Section: General Medicine

Systematic Review

SYSTEMATIC REVIEW OF DIASTOLIC DYSFUNCTION IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS

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Abstract

Background: This systematic review and meta-analysis focused on the possibilities of diastolic dysfunction development in patients with type 2 diabetes mellitus. Age and hypertension are significant risk factors for diastolic dysfunction of the left ventricle (LV). According to a previous study, diabetes may act as an independent risk factor for left ventricular diastolic dysfunction. Diabetes can cause myocardial involvement at an early stage of the disease, which initially impairs early diastolic relaxation, and when more extensive, causes decreased myocardial contraction. The initial stage of diabetic cardiomyopathy, preceding alterations in systolic function, is known as left ventricular diastolic dysfunction (LVDD). This systematic exploration highlights the prevalence of diastolic in type 2 diabetes patients. The present study revealed a strong association between diabetes mellitus and diastolic dysfunction.

INTRODUCTION

Diabetes mellitus (DM) is a major global health issue that affects over 450 million people worldwide.[1] According to the Indian Council of Medical Research-Indian Diabetes Study (ICMR-INDIAB), a nationwide study on DM, there are currently an estimated 62.4 million DM patients in India.[2] Myocardial infarction, ischaemic cardiopathy, and impaired systolic function are among the known adverse macro- and microvascular effects of diabetes. Unfortunately, because diastolic heart failure is more common than other heart conditions and has comparable morbidity and mortality rates, the role of diabetes in this condition is less understood but has begun to gain attention.[3] Diastolic dysfunction is believed to be associated with age, hypertension, and ischemic heart disease (IHD) in patients with and without diabetes.[4]

Numerous mechanisms have been proposed to explain diabetic cardiomyopathy, including autonomic dysfunction, metabolic disturbances, interstitial fibrosis, and the development of fibrosis, which may be caused by the build-up of a periodic acid Schiff-positive glycoprotein that causes diastolic dysfunction and cardiac hypertrophy.[5] One of the key pathophysiological pathways associated with diastolic dysfunction may include insulin resistance.[6] Insulin resistance has been linked to larger left ventricular mass and decreased arterial compliance. Patients with diabetes have been found to have a reduced increase in left ventricular ejection fraction by insulin infusion following submaximal exercise compared to healthy subjects.[7] Mitochondrial dysfunction is another factor that may be involved in the development of cardiomyopathy in diabetes (CMiPD). In this regard, an imbalance between mitophagy and mitochondrial biogenesis caused by excessive mitophagy may worsen the destruction of cardiac cells.[8]

Diabetes duration primarily affects systolic function through specific cardiac mechanisms, such as heart structure, tissue, and microcirculation disruptions. These effects differ in their effects on cardiac systolic and diastolic function, with left ventricular concentrated remodelling and increased fibrosis tending to affect diastolic and myocardial perfusion function and oedema correlating with both systolic and diastolic function.[9] Many antidiabetic medications can lower cardiovascular death and adverse cardiovascular events. However, it remains unknown which medications can enhance ventricular remodelling and delay the onset of heart failure.[10] Echocardiography is currently the most effective noninvasive method for evaluating ventricular diastolic function.[11]

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MATERIALS AND METHODS

This systematic literature review and meta-analysis investigated the development of diastolic dysfunction in newly diagnosed type 2 diabetes mellitus patients.

Adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, we consistently followed the PRISMA 2009 guidelines for systematic literature review, data reporting, and discussion. The articles' evaluation and data extraction were conducted following these established guidelines.[12]

The overall quality of evidence for each outcome was assessed using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) methodology.

Search strategy

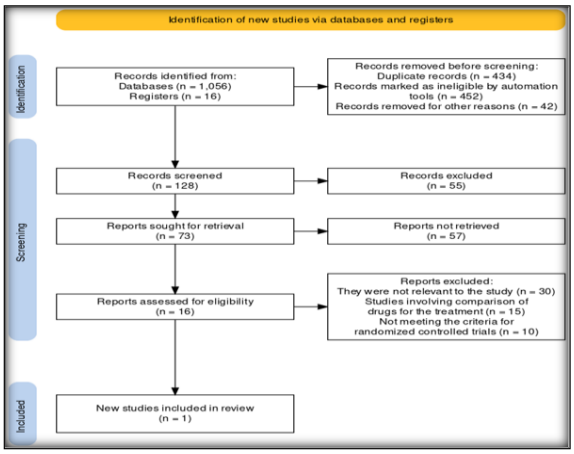
A systematic literature review was performed using PubMed (Medline database). The search methodology was aligned with the PICOS strategy, integrating Medical Subject Headings (MeSH) as search terms whenever feasible. Filters were applied to include studies with designs such as randomised controlled trials (RCTs) and observational studies as well as articles encompassing systematic reviews and meta-analyses. The selected studies were limited to those conducted between January 2019 and January 2024. No additional filters were used and the search terms used in the literature review are outlined below.

We systematically searched two online databases, PubMed and Google Scholar, to identify all reviews and meta-analyses involved in type 2 diabetes mellitus or adult-onset diabetes mellitus and diastolic dysfunction to identify those with both type 2 diabetes mellitus and diastolic dysfunction in the title.

Data extraction

The assessment of search results relied on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Participants, interventions, comparators, and outcomes (PICO) criteria were used to determine the eligibility of articles for inclusion in the meta-analysis. The inclusion criteria were individuals who met the study's enrolment conditions, and articles meeting the following criteria were included: ((type 2 Diabetes Mellitus) or (adult onset [MeSH Terms]) and (diastolic dysfunction [MeSH Terms]).



Study selection

The eligibility of all abstracts was assessed, and articles were incorporated into the qualitative synthesis if they fulfilled the following criteria.

Inclusion Criteria

We included the studies that assessed diastolic dysfunction in patients with type 2 diabetes mellitus have focused on reporting the accuracy of their development.

Exclusion Criteria

We excluded studies that lacked relevant outcome measures, had insufficient data, and were not published in English.

Data analysis

Quantitative data synthesis, when applicable, was carried out using statistical software, such as Review Manager and R. Meta-analysis was performed to compare outcomes among the studies, heterogeneity was evaluated using the I^2 statistic, values exceeding 50% indicated substantial heterogeneity, random-effects models were used in the presence of heterogeneity, and sensitivity analyses were performed to investigate the potential sources of heterogeneity and evaluate the robustness of the findings.

RESULTS

The literature search outlined above yielded 1056 articles from designated online databases for this study. After eliminating duplicate articles from automation tools and for other reasons, such as improper citations and articles in other languages, 128 records were considered. After reviewing the titles and abstracts of these 55 articles, six were excluded because they were irrelevant to the studies. The excluded articles covered various topics, including review articles; studies involving medical conditions unrelated to type 2 diabetes mellitus; studies that did not report relevant outcomes related to the accuracy, comparison, or laboratory-based investigations that lack direct applicability to human type 2 diabetes mellitus patients; studies with insufficient data quality, including those with missing or unreliable data necessary for accurate assessment of the development of diastolic dysfunction in patients with type 2 diabetes mellitus;

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and those that did not meet the inclusion criteria. After a more detailed eligibility assessment, 16 articles were considered for qualitative and quantitative synthesis.

Table 1: The outcome of the various studies

Name of the author	Study type	Number of patients	Outcome
Abhay Kumar Chaudhary et al.,	Cross-sectional study	100	Despite the confounding effects of hypertension, ischemia, and BMI, left ventricular diastolic dysfunction (LVDD) is highly prevalent at the time of type 2 diabetes diagnosis, even in patients with normotension.[2]
Rasa Kazlauskaite et al.,	Cross-sectional study	126	Diastolic dysfunction without symptoms was common in newly diagnosed diabetic patients from urban minority groups.[3]
Michaela Diamant et al.,	Prospective study	12	Patients with recently diagnosed, well-controlled, and uncomplicated type 2 diabetes may have functional changes in their left ventricle during diastole due to altered myocardial energy metabolism.[13]
Karan Jain et al.,	Cross-sectional study	50	Of the 50 patients enrolled in the study, 15 (30%) had Left Ventricular Diastolic Dysfunction (LVDD).[5]
Jung Hyun Noh et al.,	Cross-sectional study	65	Doppler echocardiographic studies revealed LV diastolic dysfunction in 15 patients (23.1%).[4]
Gani Bajraktari et al.,	Cross-sectional study	29	Insulin resistance and impaired diastolic function of the left ventricle are linked in individuals with type 2 diabetes and impaired glucose tolerance.[7]
Ricardo Fontes-Carvalho et al.,	Cohort study	1063	Before diabetes develops, there are already changes in diastolic function, which are primarily linked to the level of insulin resistance.[6]
Marijana Tadic et al.,	Cross-sectional study	140	The left ventricular hypertrophy echocardiographic parameters were considerably higher in individuals with diabetes mellitus.[14]
Jeremy M. Steele et al.,	Prospective study	331	Adolescents and young adults with T2DM who are obese have abnormal left ventricular diastolic function indices.[15]
Li Jiang et al.,	Prospective study	135	A decreased longitudinal peak systolic strain rate was linked to a longer duration of diabetes, according to univariate and multivariable analysis of systolic and diastolic function.[9]
Mami Enomoto, et al.,	Cohort study	104	In patients without hypertrophy and diastolic dysfunction, the characteristic functional abnormalities of diabetic cardiomyopathy are deterioration of left ventricular longitudinal shortening and decreased subendocardial wall thickening.[16]
Javaidur Rehman et al.,	Cross-sectional study	190	Patients with type 2 diabetes are more likely to experience diastolic dysfunction.[17]
Harikrushna Prajapati et al.,	Cross-sectional study	100	Diabetes was demonstrated in this study to be a separate risk factor for diastolic dysfunction. Of the 100 cases, diastolic dysfunction was present in 45.[11]
Sharavanan et al.,	Observational descriptive study	120	Patients with diabetes mellitus are primarily mobilised and die from cardiovascular disorders, which may also increase the risk of diabetic cardiomyopathy, which can result in congestive heart failure.[18]
Madhumathi R et al.,	Cross-sectional study	50	An early sign of diabetic cardiomyopathy is LV diastolic dysfunction. In patients with diabetes, LVDD considerably increases the morbidity of congestive heart failure.[19]
Hariprasad S et al.,	Prospective study	50	Patients with type 2 diabetes are more likely to experience diastolic dysfunction, which has a positive correlation with HbA1c level, obesity, and most crucially, length of diabetes.[20]

DISCUSSION

In this network meta-analysis, 16 studies were included. The 16 studies included nine cross-sectional studies, four prospective studies, two cohorts, and one observational descriptive study. This review showed that diastolic dysfunction is a significant issue for both men and women with type 2 diabetes.[21] The diastolic dysfunction rate is considerably higher in patients with type 2 diabetes mellitus.[22] Several studies have demonstrated that patients with diabetes may have impaired left ventricular diastolic function. Initially, cardiac catheterisation revealed diastolic LV abnormalities.

Numerous studies have explored the relationship between diabetes and myocardial histopathological abnormalities. Studies on human diabetic hearts using biopsy or post-mortem techniques have revealed interstitial accumulations of advanced-glycated end products (AGEs), which include collagen, elastin, and other connective tissue proteins, as well as fibrosis in the myocardium.[19] Evaluation of cardiac status is necessary in all diabetic patients because left ventricular diastolic dysfunction is the earliest first-stage indicator of diabetic cardiomyopathy.[18]

Another significant finding was that the prevalence of diastolic dysfunction increases with age, and diastolic dysfunction causes signs and symptoms of heart failure in approximately 50% of patients with heart failure who have a normal left ventricular ejection fraction. The general population has a prevalence of diastolic dysfunction of 27.3%, which

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highlights the significance of evaluating diastolic dysfunction even in healthy subjects.[17]

In the hypertensive diabetes mellitus subgroup, retinopathy was a significant predictor of LV longitudinal dysfunction. One possible cause of longitudinal systolic dysfunction in diabetes mellitus is microvasculopathy, a condition in which decreased coronary microcirculation results in chronic myocardial ischaemia without the capacity for compensatory angiogenesis.[16] These evidence and possibilities support the development of LVDD in patients with type 2 diabetes mellitus.

CONCLUSION

In conclusion, this systematic review and meta-analysis provides insights into the assessment of diastolic dysfunction in newly diagnosed type 2 diabetes mellitus patients, including its pathophysiology and prevalence among the diabetic population, and reveals a strong association between diabetes mellitus and diastolic dysfunction by showing references to various studies conducted at various sites, with left ventricular (LV) diastolic dysfunction being the earliest sign of diabetic cardiomyopathy. The severity and duration of diabetes are correlated. To create strategies for better managing these at-risk groups, more longitudinal studies are required to determine who patients with type 2 diabetes and LVDD will develop heart failure, after how long, and whether this varies between men and women.

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