Methodological Determinants of Left Ventricular Ejection Fraction Variability in Echocardiography: From Conventional Measurements to Advanced Three-Dimensional and Strain Imaging

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Abstract

Background: Left ventricular ejection fraction (LVEF) is one of the most widely used parameters for evaluating left ventricular systolic function and plays a central role in the diagnosis, risk stratification, and therapeutic management of cardiovascular diseases. It is a key metric in the classification and management of heart failure, guiding decisions regarding pharmacologic therapy, device implantation, and long-term patient monitoring. Echocardiography remains the primary imaging modality for assessing LVEF in clinical practice due to its non-invasive nature, widespread availability, real-time capability, and cost-effectiveness. Despite its routine use, the measurement of LVEF using echocardiography is subject to notable variability that can arise from methodological differences, image acquisition limitations, and operator-dependent interpretation.

Several echocardiographic techniques are currently used to estimate LVEF, including traditional M-mode measurements, two-dimensional (2D) approaches such as the Simpson biplane method, and more advanced modalities such as three-dimensional (3D) echocardiography and myocardial deformation imaging. Conventional methods rely on geometric assumptions regarding ventricular shape, which may not accurately represent the complex anatomy of the left ventricle, particularly in the presence of regional wall motion abnormalities, ventricular remodeling, or cardiomyopathies. As a result, discrepancies may occur when different echocardiographic methods are applied to the same patient. In addition, technical factors such as image quality, acoustic window limitations, and frame rate variability may further influence measurement accuracy and reproducibility.

Recent technological advances have introduced more sophisticated approaches for evaluating left ventricular systolic function. Real-time three-dimensional echocardiography allows direct volumetric analysis of the ventricle without relying on geometric assumptions, potentially improving the accuracy of ejection fraction measurements. Furthermore, speckle-tracking echocardiography enables the quantification of myocardial deformation through parameters such as global longitudinal strain, which provides complementary information regarding myocardial contractility and may detect subclinical ventricular dysfunction even when LVEF appears preserved.

This review aims to examine the methodological determinants responsible for variability in echocardiographic assessment of LVEF. Particular focus is placed on the influence of conventional and advanced imaging techniques, operator-related factors, and technological developments that affect measurement consistency. Understanding these determinants is essential to improve the reliability of echocardiographic LVEF assessment and to enhance its clinical value in contemporary cardiovascular practice.

Keywords: *Left Ventricular Ejection Fraction, Echocardiography, Global Longitudinal Strain.*

Introduction

Left ventricular ejection fraction (LVEF) is a fundamental parameter used in cardiology to quantify global left ventricular systolic function and to guide the diagnosis and management of a wide spectrum of cardiovascular diseases. Clinically, LVEF plays a pivotal role in the classification of heart failure phenotypes, including heart failure with reduced, mildly reduced, and preserved ejection fraction, which directly influences therapeutic strategies and prognostic evaluation. International cardiovascular guidelines rely heavily on LVEF thresholds when recommending pharmacologic therapy, device implantation, and follow-up strategies for patients with heart failure and structural heart disease. Consequently, accurate and reproducible assessment of LVEF is essential for appropriate clinical decision-making and optimal patient care. [1]

Echocardiography has become the most widely used imaging modality for evaluating LVEF because of its safety, non-invasive nature, real-time imaging capability, and accessibility across different healthcare settings. Conventional echocardiographic methods such as M-mode and two-dimensional (2D) imaging techniques have been historically used to estimate ventricular volumes and calculate ejection fraction. The Simpson biplane method of disks, recommended by major echocardiographic societies, has become the standard approach for LVEF quantification in routine clinical practice. Despite its widespread use, this method relies on geometric assumptions and accurate endocardial border delineation, which may introduce measurement variability, particularly in patients with abnormal ventricular geometry or regional wall motion abnormalities. [2]

Several technical and methodological factors contribute to the variability observed in echocardiographic LVEF measurements. These include differences in imaging techniques, acquisition protocols, ventricular modeling assumptions, and operator experience. In addition, patient-related factors such as body habitus, lung interference, and acoustic window limitations can significantly affect image quality and subsequently influence the accuracy of ventricular volume measurements. These limitations have prompted ongoing efforts to develop more advanced echocardiographic techniques that can provide more reliable and reproducible assessment of left ventricular systolic function. [3]

Recent advancements in cardiovascular imaging have introduced innovative echocardiographic modalities designed to overcome the limitations of conventional methods. Real-time three-dimensional echocardiography allows direct volumetric quantification of the left ventricle without relying on geometric assumptions, while speckle-tracking echocardiography provides detailed evaluation of myocardial deformation through parameters such as global longitudinal strain. These advanced techniques offer improved reproducibility and enhanced sensitivity for detecting early myocardial dysfunction, even before significant reductions in LVEF become evident. [4]

Despite these technological developments, discrepancies in LVEF measurements across different echocardiographic methods remain a common challenge in clinical practice. Variability between imaging techniques may influence patient classification, particularly when therapeutic decisions depend on specific ejection fraction thresholds. Furthermore, the expanding use of advanced echocardiographic modalities has raised questions regarding the optimal approach for evaluating left ventricular systolic function and integrating multiple imaging parameters into routine clinical assessment. [5]

Therefore, a comprehensive understanding of the methodological determinants influencing LVEF variability is essential. This review aims to examine the key factors contributing to differences in echocardiographic LVEF measurements, including conventional imaging techniques, advanced three-dimensional echocardiography, and myocardial strain analysis. By exploring these methodological considerations, the review seeks to highlight current challenges, identify potential sources of measurement inconsistency, and discuss emerging strategies to improve the reliability of echocardiographic evaluation of left ventricular systolic function. [6]

Evolution of Echocardiographic Assessment of Left Ventricular Function

The assessment of left ventricular function has undergone substantial evolution since the introduction of echocardiography as a clinical imaging modality. Early echocardiographic techniques relied primarily on M-mode imaging, which provided one-dimensional measurements of cardiac structures along a single ultrasound beam. M-mode allowed clinicians to estimate ventricular dimensions and fractional shortening, offering an early indirect measure of systolic function. Although this technique provided high temporal resolution and was relatively simple to perform, it was limited by its dependence on linear measurements and geometric assumptions regarding ventricular symmetry. Consequently, M-mode measurements were often inaccurate in patients with regional wall motion abnormalities or altered ventricular geometry, such as those with ischemic heart disease or cardiomyopathies. These limitations highlighted the need for more comprehensive imaging approaches capable of capturing the complex structure and dynamic motion of the left ventricle. [7]

The development of two-dimensional (2D) echocardiography represented a major advancement in cardiac imaging by enabling real-time visualization of cardiac structures in multiple planes. This innovation allowed clinicians to evaluate ventricular morphology, wall motion, and chamber volumes more accurately than earlier techniques. One of the most widely adopted methods for calculating LVEF using 2D imaging is the Simpson biplane method of disks, which estimates ventricular volumes by tracing the endocardial border in apical two- and four-chamber views. This technique has become the recommended standard for LVEF quantification in adult echocardiography due to its improved accuracy compared with M-mode–based calculations. However, the Simpson method still relies on certain geometric assumptions and requires clear delineation of the endocardial borders, factors that may introduce variability when image quality is suboptimal or when ventricular remodeling is present. [8]

Advancements in ultrasound technology have further expanded the capabilities of echocardiography through the introduction of three-dimensional (3D) imaging. Real-time 3D echocardiography enables direct volumetric analysis of the left ventricle without relying on geometric modeling assumptions. This approach provides a more anatomically accurate representation of ventricular shape and allows for improved quantification of ventricular volumes and ejection fraction. Studies comparing 3D echocardiography with cardiac magnetic resonance imaging—the reference standard for volumetric assessment—have demonstrated strong correlation and improved reproducibility compared with traditional 2D methods. As a result, three-dimensional echocardiography has become an increasingly valuable tool in modern cardiac imaging, particularly for patients with complex ventricular geometry. [9]

More recently, myocardial deformation imaging using speckle-tracking echocardiography has emerged as an important complement to traditional LVEF assessment. This technique evaluates myocardial mechanics by tracking acoustic markers within the myocardium throughout the cardiac cycle, allowing for quantitative assessment of myocardial strain. Global longitudinal strain (GLS) has been shown to provide sensitive detection of subclinical myocardial dysfunction and may identify early impairment in ventricular contractility before reductions in LVEF occur. The integration of strain imaging with conventional volumetric measurements represents a significant step forward in the comprehensive evaluation of left ventricular function, reflecting the continuous evolution of echocardiographic technology and its expanding role in cardiovascular diagnostics. [10]

Physiological Basis of Left Ventricular Ejection Fraction

Left ventricular ejection fraction represents the proportion of blood ejected from the left ventricle during systole relative to its end-diastolic volume and serves as a fundamental indicator of global systolic performance. Physiologically, LVEF reflects the integrated interaction between myocardial contractility, ventricular preload, afterload, and intrinsic myocardial structure. The parameter is calculated as the ratio of stroke volume to end-diastolic volume, expressed as a percentage, and therefore depends not only on myocardial contractile function but also on loading conditions. Variations in preload or afterload can significantly influence LVEF measurements even when intrinsic myocardial contractility remains unchanged, highlighting the importance of interpreting this parameter within the broader hemodynamic context. [11]

The mechanical process underlying ventricular ejection involves coordinated myocardial fiber contraction in multiple orientations, including longitudinal, circumferential, and radial shortening. Longitudinal fibers located predominantly in the subendocardial layer contribute significantly to early systolic shortening, while circumferential and radial fibers contribute to ventricular thickening and cavity reduction during systole. This complex three-dimensional contraction pattern enables efficient blood ejection and optimal cardiac output. However, pathological conditions such as ischemic heart disease, cardiomyopathy, or pressure overload can disrupt this coordinated myocardial mechanics, leading to impaired systolic performance and reduced ejection fraction. Importantly, early dysfunction of subendocardial longitudinal fibers may occur before global LVEF becomes abnormal, emphasizing the limitations of relying solely on ejection fraction as a marker of myocardial health. [12]

Another important determinant of LVEF is ventricular remodeling, which involves structural and geometric changes in the myocardium that occur in response to chronic pressure or volume overload. Remodeling processes may include ventricular dilation, hypertrophy, or alterations in myocardial stiffness, all of which can influence the relationship between ventricular volume and systolic function. For example, in dilated cardiomyopathy, the enlarged ventricular cavity reduces mechanical efficiency and often results in a decreased ejection fraction. Conversely, conditions such as hypertrophic cardiomyopathy or early hypertensive heart disease may present with preserved or even increased LVEF despite underlying myocardial dysfunction. These physiological and structural factors illustrate why LVEF alone cannot fully characterize myocardial performance and must be interpreted alongside other functional and structural parameters. [13]

Furthermore, LVEF plays a central role in the clinical classification of heart failure and serves as a cornerstone for therapeutic decision-making. Contemporary heart failure guidelines categorize patients based on ejection fraction into heart failure with reduced ejection fraction, mildly reduced ejection fraction, and preserved ejection fraction. Each category is associated with different pathophysiological mechanisms and treatment strategies. Because therapeutic recommendations often depend on specific LVEF thresholds, even modest measurement variability can potentially influence patient classification and management decisions. This clinical importance underscores the need for accurate and reproducible echocardiographic techniques to ensure reliable assessment of left ventricular systolic function. [14]

Conventional Echocardiographic Methods for LVEF Measurement

Conventional echocardiographic techniques have long served as the cornerstone for evaluating left ventricular systolic function in clinical practice. Among these, M-mode echocardiography was historically the earliest method used to estimate ventricular dimensions and calculate systolic performance. The Teichholz method, derived from M-mode measurements of left ventricular internal diameters in systole and diastole, estimates ventricular volumes based on geometric assumptions that treat the ventricle as a prolate ellipsoid. While this technique provides excellent temporal resolution and is technically straightforward, its reliance on linear measurements makes it highly sensitive to regional wall motion abnormalities and alterations in ventricular geometry. As a result, the Teichholz method may produce inaccurate estimates of LVEF in patients with ischemic heart disease, dilated cardiomyopathy, or asymmetric ventricular remodeling. [15]

Two-dimensional echocardiography significantly improved the evaluation of ventricular function by allowing direct visualization of cardiac structures in multiple imaging planes. The Simpson biplane method of disks, also known as the modified Simpson rule, has become the recommended standard approach for calculating LVEF using 2D echocardiography. This technique involves tracing the endocardial borders of the left ventricle in the apical four-chamber and two-chamber views to divide the ventricular cavity into a series of stacked disks, from which end-diastolic and end-systolic volumes are calculated. The difference between these volumes represents stroke volume, which is then used to determine ejection fraction. Because this method uses two orthogonal views to approximate ventricular shape, it reduces some of the geometric assumptions inherent in earlier techniques and provides improved accuracy in routine clinical assessment. [16]

Despite its advantages, the Simpson biplane method is not free from methodological limitations. Accurate tracing of the endocardial border is essential for reliable volume calculation, yet image quality can be significantly affected by patient-related factors such as obesity, lung interference, or poor acoustic windows. In addition, apical foreshortening—where the true apex of the left ventricle is not fully visualized—may lead to underestimation of ventricular volumes and overestimation of ejection fraction. Variability in endocardial border delineation between observers also contributes to interobserver and intraobserver differences in LVEF measurements. These limitations highlight the importance of standardized imaging protocols and careful acquisition techniques during echocardiographic examinations. [17]

Visual estimation of LVEF, commonly referred to as the "eyeballing" method, remains widely used in clinical practice, particularly during rapid bedside assessments or point-of-care ultrasound examinations. Experienced echocardiographers can often estimate ventricular systolic function with reasonable accuracy by visually assessing myocardial thickening and cavity reduction during systole. However, this method is inherently subjective and strongly influenced by operator experience and training. Studies have demonstrated that variability in visual estimation can be significant, especially among less experienced operators, emphasizing the need for quantitative methods whenever possible. The continued use of visual assessment nevertheless reflects its practicality and speed in clinical settings where rapid evaluation of ventricular function is required. [18]

Overall, conventional echocardiographic approaches remain essential tools for LVEF assessment due to their accessibility and well-established clinical utility. However, their dependence on geometric assumptions, image quality, and operator interpretation introduces important methodological variability. These challenges have driven the development of more advanced echocardiographic techniques aimed at improving measurement accuracy and reproducibility, particularly in patients with complex ventricular geometry or suboptimal imaging conditions. [19]

Sources of Variability in Echocardiographic LVEF Measurement

Variability in echocardiographic measurement of left ventricular ejection fraction arises from multiple technical, methodological, and operator-related factors that influence the accuracy and reproducibility of ventricular volume assessment. One of the primary contributors to measurement variability is image acquisition quality. Optimal visualization of the endocardial borders is essential for accurate delineation of ventricular contours and precise volume calculation. However, factors such as poor acoustic windows, obesity, pulmonary disease, and chest wall anatomy may limit image quality and make endocardial border detection challenging. Suboptimal imaging conditions can result in incomplete visualization of the left ventricular cavity, leading to inconsistent tracing of ventricular boundaries and inaccurate estimation of both end-diastolic and end-systolic volumes. These technical limitations remain a significant challenge in routine echocardiographic practice. [20]

Another major source of variability is related to geometric assumptions and ventricular modeling techniques used in conventional two-dimensional echocardiography. Methods such as the Simpson biplane approach attempt to approximate ventricular volume based on planar images, which may not fully capture the complex three-dimensional geometry of the left ventricle. In patients with distorted ventricular morphology—such as those with myocardial infarction, cardiomyopathies, or ventricular aneurysms—these geometric assumptions may introduce substantial errors in volume calculations. The presence of regional wall motion abnormalities can further complicate accurate modeling of ventricular shape, resulting in discrepancies between different measurement techniques or between echocardiographic assessments and reference imaging modalities. [21]

Operator experience and interpretation also play a significant role in the variability of LVEF measurements. The process of tracing endocardial borders, selecting optimal cardiac cycles, and identifying end-systolic and end-diastolic frames requires technical expertise and familiarity with echocardiographic imaging. Studies have demonstrated that interobserver and intraobserver variability can occur even when standardized measurement protocols are followed. Less experienced operators may have greater difficulty identifying accurate ventricular boundaries, which can lead to inconsistent results. Even among experienced echocardiographers, subtle differences in contour tracing and frame selection may contribute to measurable variations in calculated ejection fraction values. [22]

Temporal and physiological factors can also influence LVEF measurements during echocardiographic evaluation. Heart rate variability, loading conditions, and changes in blood pressure can affect ventricular contractility and stroke volume, thereby altering the calculated ejection fraction. Additionally, arrhythmias such as atrial fibrillation may produce beat-to-beat variations in ventricular filling and systolic performance, making it more difficult to obtain consistent measurements. These physiological fluctuations highlight the importance of averaging multiple cardiac cycles and ensuring appropriate patient conditions during echocardiographic examinations. [23]

Collectively, these sources of variability emphasize the challenges associated with obtaining precise and reproducible LVEF measurements using conventional echocardiographic techniques. Recognizing these limitations has driven the development of more advanced imaging modalities that aim to minimize geometric assumptions, improve endocardial border visualization, and enhance measurement consistency. Among these advancements, three-dimensional echocardiography has emerged as a promising approach for improving volumetric assessment of the left ventricle. [24]

Role of Three-Dimensional Echocardiography in LVEF Assessment

Three-dimensional echocardiography has emerged as a major advancement in the noninvasive assessment of left ventricular structure and function. Unlike conventional two-dimensional imaging, which relies on geometric assumptions to estimate ventricular volumes, three-dimensional echocardiography enables direct volumetric reconstruction of the left ventricle. By acquiring a full-volume dataset, this technique allows clinicians to analyze ventricular morphology and function without relying on simplified geometric models. As a result, three-dimensional echocardiography provides a more anatomically accurate representation of ventricular shape and reduces potential errors associated with planar imaging. The ability to visualize the entire ventricular cavity in a single dataset represents a substantial improvement in the evaluation of cardiac mechanics and volumetric parameters. [25]

One of the principal advantages of three-dimensional echocardiography is its ability to measure ventricular volumes and ejection fraction without the geometric assumptions inherent in two-dimensional techniques. Traditional methods such as the Simpson biplane approach approximate the ventricle as a series of stacked disks based on two imaging planes, which may not fully capture complex ventricular geometry. In contrast, three-dimensional echocardiography reconstructs the entire ventricular chamber, enabling more accurate quantification of end-diastolic and end-systolic volumes. This approach is particularly beneficial in patients with abnormal ventricular shapes, including those with ischemic cardiomyopathy, ventricular aneurysms, or structural remodeling following myocardial infarction. By minimizing geometric assumptions, three-dimensional imaging improves the reliability of volumetric assessment and reduces measurement discrepancies between observers. [26]

Another important advantage of three-dimensional echocardiography is its improved reproducibility compared with conventional two-dimensional methods. Because the entire ventricular dataset is acquired simultaneously, variability related to image plane selection and ventricular foreshortening is significantly reduced. Automated or semi-automated software algorithms can further assist in endocardial border detection and volume calculation, enhancing consistency across repeated measurements. Several studies have demonstrated that three-dimensional echocardiographic measurements of ventricular volumes and ejection fraction show strong agreement with cardiac magnetic resonance imaging, which is widely considered the reference standard for cardiac volumetric assessment. This close correlation supports the growing clinical adoption of three-dimensional echocardiography in advanced cardiac imaging laboratories. [27]

Despite its advantages, the widespread use of three-dimensional echocardiography remains influenced by certain technical considerations. Image acquisition requires adequate temporal and spatial resolution, and suboptimal acoustic windows may still affect dataset quality. Additionally, three-dimensional imaging may require specialized equipment and additional training for optimal acquisition and

interpretation. Nevertheless, ongoing technological improvements, including faster acquisition systems and more sophisticated automated analysis software, continue to enhance the feasibility and accuracy of three-dimensional echocardiography. As these technologies become more widely available, three-dimensional imaging is expected to play an increasingly important role in reducing variability and improving the reliability of LVEF assessment in routine clinical practice. [28]

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Myocardial Strain Imaging and Global Longitudinal Strain

Myocardial strain imaging has emerged as an important advancement in echocardiographic evaluation of cardiac mechanics, providing quantitative assessment of myocardial deformation during the cardiac cycle. Unlike conventional measurements such as left ventricular ejection fraction, which reflect global volumetric changes in the ventricle, strain imaging evaluates the intrinsic contractile behavior of myocardial fibers. Speckle-tracking echocardiography (STE) is the most widely used technique for this purpose and relies on tracking natural acoustic markers, or "speckles," within the myocardial tissue throughout successive ultrasound frames. By analyzing the displacement of these speckles, the technique allows for measurement of myocardial deformation in longitudinal, circumferential, and radial directions, thereby offering a more detailed understanding of ventricular contractile mechanics. [29]

Among the various strain parameters, global longitudinal strain (GLS) has gained particular clinical attention because longitudinal myocardial fibers located predominantly in the subendocardial layer are highly sensitive to early pathological changes. These fibers are often affected first in conditions such as ischemic heart disease, hypertensive heart disease, and cardiomyopathies. As a result, reductions in GLS may occur before significant changes in left ventricular ejection fraction become apparent. This ability to detect subclinical myocardial dysfunction has positioned GLS as a valuable complementary parameter in the assessment of ventricular systolic performance, particularly in patients with preserved ejection fraction or in those undergoing cardiotoxic therapies. [30]

Another advantage of strain imaging is its ability to provide more objective and reproducible quantification of myocardial function compared with visual assessment alone. Because speckle-tracking algorithms analyze myocardial motion across multiple frames of the cardiac cycle, the technique reduces operator dependency and provides standardized measurements that can be compared across serial examinations. In addition, strain analysis allows regional assessment of myocardial deformation, enabling the identification of localized dysfunction that may not significantly affect global ejection fraction. This feature is particularly useful in the evaluation of ischemic heart disease, where regional wall motion abnormalities may precede changes in overall ventricular performance. [31]

Despite its clinical advantages, strain imaging is not without limitations. Measurement accuracy can be influenced by image quality, frame rate, and differences in software algorithms between ultrasound vendors. Inter-vendor variability may lead to differences in absolute GLS values, which has prompted ongoing efforts to standardize strain measurement techniques across imaging platforms. Nevertheless, the integration of myocardial strain analysis with traditional volumetric measurements provides a more comprehensive evaluation of ventricular function. As echocardiographic technology continues to evolve, strain imaging is increasingly recognized as an essential component of modern cardiac imaging and an important adjunct to conventional LVEF assessment. [32]

Comparison With Cardiac Magnetic Resonance Imaging as a Reference Standard

Cardiac magnetic resonance imaging (CMR) is widely regarded as the reference standard for the quantification of ventricular volumes and ejection fraction because of its superior spatial resolution and ability to provide highly accurate three-dimensional volumetric measurements without geometric assumptions. CMR allows comprehensive visualization of the left ventricle across the entire cardiac cycle using cine imaging techniques, enabling precise delineation of endocardial and epicardial borders. Unlike echocardiography, CMR is less dependent on acoustic windows or operator-dependent image acquisition, which contributes to its excellent reproducibility. These characteristics make CMR an important benchmark against which other cardiac imaging modalities, including echocardiography, are frequently validated. [33]

Comparative studies have demonstrated that conventional two-dimensional echocardiographic methods often show moderate correlation with CMR measurements but may underestimate ventricular volumes due to limitations in image plane acquisition and geometric modeling assumptions. Apical foreshortening, incomplete visualization of the ventricular apex, and difficulties in accurately tracing the endocardial border are common factors that contribute to discrepancies between echocardiographic and CMR-derived measurements. As a result, LVEF values obtained using two-dimensional echocardiography may differ from those measured with CMR, particularly in patients with distorted ventricular geometry or significant regional wall motion abnormalities. These limitations highlight the need for improved echocardiographic techniques capable of more accurately reproducing true ventricular anatomy. [34]

The introduction of three-dimensional echocardiography has significantly improved the agreement between echocardiographic measurements and CMR-derived ventricular volumes. By enabling direct volumetric analysis of the left ventricle, three-dimensional imaging reduces reliance on geometric assumptions and allows more accurate representation of ventricular morphology. Several validation studies have shown strong correlation between three-dimensional echocardiographic measurements and CMR for both ventricular volumes and ejection fraction. Furthermore, three-dimensional echocardiography has demonstrated improved reproducibility compared with conventional two-dimensional methods, supporting its role as a more reliable technique for quantitative assessment of ventricular function. [35]

In addition to volumetric assessment, myocardial deformation imaging has also been validated against advanced imaging techniques. Global longitudinal strain derived from speckle-tracking echocardiography has shown good agreement with strain measurements obtained using CMR-based myocardial deformation analysis. Because strain imaging evaluates myocardial mechanics at the tissue level rather than relying solely on volumetric changes, it provides complementary information regarding ventricular contractility. The integration of advanced echocardiographic techniques with established reference imaging modalities therefore enhances the overall understanding of ventricular function and supports the growing role of multimodality imaging in contemporary cardiovascular diagnostics. [36]

Clinical Implications of LVEF Variability in Cardiovascular Disease

Left ventricular ejection fraction plays a central role in the clinical management of cardiovascular diseases, particularly in the diagnosis and classification of heart failure. Contemporary clinical guidelines stratify patients with heart failure into categories based on LVEF, including heart failure with reduced ejection fraction, mildly reduced ejection fraction, and preserved ejection fraction. These classifications are not only descriptive but also guide the selection of pharmacological therapies, device implantation strategies, and long-term management plans. Because therapeutic recommendations often depend on specific LVEF thresholds, even modest variations in measurement may lead to changes in patient classification and influence treatment decisions. Accurate and consistent evaluation of LVEF is therefore essential for appropriate clinical management and risk stratification. [37]

Variability in LVEF measurement can have important consequences for therapeutic decision-making, particularly when patients fall near clinically relevant cut-off values. For example, the initiation of certain guideline-directed medical therapies or the consideration of implantable cardioverter-defibrillators and cardiac resynchronization therapy may depend on defined LVEF thresholds. If different echocardiographic methods yield inconsistent measurements, patients may be incorrectly categorized with respect to their heart failure phenotype or eligibility for device therapy. Such discrepancies emphasize the importance of standardized imaging protocols and the use of reproducible measurement techniques in order to minimize variability and ensure reliable assessment of ventricular function. [38]

In addition to therapeutic implications, LVEF variability can influence prognostic evaluation in patients with cardiovascular disease. Numerous studies have demonstrated that reduced LVEF is associated with increased risk of mortality, hospitalization, and adverse cardiovascular events. However, when measurement variability exists between imaging techniques or between observers, the prognostic value of LVEF may be affected. Incorporating additional imaging parameters such as myocardial strain, ventricular remodeling indices, and regional wall motion analysis may improve risk assessment and provide a more comprehensive understanding of cardiac function beyond LVEF alone. [39]

The clinical significance of accurate LVEF assessment extends beyond heart failure management to include other cardiovascular conditions such as ischemic heart disease, cardiomyopathies, and valvular heart disease. In these conditions, LVEF is often used to guide the timing of surgical or interventional procedures and to monitor disease progression over time. Therefore, improving the consistency and reliability of LVEF measurements across different echocardiographic techniques remains a critical objective in modern cardiovascular imaging. Advances in imaging technology, combined with standardized acquisition protocols and increased operator training, are essential for reducing measurement variability and enhancing the clinical utility of echocardiographic evaluation. [40]

Future Directions and Technological Advances in Echocardiographic Assessment of Left

Ventricular Function

Continuous technological progress in cardiovascular imaging is expected to further improve the accuracy and reproducibility of left ventricular ejection fraction assessment. Modern echocardiographic systems increasingly incorporate automated image analysis tools, machine learning algorithms, and artificial intelligence–based software designed to enhance endocardial border detection and ventricular volume calculation. These technologies aim to reduce operator dependency and standardize measurements across different clinical settings. Automated quantification systems are capable of analyzing three-dimensional datasets and generating rapid volumetric assessments, which may significantly reduce interobserver variability and improve workflow efficiency in echocardiography laboratories. As these technologies continue to evolve, they are likely to play an important role in improving the reliability of echocardiographic measurements of ventricular function. [41]

Another promising development in echocardiographic imaging involves the integration of multimodality data and advanced computational techniques to provide a more comprehensive evaluation of cardiac mechanics. Combining volumetric analysis with myocardial deformation imaging, hemodynamic assessment, and ventricular flow dynamics allows clinicians to better understand the complex interactions between cardiac structure and function. Novel approaches, including advanced flow imaging and deformation analysis, offer deeper insights into ventricular performance beyond traditional ejection fraction measurements. These techniques may help identify subtle alterations in myocardial function that precede overt systolic dysfunction and provide additional prognostic information in patients with cardiovascular disease. [42]

Improvements in three-dimensional imaging technology are also expected to expand the clinical utility of echocardiography in the evaluation of ventricular function. Advances in transducer design, image processing algorithms, and real-time data acquisition have enhanced both spatial and temporal resolution of three-dimensional datasets. These improvements facilitate more precise volumetric analysis and enable better visualization of complex ventricular geometry. As three-dimensional echocardiography becomes more widely available and integrated into routine clinical practice, it has the potential to reduce the methodological variability associated with conventional two-dimensional techniques and provide more consistent measurements of left ventricular ejection fraction. [43]

In addition, the growing use of quantitative myocardial deformation imaging may reshape the way clinicians evaluate ventricular function. Strain-based parameters such as global longitudinal strain have already demonstrated value in detecting early myocardial dysfunction and may serve as complementary markers alongside traditional ejection fraction measurements. Future research is likely to focus on integrating strain analysis with volumetric imaging to develop more comprehensive indices of cardiac performance. Such approaches could improve early detection of myocardial disease, refine risk stratification strategies, and support personalized treatment approaches for patients with cardiovascular disorders. [44]

Conclusion

Left ventricular ejection fraction remains one of the most widely used parameters for evaluating systolic function and guiding clinical decision-making in cardiovascular medicine. However, echocardiographic measurement of LVEF is influenced by multiple methodological factors, including imaging technique, geometric assumptions, image quality, and operator experience. Conventional echocardiographic approaches such as M-mode and two-dimensional imaging have played a crucial role in routine clinical assessment but are inherently limited by their reliance on simplified ventricular modeling and susceptibility to technical variability.

Advancements in echocardiographic technology, particularly three-dimensional imaging and myocardial strain analysis, have significantly improved the accuracy and reproducibility of ventricular function assessment. Three-dimensional echocardiography enables direct volumetric evaluation of the left ventricle without geometric assumptions, while speckle-tracking strain imaging provides detailed insights into myocardial mechanics and early detection of subclinical dysfunction. These techniques have demonstrated stronger correlation with reference imaging modalities such as cardiac magnetic resonance and offer important advantages in the comprehensive evaluation of ventricular performance. Despite these advances, variability in LVEF measurement remains an important clinical consideration, particularly when therapeutic decisions depend on specific ejection fraction thresholds. Standardization of imaging protocols, improved operator training, and the integration of advanced imaging technologies are essential steps toward minimizing measurement discrepancies. Furthermore, the incorporation of complementary parameters such as myocardial strain and ventricular remodeling indices may enhance the overall assessment of cardiac function beyond LVEF alone.

In the future, continued technological innovation, including automated image analysis and artificial intelligence–assisted quantification, is expected to further improve the precision and reliability of echocardiographic evaluation. By addressing methodological determinants of variability and integrating emerging imaging techniques, echocardiography will continue to play a central role in the accurate assessment of left ventricular function and the management of patients with cardiovascular disease.

References

1. Feigenbaum H. Evolution of echocardiography. *Circulation.* 2020;142(10):984-996. doi:10.1161/CIRCULATIONAHA.120.047498
2. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr.* 2015;28(1):1-39.e14. doi:10.1016/j.echo.2014.10.003
3. Mitchell C, Rahko PS, Blauwet LA, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: Recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr.* 2019;32(1):1-64. doi:10.1016/j.echo.2018.06.004
4. Keller M, Magunia H, Rosenberger P, Koeppen M. Echocardiography as a tool to assess cardiac function in critical care—a review. *Diagnostics.* 2023;13(5):839.
5. Kouris NT, Kostopoulos VS, Psarrou GA, et al. Left ventricular ejection fraction and global longitudinal strain variability between methodology and experience. *Echocardiography.* 2021;38(4):582-589.
6. Marwick TH. Future directions of echocardiography in heart failure. *Heart Fail Clin.* 2021;17(3):479-486. doi:10.1016/j.hfc.2021.02.008
7. Teichholz LE, Kreulen T, Herman MV, Gorlin R. Problems in echocardiographic volume determinations: Echocardiographic–angiographic correlations in the presence or absence of asynergy. *Am J Cardiol.* 1976;37(1):7-11.
8. Otto CM. *Practice of Clinical Echocardiography.* 6th ed. Elsevier; 2021.
9. Jenkins C, Tsang W. Three-dimensional echocardiographic acquisition and validity of left ventricular volumes and ejection fraction. *Echocardiography.* 2020;37(10):1646-1653.
10. Gherbesi E, Gianstefani S, Angeli F, et al. Myocardial strain of the left ventricle by speckle tracking echocardiography: From physics to clinical practice. *Echocardiography.* 2024;41(1):e15753.
11. Ito S, Pislaru C, Miranda WR, et al. Left ventricular contractility and wall stress in patients with aortic stenosis with preserved or reduced ejection fraction. *JACC Cardiovasc Imaging.* 2020;13(2):357-369.
12. Smiseth OA, Torp H, Opdahl A, Haugaa KH, Urheim S. Myocardial strain imaging: How useful is it in clinical decision making? *Eur Heart J.* 2016;37(15):1196-1207. doi:10.1093/eurheartj/ehv529
13. Savarese G, Stolfo D, Sinagra G, Lund LH. Heart failure with mid-range or mildly reduced ejection fraction. *Nat Rev Cardiol.* 2022;19(2):100-116.
14. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021;42(36):3599-3726. doi:10.1093/eurheartj/ehab368

15. Venkatram P. The three basic modes of echocardiogram: 2D, M mode and Doppler. In: *Heart Diseases and Echocardiogram: Principles in Practice.* Springer; 2024:505-519.
16. Zerbib Y, Maizel J, Slama M. Echocardiographic assessment of left ventricular function. *J Emerg Crit Care Med.* 2019;3:0. doi:10.21037/jeccm.2019.03.02
17. Liu S, Churchill J, Hua L, et al. Direct planimetry of left ventricular outflow tract area by simultaneous biplane imaging. *J Am Soc Echocardiogr.* 2020;33(4):461-468.
18. Akil S, Castaings J, Thind P, et al. Impact of experience on visual and Simpson's biplane echocardiographic assessment of left ventricular ejection fraction. *Clin Physiol Funct Imaging.* 2025;45(1):e12918.
19. Knackstedt C, Schummers G, Schröder J, et al. A graphical analysis of aspects contributing to the spreading of measurements of left ventricular function. *Int J Cardiovasc Imaging.* 2023;39(5):915-927.
20. Pastore MC, Mandoli GE, Aboumarie HS, et al. Basic and advanced echocardiography in advanced heart failure: An overview. *Heart Fail Rev.* 2020;25(6):937-948.
21. Chen Y, Hua W, Yang W, et al. Reliability and feasibility of automated function imaging for quantification in patients with left ventricular dilation. *Int J Cardiovasc Imaging.* 2022;38(6):1267-1276.
22. Dissabandara T, Lin K, Forwood M, Sun J. Validating real-time three-dimensional echocardiography against cardiac magnetic resonance for the determination of ventricular mass, volume and ejection fraction: A meta-analysis. *Clin Res Cardiol.* 2024;113(3):367-392.
23. Patel MD, Myers C, Negishi K, Singh GK, Anwar S. Two-dimensional strain is more precise than conventional measures of left ventricular systolic function in pediatric patients. *Pediatr Cardiol.* 2020;41(1):186-193.
24. Mihos CG, Liu JE, Anderson KM, et al. Speckle-tracking strain echocardiography for the assessment of left ventricular structure and function: A scientific statement from the American Heart Association. *Circulation.* 2025.
25. Ahmad A, Li H, Zhang Y, et al. Three-dimensional echocardiography assessment of right ventricular volumes and function: Technological perspective and clinical application. *Diagnostics.* 2022;12(4):806.
26. Li Y, Zhang L, Gao Y, et al. Comprehensive assessment of right ventricular function by three-dimensional speckle-tracking echocardiography: Comparisons with cardiac magnetic resonance imaging. *J Am Soc Echocardiogr.* 2021;34(5):472-482.
27. Lindner JR. Contrast echocardiography: Current status and future directions. *Heart.* 2021;107(1):18-24.
28. Johnson C. A review of three-dimensional medical image visualization. *Health Data Sci.* 2022.
29. Brady B, King G, Murphy RT, Walsh D. Myocardial strain: A clinical review. *Ir J Med Sci.* 2023;192(4):1649-1656.
30. Abou R, van der Bijl P, Bax JJ, Delgado V. Global longitudinal strain: Clinical use and prognostic implications in contemporary practice. *Heart.* 2020;106(18):1438-1444.
31. Antoniou N, Iliopoulou S, Raptis DG, et al. Global longitudinal strain in stress echocardiography: A review of its diagnostic and prognostic role. *Diagnostics.* 2025;15(16):2076.
32. Mandoli GE, Pastore MC, Vasilijevaite K, et al. Speckle tracking stress echocardiography: A valuable diagnostic technique or a burden for everyday practice? *Echocardiography.* 2020;37(12):2123-2129.
33. Rajiah PS, Kalisz K, Broncano J, et al. Myocardial strain evaluation with cardiovascular MRI: Physics, principles, and clinical applications. *Radiographics.* 2022;42(4):968-990.
34. Georgiopoulos G, Aimo A, Barison A, et al. Imaging predictors of incident heart failure: A systematic review and meta-analysis. *J Cardiovasc Med.* 2021;22(5):378-387.
35. Wang S, Wang S, Zhu Q, et al. Reference values of right ventricular volumes and ejection fraction by three-dimensional echocardiography in adults: A systematic review and meta-analysis. *Front Cardiovasc Med.* 2021;8:709863.
36. Postigo A, Viola F, Chazo C, et al. Assessment of blood flow transport in the left ventricle using ultrasound: Validation against 4-D flow cardiac magnetic resonance. *Ultrasound Med Biol.* 2022;48(9):1822-1832.
37. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 guideline for the management of heart failure. *J Am Coll Cardiol.* 2017;70(6):776-803.
38. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2016;37(27):2129-2200.
39. Ostovan M, Gholami K, Rezaeian N, et al. Prognostic value of left ventricular hypertrophy by electrocardiography and echocardiography in coronary artery disease: A systematic review and meta-analysis. *Curr Probl Cardiol.* 2023;48(7):101693.

40. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J.* 2017;38(36):2739-2791.

41. Chen Y, Hua W, Yang W, et al. Automated function imaging for quantification in patients with left ventricular dilation: Comparison with cardiac magnetic resonance. *Int J Cardiovasc Imaging.* 2022;38(6):1267-1276.

42. Meyers BA, Vlachos PP. Flow measurements in clinical cardiac imaging. *Phys Rev Fluids.* 2025;10(2):020501.

43. Santarpino G, Taverna G, Calabrese V, et al. Exploring imaging depth: A pilot study about 2D vs 4D echocardiography for tricuspid valve evaluation. *Rev Cardiovasc Med.* 2025;26(5):41556.

44. Zacchigna S, Paldino A, Falcão-Pires I, et al. Towards standardization of echocardiography for the evaluation of left ventricular function. *Cardiovasc Res.* 2021;117(1):43-59.