

Type of the Paper (Review)

Evaluation of Left Ventricular Functions in Hypertensive Diabetic Patients by Speckle Tracking Imaging and its Correlation with Brain Natriuretic Peptide Levels: A systematic Review

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Abstract

The purpose of this study is to analyze diabetic and hypertensive patients who have compromised left ventricular function as determined by speckle-tracking echocardiography. These patients also had higher levels of brain natriuretic peptide (BNP), a hormone that is released by the heart in response to stress. These findings suggest that patients with diabetes and hypertension are at increased risk of developing heart failure. The systemic review included seven studies that met the inclusion criteria of patients with hypertension or diabetic hypertension and volunteers in the control group who were normotensive, non-diabetic, and free of any cardiovascular disease. However, the quality of the included studies was generally good. This study investigated the correlation between BNP levels and left ventricular function in patients with hypertension and/or diabetes. A total of seven studies were included, with a total of 601 participants. The results revealed that in patients with hypertension and/or diabetes, there was a strong relationship between BNP levels and global systolic strain. This suggests that BNP levels may be a useful biomarker for assessing left ventricular function in these patients. This systematic review found that speckle tracking imaging could be used to detect sub-clinical changes in LV function in patients with hypertension or diabetes. Speckle tracking imaging detected significant reductions in all patient groups compared to controls in early diastolic strain rate. All patient groups had BNP levels that were substantially greater than those of healthy controls, and BNP levels were associated with LV strain and strain rate measurements. These findings suggest that speckle tracking imaging may be a useful tool for the detection of subclinical heart failure in patients with diabetes and/or hypertension. Further research is needed to confirm the findings of this review. However, to provide accurate evidence on the use of speckle tracking imaging in patients with hypertension and/or diabetes, future research should use larger sample sizes and more rigorous study methods.

Key words: Speckle tracking imaging; left ventricular; hypertension; brain natriuretic peptide.

1. Introduction

Cardiovascular diseases (CVD) are conditions of the heart and blood vessels that cause significant mortality and morbidity and place a significant burden on global public health. In addition, CVDs are considered the world's most common death cause. The term

"cardiovascular disease" (CVD) is used to describe a variety of conditions that affect the heart and blood vessels [1]. These include heart failure and other cardiac disorders, as well as high blood pressure (HTN), coronary heart disease (heart attack), cerebrovascular illness (stroke),

and. Since the environment in which the field of cardiology operates has been changing quickly, reliable and timely CVD statistics are crucial for tracking and predicting the progression of the illness [2].

Furthermore, HTN is the most prevalent cause of disability in the world and a separate, manageable risk factor associated with cardiovascular disease (CVD) [3]. Besides, for those with type 2 diabetes (T2D) and type 1 diabetes, CVD continues to be the leading cause of mortality and morbidity due to the morphological and functional changes that persistent hyperglycemia produces on artery walls, which are assumed to be the cause of the development of atherosclerotic plaque [4].

The finding that people with diabetes and hypertension have a greater LV end-diastolic pressure than those with hypertension alone may help to explain some of the increased risk of developing heart failure in these patients [5]. Additionally, independent abnormalities of diastolic function are rare and are typically brought on by a subclinical impairment of systolic function. Since LV re-modelling or hypertrophy is clearly seen in the advanced stages of hypertensive heart disease (HHD), traditional echocardiography only reveals problems in LV systolic function in these cases [6]. Additionally, speckle tracking echocardiography (STE) is a non-invasive, angle-independent method that monitors myocardial characteristics throughout

the cardiac cycle. Each myocardial region has its own distinct characteristics, and they are unaffected by heart translational movements [7]. Additionally, STE is more adept at identifying early cardiac dysfunction in hypertensive patients than both tissue Doppler imaging (TDI) and conventional echocardiography. Additionally, it can be used to evaluate diabetics' subclinical cardiac impairment prior to the onset of diabetic cardiomyopathy [8].

Brain natriuretic peptide (BNP) is a hormone produced by the heart in response to volume overload and increased pressure. It acts on the kidneys and blood vessels to promote fluid excretion and vasodilation [9]. In patients suffering from heart failure and acute myocardial infarction, BNP levels are increased and considered a strong predictor of cardiovascular events. BNP expression upregulation is frequently employed in the clinic as a diagnostic indicator for heart failure, diastolic dysfunction, and LV hypertrophy [10]. According to the literature, by acting as an endogenous brake on the LV myocardium, BNP can reduce the signaling pathways that cause the transition from LV hypertrophy to re-modeling, heart failure, and death [11, 12].

The purpose of this study was to evaluate left ventricular function using speckle tracking echocardiography in individuals with diabetes and hypertension and to make a correlation with the results of the brain natriuretic peptide levels.

2. Methods

2.1. Search strategy

The recommendations of Preferred Reporting Items for Systematic Reviews (PRISMA) were followed when conducting this systematic review [13]. Using PubMed, Web of Science, Cochrane, and Scopus, a literature search was conducted to look for potential studies that had been published. The search strategy

includes "left ventricular/left ventricle/left ventricles," "hypertensive /hypertensive diabetic," "strain/ deformation/ speckle tracking," and "brain natriuretic peptide/BNP-32/brain natriuretic peptide-32." In addition, this study did not require the permission of a university review board.

2.2. PICO criteria

Population

Patients were diagnosed with hypertension if their SBP and/or DBP were consistently elevated to ≥ 140 mmHg and ≥ 90 mmHg, respectively. Bedside, patients were diagnosed with diabetes if their FPG and/or 2hPG were consistently elevated to ≥ 126 mg/dl and ≥ 200 mg/dl, respectively.

Intervention

Speckle tracking imaging.

Comparison

None.

Outcome

Left ventricular function.

Inclusion criteria

Patients in the included trials were hypertension or diabetic hypertensive, while control group were non-hypertensive and non-diabetic persons who free of any CVD disease. However, hypertensive individuals were diagnosed using ESH/ESC guidelines for hypertension therapy if their SBP was 140 mmHg and/or their DBP was 90 mmHg on two or more hospital visits at one-week intervals. Diabetic individuals were identified using the American Diabetes Association's criteria: fasting plasma glucose 126 mg/dl (7.0mmol/l) or two-hour plasma glucose 200 mg/dl (11.1mmol/l).

Exclusion criteria

Patients with reduced left ventricular systolic function, arrhythmias, coronary artery disease, valve disease, congenital heart diseases, pericardial disorders, secondary causes of hypertension, or unsatisfactory echocardiographic pictures were excluded from the study.

Study selection

Both entire full-text and abstracts underwent conventional, blind review. Selected publications' references to pertinent studies were reviewed for potential inclusion. The Excel program was utilized. Moreover, any differences among scholars were settled by senior contributors prior to final clearance.

Data extraction

Before screening, each database's search results were aggregated, and duplicates were removed. The title/abstract were initially screened, the full-texts of selected publications were collected, in addition, the eligibility was double-checked by a specified eligibility form, and data was collected using a prepared form. Two authors working independently, carried out the citation screening and extraction and conflicts were resolved through consensus.

Bias risk assessment, quality, and validity of included studies. The author evaluated the included studies for quality and bias risk, including using the Newcastle-Ottawa Scale.

3. Results

3.1. Search results and study selection

A PRISMA diagram is shown in Figure 1. A total of 300 records were found. After deleting duplicates, 279 of 300 items were discarded based on title and abstract. The

eligibility of ten full-text articles was determined. The other seven papers from ten investigations were suitable (n = 2: demonstrate an association with brain natriuretic peptide levels; n = 5: use

Speckle tracking to assess left ventricular function).

Table 1 shows the characteristics of the papers that were included. Most (2/7) were based

3.2. Evaluation of left ventricular functions and its correlation with brain natriuretic peptide levels

A study by El-Noamany 2020 et al. showed a significant positive correlation between BNP levels and global systolic strain in group 4 (hypertensive-diabetics) ($r = 0.25$, $P = 0.000$) [12]. In addition, a study by Hamed 2014 et al.

on Egyptian samples. The remainder included one paper from China, Turkey, Germany, the USA, and India. The total number of participants in the seven trials mentioned was 601.

reported that plasma BNP levels were greater in hypertension groups (groups II and III) than in controls, and that group III was significantly higher than group II ($P = 0.001$) [14].

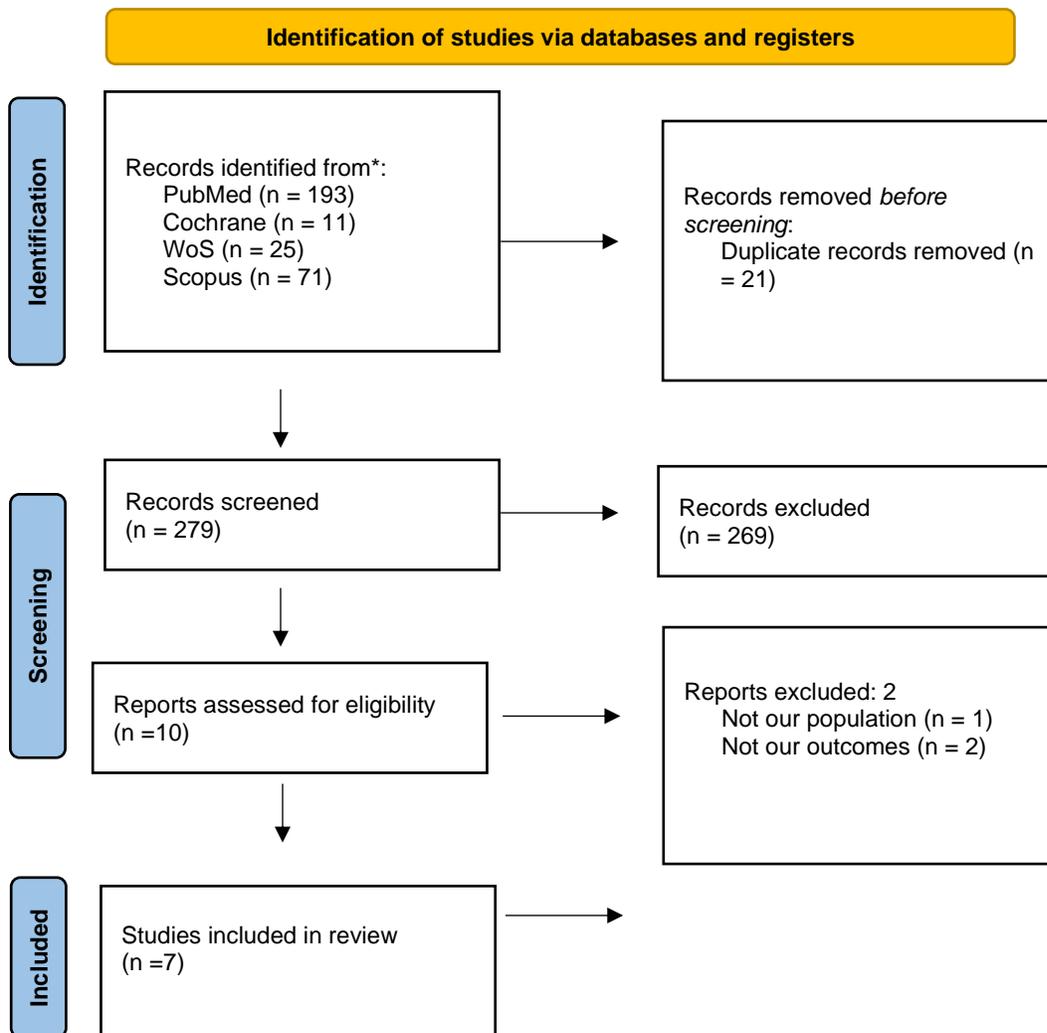


Figure 1: PRISMA flowchart.

Table 1: Summery of included studies.

Study ID	Country	Study Design	Study Population	Inclusion and exclusion criteria	Conclusion
El-Noamany et al., 2020 [12].	Egypt	Case-control study	Patients with hypertension and/or diabetes	<p>Inclusion criteria Hypertension and diabetes are diagnosed based on blood pressure and blood sugar levels.</p> <p>Exclusion Criteria Patients with heart conditions, other diseases, or poor echocardiographic images were excluded from the study.</p>	2D-STE is superior to conventional echocardiography in detecting subclinical alterations of LV systolic and diastolic functions in patients with hypertension and diabetes. In addition, even before chamber collapse occurs, increased BNP levels suggest the presence of ventricular dysfunction.
Hamed et al., 2014 [14].	Egypt	Case-control study	Hypertensive patients	<p>Exclusion Criteria The study included patients with reduced heart function (ejection fraction <50%), heart failure symptoms, diabetes, coronary artery disease, valvular disease, and atrial fibrillation or other rhythm disturbances.</p>	Hypertensive patients with apparently normal LV systolic function have substantial impairment of LV systolic and diastolic functions, especially if associated with LVH. This is evident by 2D speckle tracking echocardiography and elevated plasma BNP levels.
Han et al., 2008 [15].	China	Case series study	Hypertensive patients	<p>The study enrolled 50 patients with stage I to II essential hypertension who had their blood pressure measured before echocardiography.</p> <p>Patients with secondary hypertension, angina pectoris, previous</p>	Patients with hypertension had higher peak LV twist and slower diastolic untwisting than normal controls. This suggests that STI can be used to evaluate early changes in LV function in patients with hypertension.

				myocardial disease, or diabetes mellitus were excluded.	
Kalaycioglu et al., 2014 [16].	Turkey	Case-control study	Diabetic hypertensive	The study included 86 diabetic hypertensive patients and 30 nondiabetic hypertensive patients who were receiving antihypertensive and/or antidiabetic treatment for at least 1 year. Patients with echocardiographic evidence of either regional or global wall motion abnormalities, LV EF < 50%, and other conditions were excluded.	A Speckle Tracking Study showed that osteoprotegerin (OPG) levels are elevated in diabetic hypertensive patients with subclinical LV systolic dysfunction. This suggests that OPG could be used as a biomarker to identify these patients early, so that preventive strategies can be implemented to reduce their risk of developing LV systolic dysfunction.
Kosmala et al., 2008 [17].	Germany	Case-control study	Hypertensive patients	Coronary artery disease was excluded in patients with NYHA classes I and II by negative history and normal treadmill exercise test, and in patients with NYHA classes III and IV by normal coronary angiograms. <ul style="list-style-type: none"> • Inadequate acoustic window • Moderate and severe valvular heart disease • Diabetes mellitus and other endocrine or systemic diseases 	Speckle tracking can be used to assess the extent of myocardial damage in patients with hypertension and to predict its progression over time. However, the reproducibility of radial strain measurements may be less reliable than Doppler strain measurements.

				<ul style="list-style-type: none"> •Renal insufficiency with serum creatinine > 2.5 mg/dL. •Conduction or rhythm disturbances •Frequent supraventricular and ventricular extra-systolic beats •Atrial fibrillation and flutter •Other active non-sinus rhythms
Nakai et al., 2009 [17].	USA	cross-sectional study	Diabetic patients	<p>The study includes all patients had normal left ventricular ejection fraction (LVEF) and no regional wall motion abnormalities on two-dimensional echocardiography. The study excluded patients with a history of coronary artery disease, moderate-to-severe valvular heart disease, and/or significant rhythm disturbances.</p> <p>Diabetic patients with diastolic dysfunction have early signs of systolic dysfunction, even if LVEF is normal. 2DSTE can detect subclinical LV systolic dysfunction in diabetic patients and may be useful for risk stratification.</p>

<p>Sengupta et al., 2013 [18].</p>	<p>India</p>	<p>Case-control study</p>	<p>Patients with systemic hypertension</p>	<p>Exclusion criteria</p> <ul style="list-style-type: none"> • Established coronary artery disease • Hypertrophic cardiomyopathy • Valvular heart disease • Diabetes mellitus • Echocardiographic evidence of either regional or global wall motion abnormalities 	<p>The study found that the patients with systemic hypertension, the left ventricle (LV) wall thickens to compensate for reduced longitudinal shortening. This preserves the global LV ejection fraction, but masks subclinical LV dysfunction. Characterizing the disparities in LV principal strains can help to identify these patients and provide insights into the functional adaptations that maintain LV function.</p>
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3.3. LV and Speckle Tracking Imaging

A study by Han et al. (2008) reported that, in comparison to the healthy control group, patients with hypertension had a higher peak LV twist and delayed diastolic untwisting. This shows that STI can be used to assess early LV function changes in hypertensive patients [15]. Furthermore, a study by Kosmala et al. (2008) reported that in individuals with hypertension, speckle tracking can be used to evaluate the severity of cardiac damage and forecast how it

will evolve over time. Radial strain measures' reproducibility, however, might be less trustworthy than Doppler strain measurements [17]. A study by Nakai et al. (2009) found that in diabetic patients, 2DSTE can identify subclinical LV systolic dysfunction, which may be helpful for risk assessment [18].

Publication bias and study quality

The small number of included studies made it impossible to assess publication bias. However, the quality of the studies was good.

Table 2: Bias Risk Assessment Using Newcastle-Ottawa Scale.

Study ID	Country	Year	Journal	Newcastle–Ottawa Scale
El-Noamany et al., [12].	Egypt	2020	Cardiology and Cardiovascular Research	Good quality
Hamed et al., [14].	Egypt	2014	The Egyptian Heart Journal	Good quality
Han et al., [15].	China	2008	Journal of Huazhong University of Science and Technology	Good quality
Kalaycioglu et al., [16].	Turky	2014	Canadian Journal of Cardiology	Fear quality
Kosmala et al., [17].	Germany	2008	Journal of the American Society of Echocardiography	Good quality
Nakai et al., [17].	USA	2009	European Journal of Echocardiography	Good quality
Sengupta et al., [18].	India	2013	Indian heart journal	Good quality

4. Discussion

Using speckle tracking echocardiography, this systematic review summarizes the most recent research on the assessment of left ventricular functions in patients with hypertension and/or diabetes who appear to maintain LV. systolic function and compares the results to plasma brain natriuretic peptide levels.

To evaluate LV systolic function, conventional echocardiographic measures have been developed over time. The most clinically pertinent metric for this reason is LVEF, which is one of them. LVEF, however, has a number of drawbacks. Second, it is impacted by factors including heart rate, loading conditions, and other factors. The first of these three problems, which is the most important, is that it lacks the sensitivity to recognize minute alterations in

contractile performance, making it unsuitable for detecting sub-clinical myocardial injury, Thus, depending on the clinical context, could have significant therapeutic and prognostic implications.

Measurement of LV systolic function that can precisely identify minor changes in myocardial function is the most important function of STE. In this study, conventional echocardiogram measurements of LV systolic function revealed no appreciable differences between the two groups in terms of LV. However, these results were consistent with those of Wang et al., (2015) who included 90 diabetes patients, 36 of whom had concurrent hypertension, and classified them into three groups.: controls, individuals with diabetes, and individuals who also had hypertension [20]. The study found that

the three groups displayed comparable LVEF values when it came to heart function as measured by traditional echocardiography.

The results for early diastolic strain rate agreed with those from Hamed et al., (2014) who found that early diastolic strain rate was considerably lower in hypertension patients than in controls [14]. According to Yu Kolesnyk patients with diabetes and hypertension exhibited a considerably early diastole, reduced longitudinal strain rate than the other study groups [21].

The results of this study support earlier studies' findings that TDI or 2DSTE could detect early subclinical alterations in heart function [22–24]. However, TDI only reports velocity and strain information in the long axis direction and is angle dependent. Although 2DSTE eliminates TDI's angle dependency [25].

However, according to the current study, all patient groups had BNP levels that were significantly higher than those of healthy controls. These levels rose from the hypertension group to the diabetic group over time, peaking in the diabetic hypertensive group. In all patients, BNP levels were associated with LV strain and rate measurements, along with findings from traditional echocardiography and TDI. These results contradict those of Bakhoun et al., who claimed that there was no significant difference between control subjects and patients in terms of serum BNP level [26].

The present results, however, in line with those of Sadlecki et al. noted that BNP in pregnant women typically have higher amounts than non-pregnant ones, the study's participants showed that gestational hypertension dramatically increased BNP levels compared to normotensive pregnancy [27]. The most recent findings concurred with those of Hamed et al., (2014) who found that BNP levels were

considerably greater in hypertension patients than in control individuals [14].

Our findings differed slightly from those of Wang et al., (2015) that is concluded that the most of the diabetic research participants' BNP levels were normal, and echocardiography revealed diastolic dysfunction and abnormal strain. [20]. Despite the apparent discrepancy among diverse studies, BNP's examination is beneficial for excluding cardiac dysfunction in emergency situations with symptoms that may mirror those of cardiac origin because of its negative predictive value, which cannot be disregarded [14].

It has been demonstrated that natriuretic peptides are linked to left ventricular hypertrophy, changes in cardiac function, and overt heart failure in people with chronic renal illness. They are also linked to LV systolic and/or diastolic dysfunction in those with CVDs [28, 29]. Additionally, earlier research has demonstrated that BNP is elevated in the presence of asymptomatic LV systolic failure [30, 31].

Conclusion

This systematic review found that in individuals with diabetes or hypertension who appear to have intact LV systolic function, speckle tracking echocardiography was found to be able to detect sub-clinical alterations in left ventricular function. Speckle tracking echocardiography was able to detect significant reductions in early diastolic strain rate in all three patient groups, in comparison to controls. Additionally, all patient groups had BNP levels that significantly greater than those of healthy controls, and BNP levels were associated with LV strain and strain rate measurements. These findings suggest that speckle tracking echocardiography might be a useful tool for early identification of subclinical heart failure in patients with hypertension and/or diabetes.

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Conflicts of Interest: All authors declare no conflict of interest.

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