and hypertension might also play a role.	An increased left ventricular wall thickness is associated with an increased risk of cardiac events (CVEs). Echocardiography is used for the early diagnosis and risk stratification of these events.
LAD	Factors such as hypertension, valve malformations, inflammation, and cardiomyopathies increase the risk of CH by enlarging the left atrial (LA) cavity.	There is an increased risk of CVEs. It is important to use echocardiography to measure left atrial size and function in order to predict atrial fibrillation.
Aortic root dilation	The pathological dilation of the aortic root can result in an aneurysm, aortic dissection, or aortic rupture. Genetic mutations and hypertension have been demonstrated to exacerbate this condition.	Early detection and surgical intervention are of paramount importance due to the potential for severe cardiovascular complications. EchoCG is utilized for the purposes of evaluation and monitoring.
Left ventricular dysfunction	Diastolic dysfunction can lead to dyspnea and an increased risk of hospitalization. Pathogenesis includes genetic and hemodynamic factors that affect myocyte metabolism and structure.	Left ventricular diastolic dysfunction has been identified as a significant marker of CVD risk. Early diagnosis is imperative for the prevention of heart failure (HF), particularly in patients with diabetes or hypertension.

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ventricular wall stress. The study revealed that hypertrophied LV exhibited structural and molecular alterations, including the accumulation of lipid droplets in cardiomyocytes, the upregulation of fatty acid transporter CD36, protein kinase C, and matrix metalloproteinase-2, and the enhanced activation of the phosphatidylinositol 3-kinase/activated protein kinase pathway [14].

Prolonged and strenuous physical activity has been demonstrated to induce physiological alterations in the cardiovascular system, manifesting in the augmentation of left ventricular wall thickness and cavity diameter. These adaptations often meet diagnostic criteria for LVH, though are considered physiological [15], align with the diagnostic criteria for left ventricular hypertrophy, yet are typically regarded as physiological responses rather than pathological manifestations [15]. Intense aerobic exercise has been demonstrated to result in a substantial decrease in blood pressure (BP), thereby reducing the hemodynamic load on the heart and potentially diminishing the stimulus for pathologic LVH [16]. These alterations are deemed safe and reversible, representing a physiological response to an elevated cardiovascular workload. However, the degree to which physical activity contributes to cardiac health varies significantly. A study by Holtermann A. et al. found that individuals engaged in high-intensity occupational activities, characterized by static loads and repetitive movements, exhibited a 35% increased risk of CVD and a 27% increased risk of mortality compared to those with low levels of activity (odds ratio (OR)=1.35 for CVD and OR=1.27 for mortality). Conversely, active leisure time has been shown to reduce these risks: high leisure time physical activity has been demonstrated to reduce the risk of cardiovascular disease by 23% and the risk of mortality by 41% [17]. Such activity has been shown to enhance cardiovascular and metabolic function, in contrast to occupational activity, which is often not dynamic enough and does not involve recovery periods.

Epidemiology studies confirm LVH is a significant independent cardiovascular disease risk factor [16, 18]. LVH can result in CVD through various mechanisms, including the development of arrhythmias and alterations in the structure and function of the heart muscle [18]. A study by Fernandes L. P. et al. demonstrated that increased LV wall thickness is associated with non-fatal CVD (relative risk (RR) 2.16), CVD death (RR 2.58), and total mortality (RR 2.02) [19].

The assessment of LVH geometry serves as a critical risk stratification tool, facilitating the identification of patients at high risk of developing CVD prior to the manifestation of any clinical signs.

The management of patients with LVH requires a comprehensive approach, including pharmacological treatment to control BP, lifestyle modifications, and potentially a cardioverter-defibrillator implantation (ICD) to prevent sudden cardiac death. In summary, a comprehensive understanding of the underlying pathophysiology of LVH, including its epidemiological associations with CVD, is imperative for the development of effective diagnostic strategies and management plans for this condition.

Left ventricular dysfunction

Left ventricular dysfunction is a diastolic dysfunction that has been associated with an elevated risk of fatal and nonfatal CVEs. The study reported an odds ratio (OR) of 2.01, with a 95% confidence interval (CI) of 1.32-3.07 [19]. The primary mechanisms underlying LVD development are impaired ventricular relaxation and increased viscoelastic stiffness, resulting in dyspnea and an elevated risk of hospitalization [20].

Physical exercise exerts a substantial influence on diastolic function, particularly in patients diagnosed with systolic left ventricular dysfunction with normal ejection fraction (sLVD-nEF), leading to a deterioration in systolic function during periods of exercise [12]. This contributes to increased left ventricular pressure and the development of sLVD-nEF.

Genetic factors have been demonstrated to play a pivotal role in the development of LVD. It has been established that certain genetic variations exert an influence on the metabolism and structural characteristics of cardiomyocytes, thereby contributing to alterations and impaired relaxation with an increased myocardial stiffness [12, 14]. In particular, TTN, PLN, and GJA1 genes have been associated with diastolic function [20].

Risk stratification is a central component of the assessment of LVD. Diastolic dysfunction can serve as an important marker for determining CVD risk in patients without a prior history of HF, thereby allowing the detection of an occult cardiac disease and timely therapeutic interventions to prevent HF. For instance, a study by Chee et al. has demonstrated that diastolic LV dysfunction affects the majority of patients with type 2 diabetes mellitus with no prior history of CVD, indicating the high prevalence of this condition and the importance of its early detection [21].

Furthermore, a study by Kiel P. et al. revealed a considerably higher median coronary artery calcium (CAC) score in patients with LVD, emphasizing the importance of CAC assessment in the diagnosis of LVD in patients with AH [22]. Also, a study by Han B. G. et al. indicated that patients with diabetic kidney disease of stages 3 and 5 exhibited an elevated risk of cardiovascular disease. This finding highlights the necessity for the early detection and prevention of CVD risk factors in these patients [23]. A study by Lindstedt M. et al. found that diastolic dysfunction affected 50% of patients with idiopathic inflammatory myopathy, suggesting a high risk of developing sLVD-nEF in this group [24]. These data reinforce the significance of risk stratification and early diagnosis of diastolic dysfunction to avoid the development of severe cardiovascular disease.

Left atrial dilation

LAD is defined as a dilation of the left atrial cavity that may be caused by various pathological conditions, including hypertension, valve defects, cardiomyopathy, inflammation, or fibrosis. This condition can potentially impact cardiovascular function and elevate the risk of developing heart failure.

Risk stratification is a critical component of evaluating patients with LAD, as this condition is associated with an elevated risk of CVEs (RR 1.78; 95% CI 1.16-2.73) [19]. Alterations in the PITX2 gene, associated with LA development and function, serve as a significant risk marker. Epigenetic modifications, including hypermethylation of the Pitx2 gene, have been associated with an elevated risk of developing atrial fibrillation [24].

The mechanisms affecting LAD include pressure and volume overload, as well as increased levels of matrix metalloproteinases that promote fibrosis and tissue remodeling. This emphasizes the potential role of therapeutic targets in preventing and reversing changes in LA structure.

The assessment of left atrial dimensions and functionality through echocardiography, including the indexed maximum left atrial volume, facilitates accurate risk stratification [24]. This measurement is closely related to cardiac outcomes and is particularly important for predicting atrial fibrillation in patients with severely dilated LA.

For instance, a study by Jagadeesan V. et al. demonstrates the necessity of incorporating LA dilation into risk assessments for re-hospitalization following embolic strokes [25]. This suggests that LA dilation may have a role in predicting outcomes for patients with embolic stroke of unknown etiology and other cardiovascular diseases.

Aortic Root Dilation

The anomaly is characterized by the presence of an abnormal dilation of the aortic root. This condition can lead to serious complications, including aneurysm, dissection, or rupture of the aorta. These complications are often associated with abnormalities in the structure and function of the aortic valve and vascular wall.

The following mechanisms have been identified as contributing to the development of dilation:

Genetic factors. Genetic factors play a significant role in the development of aortic dilation. Mutations in genes such as FBN1, TGFBR1, and TGFBR2 can result in abnormalities in the structure of connective tissue, which can contribute to the dilation of the aortic wall [26].

Molecular Mechanisms. Abnormalities in the transforming growth factor beta (TGF-ß) signaling pathway may contribute to the breakdown of elastic fibers and collagen matrix, weakening the aortic wall [27].

Hemodynamic factors. The hemodynamic factors involved in this condition include high blood pressure, which exerts a mechanical load on the aortic wall, contributing to its dilation [28].

Aortic root dilation has been identified as a significant risk factor for the development of CVD. This condition can lead to aortic regurgitation, aneurysms, and dissections, significantly increasing the risk of mortality and the need for surgical intervention [26]. Thus, aortic root dilation is associated with an elevated risk of CVEs (RR 1.25; 95% CI 1.09-1.43) [19]. The early identification of patients at high risk of complications is of paramount importance for the timely initiation of treatment and prophylaxis. This can be achieved through the use of risk stratification tools, such as echocardiography and other imaging techniques, that can accurately assess the risk of complications.

EchoCG, being a non-invasive method, plays a crucial role in the diagnosis of aortic root dilation due to its accessibility and high degree of diagnostic accuracy.

Current challenges in the early diagnosis of cardiovascular disease review

Early diagnosis of cardiovascular disease poses a significant challenge in contemporary cardiology, particularly in cases involving asymptomatic patients. The complexity of this task is further compounded by the fact that the majority of cardiovascular disorders develop subtly and often do not manifest until serious events, such as myocardial infarction or stroke, occur [30].

Difficulties in early diagnosis

The absence of symptoms. The absence of symptoms is a hallmark of most cardiovascular diseases in their early stages, rendering them challenging to detect early. A multitude of symptoms, including fatigue and stress, may be erroneously attributed to less severe conditions, thereby delaying the diagnosis [31].

Patient Unawareness. Low level of awareness regarding the signs of CVD and its risk factors among the population can result in a delay in medical care seeking [31].

Lack of informativeness of traditional methods. Traditional diagnostic methods, such as BP and cholesterol levels measurements, are not always effective in identifying diseases before they progress [30].

Statistical significance

According to a study by Tsai et al., nearly half of the adult population in the United States has some form of CVD, with many remaining asymptomatic in the initial stages [30]. A study by Zwartkruis et al., involving 100,311 participants, revealed that 1325 participants had undiagnosed cardiovascular disease, which underscores the significance of early screening and diagnosis [31].

A proactive screening, incorporating both symptom-based assessment and a comprehensive questionnaire, has been demonstrated to enhance the efficacy of early detection of CVD in primary care settings. This approach has the potential to prevent CVEs and disease progression. The study accentuates the necessity to develop and implement simple yet effective screening methods that can be seamlessly integrated into routine clinical practice [30].

The efficacy of timely diagnosis and prevention of CVD has been demonstrated to markedly enhance patient prognoses and quality of life, while concurrently reducing the economic burden associated with advanced-stage disease management. The implementation of enhanced methods for early diagnosis and screening, aimed at identifying patients in the early stages of the disease, has emerged as a priority task in contemporary medical practice.

Early Signs of Echocardiographic Abnormalities Review

Echocardiography is a non-invasive technique that plays a critical role in detecting early signs of CVD, even in patients presenting with no symptoms. This method can detect changes such as LAD, abnormalities in aortic root structure and function, LVH, and LVD. This capability is essential for initiating timely treatment and preventing serious CVEs.

Early signs of aortic root changes

A slight increase in aortic root diameter: this change has been observed, which may be indicative of the initial stages of aortic aneurysm or other pathologic conditions that may not be symptomatic in the early stages. Early detection of such changes is critical to assess the risk of developing serious complications [26].

Aortic valve cusps thickening. Aortic valve cusps thickening may indicate the initial processes of fibrosis or calcification. EchoCG has been demonstrated to detect these changes in patients who are not yet symptomatic, which is important for early diagnosis and prevention of aortic stenosis [26].

Subvalvular fibrous ridges. Subvalvular fibrous ridges are a common finding in patients with ankylosing spondylitis, potentially indicative of inflammatory processes or the initial stages of structural changes of the aorta. Early detection of these signs may prevent the development of serious aortic disease [26].

The two-dimensional EchoCG is utilized to evaluate these changes, enabling their detection prior to the manifestation of clinical symptoms of aortic regurgitation [26].

Early signs of left atrial changes

Changes in LA volume and function can be detected echocardiographically in asymptomatic patients, indicating early cardiac involvement in the pathologic process [24].

A study by Christensen et al. demonstrated that in patients with asymptomatic severe aortic stenosis, LA dilation may serve as an indicator of advanced disease stage. It has been associated with an increase in LA mass and end-diastolic volume, which are the risk factors for cardiac events [32].

An additional study by Cameli et al. emphasizes that LA deformation is a useful index for early detection of cardiac damage in chronic mitral regurgitation. Speckle-tracking echocardiography allows analyzing LA function and can indirectly identify structural tissue changes in the early stages of the disease before complete deterioration of atrial function [33].

Early signs of left ventricular hypertrophy

LVH is prevalent among patients with long-term AH and can be detected early through echocardiographic imaging. Increased LV myocardial mass and structural changes can be detected before the onset of clinical symptoms, thereby providing an opportunity for an early intervention [33]. The CHELLO study has demonstrated that 44% of elderly patients with asymptomatic hypertension had LVH, emphasizing the importance of early detection for improving outcomes [33].

Early signs of Left Ventricular Dysfunction

LV diastolic and systolic dysfunction can be detected at an early asymptomatic stage, thus preventing the development of HF. Diastolic dysfunction, defined as impaired ventricular relaxation and filling, can be detected through analysis of isovolumic relaxation and changes in filling velocities [33]. Systolic dysfunction, evaluated by decreased EF and global longitudinal strain, can be identified in a presymptomatic stage, which is crucial for timely diagnosis [33].

Early diagnosis of CVD remains a critical component of contemporary cardiology. The recognition and detection of asymptomatic changes with echocardiography has been demonstrated to result in a substantial improvement in patient outcomes, thereby enabling the initiation of treatment before the onset of serious complications. This approach not only reduces the economic burden associated with advanced stages of CVD but also presents an opportunity to improve patients' quality of life.

EchoCG is an invaluable tool in the early diagnosis of asymptomatic CVD. It provides essential data on heart muscle condition and function, enabling the well-timed administration of required treatment. Early detection and diagnosis of CVD play a key role in preventing disease progression and improving patient prognosis. For this reason, EchoCG is considered an indispensable method in modern cardiology practice.

Selection of patients without signs of cardiovascular disease for echocardiographic examination

EchoCG is a valuable tool in the preventive screening of CVD, especially among patients who do not exhibit explicit symptoms. However, studies have demonstrated that its efficacy and cost-effectiveness depend on the selection of suitable candidates for screening.

Screening Using Echocardiography

Paton et al. demonstrated in their study that widespread screening using EchoCG in the general population did not result in a substantial decrease in mortality or the risk of CVEs, including MI and stroke. These data emphasize that without careful selection of patients by risk, this approach may not be effective [34].

Risk Assessment and Feasibility of Echocardiography

Winchester et al. discuss the use of echocardiography for risk assessment in asymptomatic patients, especially those with AH. They emphasize that the direct benefit of EchoCG in the prevention of heart disease has not been proven and that its use should be carefully justified, taking into account the individual risks of the patient [35].

Preventive Use of Echocardiography

Post-hoc data from the Irish STOP-HF randomized controlled trial, published by Cannone et al., demonstrated that in patients with cardiovascular risk factors, applying a threshold level of endogenous BNP to refer individuals for transthoracic EchoCG and subsequent interdisciplinary management enabled the timely detection of asymptomatic systolic LVD and shown statistically significant reduction in the risk of progression to clinical HF [36].

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Patient selection criteria for echocardiographic examination

Studies emphasize the importance of selecting patients for echocardiographic screening based on the presence of relevant risk factors:

Age and comorbid conditions. A new prospective analysis from the Australian SCREEN-HF study (Coller et al.) showed that in individuals aged ≥60 years with at least one classical cardiovascular risk factor — including CHD, arterial hypertension, diabetes mellitus, or chronic kidney disease — targeted echocardiography effectively detects asymptomatic systolic LVD and helps to prevent progression to symptomatic HF. The novel formulation below is based on these findings and aligns with current ESC 2021 and ACC/AHA/HFSA 2022 guidelines, which also emphasize the importance of early detection of stage B/pre-HF in such populations [37].

Cardiooncology. In the field of cardio-oncology, echocardiography plays a central role in the early detection and monitoring of cancer therapy–related cardiotoxicity. This is particularly evident in patients receiving cardiotoxic treatments with echocardiographically revealed early signs of cardiac dysfunction [29].

Clinical Guidelines. Based on Framingham risk score or other validated risk assessment models, echocardiography may be recommended for individuals at intermediate or high cardiovascular risk. This allows for the detection of conditions such as left ventricular hypertrophy and LVD even in asymptomatic patients [29, 35].

The preventive use of echocardiography is a vital component of early diagnosis and risk management in asymptomatic individuals. Careful patient selection, grounded in thorough risk assessment, can contribute to more effective prevention of CVD and improved treatment outcomes.

Conclusion

Echocardiography remains a cornerstone of preventive cardiology, with the ability to identify subclinical structural and functional cardiac abnormalities long before symptoms arise. Systematic analysis has shown that targeted screening of individuals aged ≥60 years with major cardiovascular risk factors or elevated BNP levels provides the best balance between clinical effectiveness and cost-efficiency, helping to prevent the progression to heart failure and reducing the incidence of major cardiovascular events. The integration of modern technologies, such as global longitudinal and left atrial strain assessment, three-dimensional EchoCG, and AI-powered post-processing algorithms, further enhances the diagnostic value of echocardiography. Developing standardized protocols for patient selection and management could transform echocardiography from a diagnostic tool into an effective mechanism for primary prevention.

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