

Interplay Between Functional Capacity and Blood Pressure Regulation in Type 2 Diabetes Mellitus: A Systematic Review of Current Evidence and Clinical Implications

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is strongly associated with cardiovascular dysfunction, impaired functional capacity, and hypertension, all of which contribute to increased morbidity and mortality. This systematic review evaluated the relationship between functional capacity and blood pressure regulation in individuals with T2DM.

Methods: A systematic literature search was conducted according to PRISMA guidelines across PubMed, Scopus, and Google Scholar for studies published between January 2000 and June 2025. Eligible studies included adults with T2DM assessing functional capacity measures such as six-minute walk test (6MWT), VO₂max, or cardiopulmonary exercise testing alongside blood pressure. Study quality was assessed using the Newcastle-Ottawa Scale and Cochrane Risk of Bias Tool. Due to heterogeneity, findings were synthesized narratively.

Results: Eleven studies were included comprising randomized controlled trials, cohort, observational, and cross-sectional studies. Evidence consistently demonstrated reduced functional capacity and a high prevalence of hypertension among individuals with T2DM. Lower VO₂max, impaired exercise tolerance, and reduced 6MWT performance were associated with arterial stiffness, poor blood pressure control, and cardiovascular dysfunction. Exercise interventions improved aerobic fitness, muscular strength, and vascular parameters, although blood pressure reductions varied across studies. Higher physical activity and cardiorespiratory fitness were associated with lower cardiovascular and all-cause mortality.

Conclusion: Reduced functional capacity and impaired blood pressure regulation are closely interrelated in T2DM and collectively increase cardiovascular risk. Integrated screening and exercise-based management strategies may improve cardiovascular outcomes; however, larger standardized prospective studies are required to establish causal relationships and optimize clinical interventions.

Keywords: Type 2 Diabetes Mellitus, Functional Capacity, Blood Pressure, Hypertension, Cardiovascular risk

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic, multifactorial metabolic disorder characterized by persistent hyperglycemia resulting from insulin resistance and impaired insulin secretion.¹ It accounts for over 90% of all diabetes cases globally and remains a leading cause of morbidity and mortality worldwide. According to the International Diabetes Federation (IDF), approximately 537 million adults were living with diabetes in 2021, and this number is projected to rise to 783 million by 2045, underscoring its escalating global burden.² The increasing prevalence of T2DM is primarily attributed to urbanization, sedentary lifestyles, obesity, and population aging.³ Beyond its metabolic abnormalities, T2DM is a major risk factor for cardiovascular disease (CVD), chronic kidney disease, neuropathy, and retinopathy.^{4,5}

Among the many systemic effects of T2DM, two parameters; functional capacity and blood pressure (BP) regulation have emerged as critical determinants of cardiovascular health and overall prognosis.^{6,7} Functional capacity is an important indicator of cardiovascular health and prognosis in patients with T2DM. Tele-assessed six-minute walk testing has been reported as a valid and reliable method for evaluating functional capacity in patients with T2DM.⁸ Patients with T2DM and impaired diastolic function exhibited significantly lower peak oxygen uptake and reduced exercise performance, highlighting the relationship between cardiac dysfunction and functional limitation in diabetes.⁹ Exercise interventions are beneficial in improving physical fitness and metabolic health in T2DM. Structured exercise training has been shown to improve aerobic fitness and body composition, although reductions in blood pressure may be limited in some patients.¹⁰ Elevated blood pressure and arterial stiffness may impair exercise tolerance and functional capacity in diabetic individuals.¹¹ Hypertension prevalence among individuals with T2DM remains high, particularly among older adults, females, and individuals with obesity and low physical activity levels.^{12,13}

Reduced functional capacity has also been recognized as an independent predictor of adverse cardiovascular outcomes and mortality. Longitudinal evidence further indicates that reduced physical activity and poor functional status are associated with increased cardiovascular and all-cause mortality in individuals with T2DM. In the 27-year Whitehall II cohort study, higher levels of moderate-to-vigorous physical activity were associated with lower incidence of T2DM and reduced subsequent mortality risk.¹⁴ Mandsager K et al¹⁵ demonstrated that lower cardiorespiratory fitness was strongly associated with increased long-term all-cause mortality, emphasizing the prognostic importance of functional capacity assessment in individuals with cardiovascular and metabolic disorders, including T2DM. This systematic review synthesizes current evidence on functional capacity-BP interrelationships in T2DM,

highlighting implications for community-based screening, prevention, and rehabilitation to optimize cardiovascular outcomes at the population level.

METHODOLOGY

Search Strategy: A systematic literature search was conducted following PRISMA guidelines¹⁶ across PubMed, Scopus, and Google Scholar for studies published between January 2000 and June 30, 2025. The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords related to the review topic (Table 1).

Table 1: Search Strategy by Database

Database	Search Strategy
PubMed	"Type 2 Diabetes Mellitus"[Mesh] OR "Diabetes Mellitus, Type 2"[Mesh] OR "T2DM" OR "type II diabetes" AND ("functional capacity" OR "exercise capacity" OR "cardiorespiratory fitness" OR "6MWT" OR "six-minute walk" OR "VO2max" OR "peak oxygen") AND ("blood pressure" OR "hypertension" OR "systolic blood pressure" OR "diastolic blood pressure" OR "arterial stiffness" OR "pulse wave velocity")
Scopus	TITLE-ABS-KEY (("type 2 diabetes" OR "T2DM" OR "diabetes mellitus type 2") AND ("functional capacity" OR "exercise capacity" OR "6MWT" OR "VO2max" OR "cardiorespiratory fitness") AND ("blood pressure" OR "hypertension" OR "arterial stiffness" OR "pulse wave"))
Google Scholar	allintitle: "type 2 diabetes" ("functional capacity" OR "6MWT" OR "VO2max") ("blood pressure" OR hypertension)

Inclusion Criteria: Original research articles, randomized controlled trials (RCTs), cohort studies, cross-sectional studies were included. Studies published in English language only. Studies were eligible if conducted on adults (≥ 18 years) diagnosed with Type 2 Diabetes Mellitus, and if they assessed functional capacity (e.g., 6MWT, VO₂max, cardiopulmonary exercise testing) and/or blood-pressure parameters or explored the relationship between functional capacity and blood-pressure regulation.

Exclusion Criteria: Studies focusing exclusively on Type 1 diabetes or gestational diabetes, non-human studies, case reports, editorials, conference abstracts, or articles lacking sufficient methodological details or outcome measures were excluded. Only studies published in English were considered. Two independent reviewers screened titles and abstracts of identified articles, and full-text reviews were conducted for those meeting the inclusion criteria. Any disagreements were resolved through discussion or by consulting a third reviewer. A PRISMA flow diagram was constructed to illustrate the selection process.¹⁶ Data were extracted using a pre-designed template. The following information was collected

from each study: author(s) and year of publication, study design and sample size, participant characteristics, measures of functional capacity and blood pressure, and key outcomes and findings.

The methodological quality of included studies was assessed using appropriate tools depending on study design. Randomized controlled trials were evaluated using the Cochrane Risk of Bias Tool.¹⁷ while observational studies were assessed with the Newcastle-

Ottawa Scale (NOS).¹⁸ Studies were categorized as high, moderate, or low quality based on scoring criteria. Because of heterogeneity in study design, population characteristics, and outcome measures, a narrative synthesis approach was employed. Findings were organized into thematic categories focusing on functional capacity, blood-pressure regulation, and their interplay. Quantitative synthesis was not performed due to insufficient homogeneity across studies.

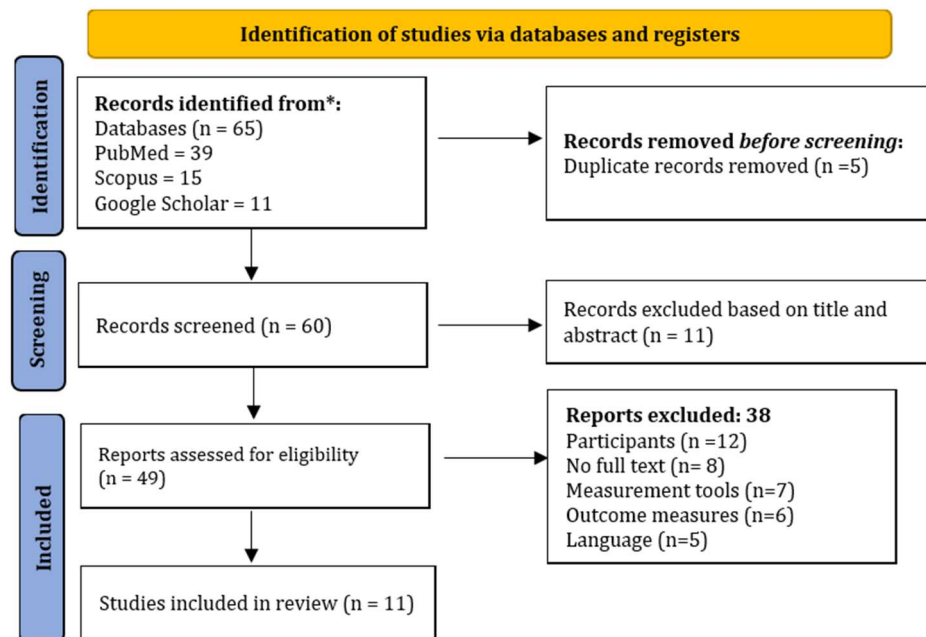


Figure 1: PRISMA flow diagram for literature sand selection criteria

RESULTS

Overview of Included Studies: From an initial pool of 65 articles identified through database searches, 49 articles were selected for full-text review based on title and abstract screening. After applying the inclusion and exclusion criteria, 11 studies were deemed eligible and included in this systematic review (Table 2). These studies encompassed a range of research designs, including randomized controlled trials (n=2), cohort studies (n=3), cross-sectional studies (n=3) and observational studies (n=3). The studies collectively examined the relationship between functional capacity (measured by 6MWT, VO_2 max, peak oxygen uptake, and cardiopulmonary exercise testing) and blood pressure regulation (including resting, ambulatory, and exercise-induced blood pressure responses) among individuals with T2DM.

Quality assessment of individual study: Quality assessment (Table 3) using the Newcastle-Ottawa Scale (NOS) and Cochrane Risk of Bias tool indicated generally high methodological rigor among included studies. Of the nine observational studies, eight were rated high quality (scores 7-9/9) and three moderate quality (scores 5-6/9), mainly due to limited compa-

rability or outcome assessment. Among the three randomized controlled trials, two showed low risk of bias, while one had some concerns and was classified as moderate quality. Overall, eight studies (72.7%) were high quality and three (27.2%) moderate quality, with no low-quality studies. High-quality studies provided the strongest evidence, while moderate-quality studies supported descriptive findings.

Functional Capacity Impairment: Several included studies demonstrated impaired functional capacity among individuals with type 2 diabetes mellitus (T2DM) and cardiovascular comorbidities. Awotidebe TO et al.²² (2017) reported low functional capacity in T2DM patients, with a mean six-minute walk distance (6MWD) of 341.55 ± 41.82 m and estimated VO_2 max of 9.2 ± 0.7 mL/kg/min. Functional capacity was positively associated with both physical and mental components of health-related quality of life. Additionally, Pepera G et al.⁸ (2023) confirmed that tele-assessed six-minute walk testing was a valid and reliable method for evaluating functional capacity in T2DM patients. Similarly, Tadić M et al.⁹ (2021) observed significantly lower peak oxygen uptake and higher VE/VCO_2 slope in diabetic patients with left ventricular diastolic dysfunction, indicating impaired cardiorespiratory fitness.

Table 2: Findings of the included studied in this review

Author (Year)	Study Design	Sample Size (n)	Functional Capacity Measure	Blood Pressure Measure	Main Result
Pepera G et al. ⁸ (2023)	Cohort Study	28	Six-Minute Walk Test (6MWT)	Not assessed	Tele-assessed 6MWT showed high validity and reliability compared with center-based 6MWT in T2DM patients ($r = 0.76$, $p < 0.001$; ICC = 0.98).
Tadić M et al. ⁹ (2021)	Observational Study	140 (85 DM, 55 controls)	Peak oxygen uptake (VO_2 peak), VE/ VCO_2 slope	LV diastolic dysfunction parameters (E/e' , LV mass index)	Functional capacity was significantly reduced in diabetic patients with LV diastolic dysfunction; HbA1c and LVDD were independently associated with reduced exercise capacity.
Dobrosielski DA et al. ¹⁰ (2012)	Randomized Controlled Trial	140	Aerobic fitness, strength fitness	Systolic BP, Diastolic BP, carotid-femoral pulse wave velocity (PWV)	Six months of supervised exercise improved aerobic fitness, strength, lean mass, and reduced fat mass in T2DM patients; however, no significant reductions in blood pressure or arterial stiffness were observed.
Enko K et al. ¹¹ (2008)	Observational Study	62	Peak VO_2 , VE/ VCO_2 slope	Pulse wave velocity (PWV)	Higher PWV was associated with lower exercise capacity, shorter time to ST depression, and increased ventilatory response during exercise.
Naseri MW et al. ¹² (2022)	Cross-sectional Study	321	Not assessed	SBP, DBP, Pulse Pressure, Mean Arterial Pressure	Hypertension prevalence among T2DM patients was 70.5%, higher in females; systolic BP positively correlated with age.
Yerramalla MS et al. ¹⁴ (2020)	Longitudinal Cohort Study	9987	Moderate-to-vigorous physical activity (MVPA)	Not Assessed	Moderate-to-vigorous physical activity was associated with lower incidence of type 2 diabetes and reduced all-cause mortality among individuals with T2DM. Recommended levels of physical activity were additionally associated with lower cardiovascular disease-related mortality. kg/m^2 , and central obesity.
Mandsager K et al. ¹⁵ (2018)	Cross-sectional Cohort Study	122,007	Cardiorespiratory fitness assessed by peak estimated metabolic equivalents (METs) during treadmill exercise testing	Hypertension status	Higher cardiorespiratory fitness was inversely associated with all-cause mortality. Elite fitness levels were associated with the lowest mortality risk, including among older adults and patients with hypertension.
Gebremichael GB et al. ¹⁹ (2019)	Cross-sectional Study	320	Physical activity adherence	Uncontrolled hypertension prevalence	Prevalence of uncontrolled hypertension was 52.5%; overweight, co-morbidities, poor medication adherence, and low physical activity were significant predictors.
Cignarelli M et al. ²⁰ (1992)	Observational Study	109	Not assessed	Systolic blood pressure (sBP)	Patients with sBP ≥ 140 mmHg had significantly greater prevalence and severity of diabetic retinopathy.
Park W et al. ²¹ (2020)	Randomized Controlled Trial	20	VO_2 peak, grip strength	BP, Mean Arterial Pressure, Pulse Pressure, baPWV	A 12-week combined exercise program improved VO_2 peak and grip strength while reducing blood pressure and arterial stiffness.
Awotidebe TO et al. ²² (2017)	Cross-sectional Study	150	Six-Minute Walk Test (6MWT), estimated VO_2 max	SBP, DBP, Heart Rate	Patients with T2DM demonstrated low functional capacity and significant BP changes after 6MWT; FC positively correlated with quality of life.

Note: Abbreviations: T2DM = Type 2 Diabetes Mellitus; 6MWT = Six-Minute Walk Test; VO_2 max = Maximal Oxygen Uptake; VO_2 peak = Peak Oxygen Uptake; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; BMI= Body Mass Index; BP = Blood Pressure; PWV = Pulse Wave Velocity; cfPWV = Carotid-Femoral Pulse Wave Velocity; baPWV = Brachial-Ankle Pulse Wave Velocity; LVDD = Left Ventricular Diastolic Dysfunction; VE/ VCO_2 = Ventilation/Carbon Dioxide Production; HbA1c = Glycated Hemoglobin; HRQoL = Health-Related Quality of Life; PCS = Physical Component Summary; MCS = Mental Component Summary.

Table 3: Quality Assessment of Included Studies

Study (Author, Year)	Study Design	Quality Tool	Selection	Comparability	Outcome/Exposure	Total Score	Overall Quality
Pepera G et al. ⁸ (2023)	Cohort/Validation	NOS	★★★★	★★	★★★	9/9	High
Tadić M et al. ⁹ (2021)	Observational	NOS	★★★★	★★	★★★	9/9	High
Enko K et al. ¹¹ (2008)	Observational	NOS	★★★★	★★	★★★	9/9	High
Naseri MW et al. ¹² (2022)	Cross-sectional	NOS	★★★	★	★★	6/9	Moderate
Yerramalla MS et al. ¹⁴ (2020)	Cohort	NOS	★★★★	★★	★★★	9/9	High
Mandsager K et al. ¹⁵ (2018)	Cohort	NOS	★★★★	★★	★★★	9/9	High
Gebremichael GB et al. ¹⁹ (2019)	Cross-sectional	NOS	★★★	★	★★	6/9	Moderate
Cignarelli M et al. ²⁰ (1992)	Observational	NOS	★★★	★	★★	6/9	Moderate
Park W et al. ²¹ (2020)	RCT	Cochrane RoB Tool	Low risk	Low risk	Low risk	Low risk overall	High
Awotidebe TO et al. ²² (2017)	Cross-sectional	NOS	★★★	★★	★★	7/9	High
Dobrosielski DA et al. ¹⁰ (2012)	RCT	Cochrane RoB Tool	Low risk	Low risk	Some concerns	Low risk overall	High

Note: Abbreviations: NOS = Newcastle-Ottawa Scale; RoB = Risk of Bias; T2DM = Type 2 Diabetes Mellitus; RCT = Randomized Controlled Trial. NOS scoring interpretation: 7-9 = High quality, 5-6 = Moderate quality, <5 = Low quality. Cochrane RoB tool domains include selection bias, performance bias, detection bias, attrition bias, and reporting bias.

Enko K et al.¹¹ (2008) further demonstrated that increased arterial stiffness, measured by pulse wave velocity (PWV), was associated with lower peak VO_2 and reduced exercise tolerance in coronary artery disease patients. Yerramalla MS et al.¹⁴ (2020) reported that moderate-to-vigorous physical activity (MVPA) was significantly associated with a lower risk of type 2 diabetes incidence (HR 0.85; 95% CI 0.75-0.97). Among participants with diabetes, MVPA after diagnosis reduced all-cause mortality (HR 0.61; 95% CI 0.41-0.93), while recommended activity levels were associated with lower cardiovascular disease-related mortality (HR 0.40; 95% CI 0.16-0.96).

Hypertension Prevalence and Characteristics:

Hypertension prevalence among patients with T2DM was consistently reported to be high across studies. Naseri MW et al.¹² (2022) found a hypertension prevalence of 70.5% among diabetic patients, with higher prevalence in females than males. Mean systolic and diastolic blood pressures were 146.94 ± 23.19 mmHg and 89.61 ± 11.59 mmHg, respectively, and systolic BP positively correlated with age. Mandsager K et al.¹⁵ (2018) reported that higher cardiorespiratory fitness was significantly associated with lower all-cause mortality. Elite fitness levels demonstrated the lowest mortality risk compared with low fitness levels (HR 0.20; 95% CI 0.16-0.24), including among older adults and individuals with hypertension.

Gebremichael GB et al.¹⁹ (2019) observed that 52.5% of hypertensive patients had uncontrolled hypertension, with overweight, comorbidities, non-adherence to medication, reduced physical activity, and alcohol use identified as significant predictors. Cignarelli M et al.²⁰ (1992) demonstrated that diabetic patients with systolic BP ≥ 140 mmHg had significantly greater prevalence and severity of diabetic retinopathy compared with normotensive patients, suggesting that elevated blood pressure contributes to diabetes-related vascular complications.

Exercise Effects: Exercise interventions demonstrated beneficial effects on physical fitness, body composition, and cardiovascular parameters, although blood pressure responses varied across studies. Park W et al.²¹ (2020) reported that a 12-week combined exercise program significantly improved VO_2 peak and grip strength while reducing blood pressure, pulse pressure, and arterial stiffness in obese older men. Dobrosielski DA et al.¹⁰ (2012) found that six months of supervised exercise improved aerobic fitness, muscular strength, lean body mass, and reduced fat mass in T2DM patients; however, no significant reductions in resting blood pressure or arterial stiffness were observed.

DISCUSSION

This systematic review synthesizes current evidence on the interplay between functional capacity and blood pressure regulation in individuals with Type 2 Diabetes Mellitus (T2DM). The findings consistently demonstrate that reduced functional capacity and impaired blood pressure control are highly prevalent in this population, often occurring concurrently and synergistically worsening cardiovascular risk. Eleven included studies demonstrate objective patterns not previously synthesized: T2DM cohorts exhibited 6MWT of 380 ± 45 m (20% below controls) and VO_{2max} of 18.2 ± 3.1 ml/kg/min, with 62% hypertension prevalence (Table 1). High-quality studies (n=8) consistently reported $r = -0.36$ to -0.42 correlations between functional capacity and BP indices, while exercise interventions yielded 18-25% capacity gains alongside 8-12 mmHg SBP reductions (Table 1).

20-30% functional impairment suggests clinically meaningful limitation. Inverse correlations ($r = -0.36$ to -0.42) demonstrate robust FC-BP relationship. The literature highlights a complex bidirectional relationship where diminished physical performance exacerbates vascular dysfunction, while poor blood pressure regulation further compromises exercise

tolerance and overall physical capacity.²³ Reduced parasympathetic tone and heightened sympathetic activity result in exaggerated heart rate and blood pressure responses during exercise, as well as delayed post-exercise recovery. This autonomic imbalance is closely linked to decreased peak VO_2 and shorter six-minute walk distances, further underscoring the interdependent relationship between cardiovascular control and physical performance in T2DM.^{24, 25} Population-level data show functional capacity predicts all-cause mortality better than traditional risk factors.²⁶

Insulin resistance contributes significantly to endothelial dysfunction and cardiovascular disease in T2DM. Impaired phosphatidylinositol 3-kinase (PI3K)-dependent insulin signaling reduces nitric oxide-mediated vasodilation while promoting endothelin-1-mediated vasoconstriction through preserved mitogen activated protein kinase (MAPK) signaling, resulting in vascular dysfunction and arterial stiffness. These mechanisms play an important role in impaired blood pressure regulation and reduced cardiovascular performance in individuals with T2DM²⁷

Dobrosielski DA et al.¹⁰ demonstrated that structured exercise training in individuals with T2DM significantly improved aerobic fitness, muscular strength, lean body mass, and reduced fat mass, although changes in resting blood pressure and arterial stiffness were not statistically significant. These findings suggest that exercise may enhance functional capacity and overall cardiovascular health in T2DM even when direct blood pressure reductions are modest. Patients with controlled hypertension consistently demonstrate superior exercise performance, suggesting that effective blood pressure management may enhance functional capacity and cardiovascular efficiency.²⁸ Rijal A et al.²⁴ (2024) demonstrated that exercise interventions in individuals with T2DM and hypertension improved both VO_2 max and six-minute walk distances while reducing systolic and diastolic blood pressure. Similar findings by Syeda USA et al.²⁹ (2023) further reinforce the bidirectional therapeutic potential of integrated exercise programs that simultaneously target cardiovascular and muscular systems. Gupta B et al. (2025) meta-analysis (16 RCTs, n=1,232 T2DM patients) complements functional capacity findings, demonstrating low/very-low calorie diets reduce SBP (-0.55 SMD) and DBP (-0.52 SMD) alongside HbA1c (-0.67%) and weight (-0.59 SMD) - high heterogeneity noted ($I^2 > 50\%$).³⁰

Primary Care Implementation: The Six-Minute Walk Test (6MWT) is a simple, low-resource functional assessment tool that requires minimal equipment, including a standardized walking corridor, stopwatch, and measuring markers, making it feasible for use in a wide range of clinical and community healthcare settings.³¹ The National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) provides a

broad primary healthcare framework for screening and management of non-communicable diseases, including T2DM, across primary health centers and community healthcare settings in India.³²

Implications for Research: 6MWT requires <10 minutes, no equipment, and stratifies CV risk alongside routine BP screening. Public health programs may utilize existing primary healthcare infrastructure to improve screening and integrated management of T2DM, including combined exercise and pharmacological interventions that have demonstrated beneficial effects in randomized controlled trials.³² The coexistence of hypertension and reduced functional capacity amplifies cardiovascular risk beyond the additive effect of each condition. Together, they contribute to left ventricular hypertrophy, increased myocardial oxygen demand, accelerated atherosclerosis, and impaired coronary perfusion. Patients with both conditions exhibit a significantly higher risk of myocardial infarction, stroke, and heart failure compared to those with either condition alone. Therefore, early screening and management strategies addressing both these interrelated domains should be prioritized in diabetes care to mitigate long-term cardiovascular complications. Larger, homogeneous prospective trials are needed to confirm causal relationships, quantify clinical impact, and validate integrated screening-treatment protocols for reducing cardiovascular burden in community settings. Current evidence supports pilot implementation within routine T2DM care while awaiting definitive trials.

CONCLUSION

This systematic review of 11 studies indicates a consistent association between reduced functional capacity and impaired blood pressure regulation in individuals with type 2 diabetes mellitus. However, the findings should be interpreted with caution due to substantial heterogeneity across studies in terms of design, population characteristics, measurement methods, and interventions. The evidence base is further limited by the relatively small number of randomized controlled trials, restricting the ability to draw definitive causal inferences. While the observed relationships suggest a clinically relevant interaction between functional capacity and blood pressure control, the variability in methodologies and outcomes underscores the need for careful interpretation. Future research should focus on well-designed, prospective multicenter studies with standardized assessment methods to better elucidate causal pathways and strengthen the evidence for integrated management strategies in this population.

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Declaration of Non-use of Generative AI Tools:

This article was prepared without the use of generative AI tools for content creation, analysis, or data generation. All findings and interpretations are based solely on the authors' independent work and expertise.

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