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Review article

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Erectile dysfunction and cardiovascular health

Emil Durukan[1] ✉, Christian Fuglesang S. Jensen[1], Kristoffer Grundtvig Skaarup[2] & Mikkel Fode[1,3]

Abstract

Erectile dysfunction (ED) is a prevalent condition, recognized as a sentinel marker of cardiovascular disease. Epidemiological and mechanistic evidence link ED to cardiovascular risk, with a prominent role of low-grade inflammation, endothelial dysfunction and atherosclerosis. ED might serve as an early indicator of subclinical vascular disease, and diagnostic strategies, including coronary artery calcium scoring and echocardiography, can be considered to enhance risk stratification. Management approaches that integrate sexual and cardiometabolic health are beneficial to improve care in this at-risk population.

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[1]Department of Urology, Copenhagen University Hospital - Herlev and Gentofte Hospital, Herlev, Denmark. [2]Cardiovascular Non-Invasive Imaging Research Laboratory, Department of Cardiology, Copenhagen University Hospital - Herlev and Gentofte Hospital, Gentofte, Denmark. [3]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark. ✉e-mail: Emil.durukan.01@regionh.dk

Key points

- Erectile dysfunction (ED) is associated with increased cardiovascular risk.
- Inflammation and endothelial dysfunction are shared pathophysiological mechanisms linking ED and cardiovascular disease.
- ED often precedes manifest cardiovascular disease, offering a window for early detection.
- Coronary artery calcium scoring and echocardiography show promise in risk stratification of patients.
- Integrated management of ED and cardiovascular health is clinically beneficial.

Introduction

Cardiovascular disease (CVD) remains the leading cause of death globally, accounting for an estimated 17.9 million deaths each year[1]. Accordingly, early identification of individuals at increased risk is a crucial public health priority. Erectile dysfunction (ED), defined as the persistent inability to attain or maintain an erection sufficient for satisfactory sexual performance, affects ~30% of men over the age of 40 years[2,3]. ED has emerged as an important clinical marker of cardiovascular risk, and the two conditions share several risk factors such as diabetes, hypertension, obesity, smoking and dyslipidaemia[4–6]. Historically, the association between ED and CVD has been attributed to atherosclerosis and the artery size hypothesis, which proposes that penile arteries are smaller and, therefore, more susceptible to occlusion than larger coronary arteries, thereby manifesting symptoms of ED earlier than heart symptoms[7]. Subsequent evidence suggests that low-grade inflammation and endothelial dysfunction also have crucial roles in linking ED to CVD, contributing to systemic vascular injury and localized penile vascular impairment[8].

In this narrative Review, we evaluate the published literature on ED and cardiovascular health, with particular emphasis on epidemiology, shared pathophysiological mechanisms, cardiovascular risk stratification and management strategies. In addition, we highlight crucial gaps in knowledge and propose future research directions.

Epidemiology

Results from seminal studies have established a robust association between ED and subsequent cardiovascular events (Table 1). In an analysis of 9,457 men from the placebo arm of the Prostate Cancer Prevention Trial, ED was identified as an independent predictor of cardiovascular events[9]. In this study, both incident ED (hazard ratio (HR) 1.25) and prevalent ED (HR 1.45) were associated with a statistically significant increased risk of subsequent CVD events, including myocardial infarction (HR 1.50, 95% CI 1.20–1.87), angina (HR 1.72, 95% CI 1.26–2.33), stroke (HR 1.79, 95% CI 1.15–2.80), transient ischaemic attack (HR 1.92, 95% CI 1.12–3.26) and any cardiovascular event (HR 1.45, 95% CI 1.25–1.69), after adjustment for potential confounders such as age, BMI and serum lipids. Interestingly, the magnitude of risk conferred by ED was comparable to that of established risk factors, including smoking and a family history of myocardial infarction[9]. These findings underscore the crucial role of ED in cardiovascular risk assessment and suggest that ED can precede overt CVD, offering a window for early detection and intervention[9]. However, this cohort is constituted by a selected population of relatively healthy trial participants aged 55 years or older, which might limit generalizability to broader clinical populations. In addition, non-fatal cardiovascular events were based on participant or investigator report and were not centrally adjudicated; similarly, ED assessment relied on patient-reported measures rather than a contemporary multidimensional instrument. Since this first analysis, results from numerous studies have supported a link between ED and CVD severity. One notable example was the COBRA trial, in which 285 men were stratified based on coronary artery disease (CAD) burden and presentation[10]. Results from this trial showed a stepwise increase in ED prevalence corresponding to CAD severity and chronicity (ED reported in 65% of men with chronic coronary syndrome and multivessel disease versus 22% of men with acute coronary syndrome with single-vessel involvement). Importantly, the onset of ED preceded CAD diagnosis by 2–3 years in most patients, supporting the utility of this measure as a window for early vascular risk detection[10].

In a large prospective study in which over 95,000 of men were monitored, a dose-dependent relationship was observed between ED severity, assessed through self-reported ability to achieve and maintain an erection (none, mild, moderate or severe), and specific cardiovascular outcomes[11]. In this study, the risk of all CVD increased progressively across mild, moderate and severe ED compared with no ED (*P* for trend <0.001), indicating a clear dose–response relationship. Severe ED was associated with a relative risk (RR) of 1.35 (95% CI 1.19–1.53) for all CVD, alongside increased risks of ischaemic heart disease (RR 1.60), heart failure (RR 8.00) and all-cause mortality (RR 1.93). The rigorous adjustment for confounders and the size of the cohort strengthened the study's conclusions, emphasizing the role of ED severity as a determinant of cardiovascular risk[11]. Nevertheless, ED was assessed using a single self-reported question, and follow-up time was relatively short. Moreover, although the analyses were adjusted for a broad range of covariates, measured blood pressure and lipid data were not available, and residual confounding cannot be excluded. In another study, higher estimated 10-year coronary heart disease and stroke risk were reported among men with moderate-to-severe ED compared with men without ED. However, this analysis was based on Framingham risk calculation rather than observed cardiovascular events. Thus, results from this study support an association between ED and cardiovascular risk burden, but is not very informative regarding actual event prediction. In addition, the cross-sectional nature of the analysis limits causal interpretation[12]. In a substudy of the ONTARGET and TRANSCEND trials, including patients with established CVD (n = 1,549), ED independently predicted all-cause mortality (HR 1.84, 95% CI 1.21–2.81), cardiovascular death (HR 1.93, 95% CI 1.13–3.29), myocardial infarction (HR 2.02, 95% CI 1.13–3.58) and the composite cardiovascular end point (HR 1.42, 95% CI 1.04–1.94), despite intensive cardiovascular risk factor management[12]. These findings underscore that ED provides incremental prognostic information beyond traditional risk factors, even in patients under optimized medical therapy. These results are strengthened by the use of validated ED instruments and centrally adjudicated cardiovascular end points. However, this substudy included only a small proportion of the overall trial population, limited to men with pre-existing high cardiovascular risk, which limits generalizability to lower-risk populations. In addition, associations with individual outcomes were not uniform, with statistical significance reached for findings in cardiovascular death and myocardial infarction, but not for stroke or heart failure when considered separately.

Table 1 | Epidemiological studies linking erectile dysfunction and CVD

Design and population	ED assessment	Main outcomes	Key limitations	Ref.
Prospective cohort; 8,063 men without CVD at baseline	Investigator-administered assessment every 3 months plus annual self-reported sexual function questionnaire; ED graded as absent, reduced erectile function or no erections	Incident ED predicted future CVD (HR 1.25, 95% CI 1.02–1.53). Incident and prevalent ED combined: HR 1.45 (95% CI 1.25–1.69)	Selected trial population; non-validated ED assessment; non-adjudicated CVD events	9
Cross-sectional angiographic study; 285 men with CAD and 95 men without CAD	Erectile Function Domain of the 15-item IIEF (IIEF-EF); ED defined as IIEF-EF <26	ED prevalence increased with CAD burden (22% in ACS with single-vessel disease versus 65% in CCS). ED preceded CAD by ~24 months in 93% of patients with CCS	Cross-sectional design; selected angiography population; recall bias	5
Prospective population-based cohort; 95,038 men ≥45 years	Single validated self-assessment question on erectile function; responses categorized as none, mild, moderate or severe ED	Progressive increase in CVD risk with ED severity. Severe ED associated with IHD (RR 1.60), HF (RR 8.00), all CVD (RR 1.35) and all-cause mortality (RR 1.93)	Single-item ED assessment; short follow-up monitoring; residual confounding	11
Prospective cohort; 2,506 men without baseline CVD	IIEF-5; categorized as no ED (22–25), mild ED (17–21) and moderate-to-severe ED (5–16)	ED associated with increased event rates, but not an independent predictor after adjustment (HR 0.92, 95% CI 0.53–1.61)	Few events; relatively young cohort	62
Prospective ONTARGET/TRANSCEND substudy; 1,549 men at high risk of CVD	Combined IIEF-5 and Cologne Evaluation of Erectile Dysfunction questionnaires; ED severity classified from IIEF-5	ED predicted all-cause mortality (HR 1.84) and major CV events (HR 1.42), with increasing risk according to ED severity	High-risk population; selected substudy cohort	12

ACS, acute coronary syndrome; CAD, coronary artery disease; CCS, chronic coronary syndrome; CVD, cardiovascular disease; ED, erectile dysfunction; IIEF-5, 5-item International Index of Erectile Function; IIEF-EF, Erectile Function domain of the International Index of Erectile Function; RR, relative risk.

A 2019 systematic review and meta-analysis synthesized data from 25 studies involving over 154,000 men with and without ED[4]. In this analysis, CVD outcomes encompassed a broad range of events, including myocardial infarction, CAD, congestive heart failure, cerebrovascular disease, arrhythmia and cardiovascular death. ED was shown to significantly increase the risks of CVD (RR 1.43), coronary heart disease (RR 1.59), stroke (RR 1.34) and all-cause mortality (RR 1.33). Notably, subgroup analyses showed that severe ED, defined as a five-item International Index of Erectile Function (IIEF-5) score of 5–7, was associated with the highest cardiovascular risk (RR 2.52, 95% CI 1.48–4.28). Separate subgroup analyses further suggested that the association between ED and CVD was strongest in studies including men aged ≥55 years, with an ED duration <7 years and a diabetes prevalence ≥20%. This meta-analysis included findings across diverse populations and methodologies, providing the most comprehensive evidence so far about the role of ED as a crucial marker for cardiovascular risk[4].

Taken together, results from these studies support ED as a clinically relevant marker of cardiovascular risk. However, the evidence remains predominantly observational and heterogeneous in terms of study design, outcome definition and population. Thus, ED should be viewed as a marker that might refine clinical suspicion and risk assessment, rather than as proof of a causal relationship or a stand-alone indication for advanced cardiovascular testing.

Pathophysiological mechanisms

The association between ED and CVD is thought to arise from shared mechanisms, including low-grade inflammation, endothelial dysfunction and atherosclerosis (Fig. 1). Vascular mechanisms have a central role, but ED is a multifactorial condition. Indeed, hormonal, neurogenic and psychological factors might contribute to ED, and can present with distinct pathophysiological pathways that do not necessarily reflect the same cardiovascular risk profile as vasculogenic ED (Fig. 2).

Low-grade inflammation is increasingly recognized as a central driver of vascular diseases, initiating a cascade of processes that disrupt endothelial function. Inflammatory cytokines such as interleukin-6 (IL-6) and tumour necrosis factor (TNF) contribute to vascular dysfunction through several interconnected mechanisms, including increased oxidative stress, upregulation of adhesion molecules and inhibition of endothelial nitric oxide synthase activity, leading to reduced nitric oxide bioavailability and impaired vasodilation[13–15]. Concomitantly, chronic low-grade inflammation promotes insulin resistance and dyslipidaemia, crucial components of the metabolic syndrome, which further exacerbate endothelial dysfunction and vascular injury[16]. In a cross-sectional study including 141 men with and without ED stratified according to the presence of angiographically confirmed CAD, ED was associated with increased circulating levels of inflammatory markers, including high sensitivity C-reactive protein ($P = 0.005$), IL-6 ($P < 0.001$) and TNF ($P < 0.001$), irrespective of CAD status (except for IL-6)[17]. These findings support the concept that systemic inflammation is a shared upstream mechanism linking ED and vascular disease, although the cross-sectional design precludes conclusions regarding temporality or causality[18]. In a cross-sectional study including 190 men with type 2 diabetes mellitus without symptomatic coronary heart disease (150 and 40 with and without ED, respectively), patients with ED showed a predominance of pro-inflammatory over anti-inflammatory signalling, reflected by increased TNF:IL-10 ratio ($P = 0.016$), together with increased circulating E-selectin levels ($P = 0.003$), a marker of endothelial activation[18]. Furthermore, erectile function was inversely correlated with circulating TNF ($r = -0.296$, $P = 0.044$), E-selectin ($r = -0.308$, $P = 0.026$) and intracellular adhesion molecule 1 (ICAM1; $r = -0.353$, $P = 0.013$). These findings further support the concept that endothelial activation and an imbalanced inflammatory milieu are shared pathophysiological features associated with ED[18]. Consistent with these findings, results from a prospective cross-sectional study including 104 men with ED and 54 age-comparable men without ED showed higher systemic oxidative stress and inflammatory burden in the ED group, with increased oxidative stress index ($P = 0.001$), multi-inflammatory index-1 (MII-1; $P = 0.012$), and multi-inflammatory

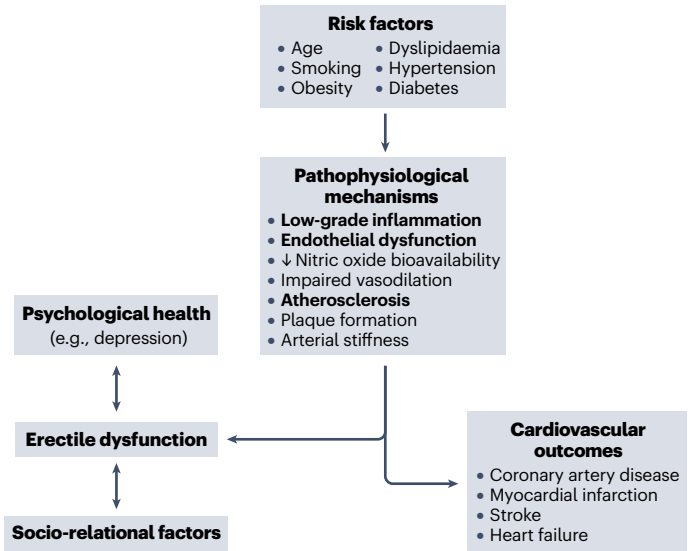

Fig. 1 | Pathophysiological links between ED and CVD. Erectile dysfunction (ED) and cardiovascular disease (CVD) share common risk factors, including age, smoking, obesity, dyslipidaemia, hypertension, and diabetes. These factors contribute to overlapping pathophysiological mechanisms between these two conditions, such as low-grade inflammation, endothelial dysfunction, reduced nitric oxide bioavailability, impaired vasodilation and atherosclerosis. ED might be an early manifestation of systemic vascular dysfunction and precede overt cardiovascular outcomes, including coronary artery disease, myocardial infarction, stroke and heart failure. Psychological health (for example, depression) and socio-relational factors, such as relationship satisfaction and partner support, are bidirectionally linked with ED, highlighting the interplay between vascular, psychological and relational domains.

index-2 (MII-2; $P = 0.031$). In addition, erectile function was inversely correlated with oxidative stress index ($r = -0.387$, $P < 0.0001$), MII-1 ($r = -0.298$, $P = 0.009$) and MII-2 ($r = -0.341$, $P = 0.006$). These findings further support an association between systemic inflammation, oxidative stress and ED, although the cross-sectional design precludes conclusions regarding temporality or causality[19].

Chronic inflammation might have deleterious effects by damaging the vascular endothelium[20]. The endothelium, a dynamic regulator of vascular tone, depends on nitric oxide to maintain vasodilation and vascular health. Inflammatory mediators impair nitric oxide bioavailability, contributing to endothelial dysfunction — a hallmark of both ED and CVD[20,21]. This link was shown in an observational study including 56 men without obstructive CAD who underwent invasive coronary endothelial function testing. In this study, men with coronary endothelial dysfunction had lower erectile function scores than those with normal endothelial function (median IIEF score 17 versus 22.5; $P = 0.008$). Moreover, erectile function correlated positively with both epicardial ($r = 0.31$, $P = 0.021$) and microvascular coronary endothelial function ($r = 0.39$, $P = 0.003$), independent of age, BMI, HDL cholesterol, C-reactive protein, insulin resistance and smoking status[22]. In this study, elevated levels of asymmetric dimethylarginine, an endogenous nitric oxide synthase inhibitor, were associated with both coronary endothelial dysfunction and ED, suggesting that impaired nitric oxide bioavailability might be a shared pathophysiological mechanism. In a retrospective cross-sectional analysis including 988 men aged 46–81 years, participants were classified according to erectile function (very poor, poor, fair, good or very good). Increasing ED severity was independently associated with increased circulating levels of soluble ICAM1 ($P = 0.009$) and soluble vascular cell adhesion molecule 1 ($P = 0.05$) after multivariable adjustment[23]. Lifestyle-related factors such as obesity, physical inactivity and metabolic disturbances also impair nitric oxide bioavailability and contribute to both ED and CVD, further supporting a shared vascular pathophysiology[24]. Persistent endothelial dysfunction contributes to vascular injury. However, atherosclerosis develops through a combination of additional mechanisms beyond endothelial damage[25], including lipid accumulation and oxidation, infiltration of inflammatory cells, smooth muscle cell migration and proliferation, matrix degradation, and alterations in vascular wall biology that collectively drive plaque development and progression[26,27]. In a population-based study including 614 men aged 45–74 years, men with ED had greater carotid intima-media thickness than men without ED (0.762 ± 0.151 mm versus 0.718 ± 0.114 mm; $P < 0.001$) and a higher prevalence of carotid plaques (63.8% versus 44.8%; $P < 0.001$)[28]. Moreover, carotid intima-media thickness and plaque prevalence increased progressively with ED severity (P for trend 0.004 and <0.001, respectively), supporting an association between worsening erectile function and increasing carotid atherosclerotic burden[28]. In addition, results from another study showed that atherosclerosis in patients with ED often shows an asymmetric distribution, with pronounced changes in both femoral and carotid arteries[29]. These findings highlight that endothelial dysfunction in ED is not an isolated phenomenon but is part of a broader disturbance in vascular homeostasis, reinforcing the concept that ED reflects systemic vascular health rather than a localized penile disorder. This evidence underscores the importance of considering ED within the context of overall vascular health. Low-grade inflammation, alongside lipid accumulation and oxidative stress, has a crucial role in promoting vascular dysfunction and the development of atherosclerosis[27,30]. Although direct evidence linking these pathways to both penile and systemic vascular dysfunction is limited, the available data support a mechanistic hypothesis whereby shared inflammatory and oxidative pathways contribute to endothelial dysfunction across multiple vascular beds, providing a biologically plausible explanation for the association between ED and adverse cardiovascular outcomes.

In addition to vascular mechanisms, endocrine dysfunction might further contribute to the link between ED and CVD. Testosterone deficiency has been associated with endothelial dysfunction, increased inflammation, insulin resistance and adverse metabolic profiles, all of which are established risk factors for CVD[31]. Low testosterone levels have also been linked to impaired nitric oxide bioavailability and reduced vascular reactivity, suggesting a potential mechanistic role in both ED and cardiovascular dysfunction[32]. However, the extent to which testosterone deficiency independently contributes to cardiovascular risk remains an area of ongoing investigation[32–34].

Diagnostic considerations

The diagnostic evaluation of ED in the context of cardiovascular risk requires a multidimensional approach that integrates sexual health with systemic risk profiling[35].

Cardiovascular risk stratification is recommended for all men with ED to identify those requiring lifestyle interventions, pharmacotherapy or referral for cardiological evaluation, according to the Princeton Consensus Recommendations, which have been adapted by the European Association of Urology and other international guidelines[36,37] Initial assessment should include a detailed medical

and sexual history, with particular attention to the onset, duration, and severity of ED; the presence of cardiovascular symptoms such as angina or exertional dyspnoea; and relevant lifestyle factors including smoking, alcohol consumption, physical activity and psychosocial stress[35,38]. A thorough physical examination is recommended to assess parameters such as BMI, waist circumference and blood pressure. Laboratory investigations should routinely include fasting plasma glucose or glycated haemoglobin (HbA1c), lipid profile and total testosterone levels.

In a 2024 update from the Fourth Princeton Consensus Conference (Princeton IV), a detailed and risk-oriented algorithm was proposed for assessing cardiac risk in men with ED who do not have overt CVD[38]. These guidelines recommend initiating risk assessment using the 10-year atherosclerotic CVD risk calculator developed by the American College of Cardiology/American Heart Association (ACC/AHA), which incorporates factors such as age, cholesterol levels, blood pressure and smoking status[39]. This online tool stratifies patients into low (<5%), borderline (5% to <7.5%), intermediate (≥7.5% to <20%) or high (≥20%) risk of experiencing a major cardiovascular event within the next decade. For patients categorized as having borderline or intermediate cardiovascular risk, the Princeton IV guidelines recommend coronary artery calcium (CAC) scoring to refine risk stratification. CAC scoring is a non-invasive CT-based technique that quantifies the burden of calcified atherosclerotic plaque within the coronary arteries, providing a direct measure of subclinical CAD. Identifying this hidden disease can help reclassify patients' risk profiles and guide decisions regarding preventive therapies or referral to preventive cardiology[38]. In selected patients with a low estimated cardiovascular risk but a strong clinical suspicion of vasculogenic ED, CAC testing might also be considered[38]. Conversely, patients identified as having a high cardiovascular risk should be referred directly to preventive cardiology services without additional risk stratification. CAC scoring, carried out through non-contrast, electrocardiogram-gated CT, has shown strong diagnostic and prognostic value in predicting future coronary events[40]. Evidence from prospective observational cohort studies, summarized in the ACCF/AHA Expert Consensus Document, shows that increasing CAC burden is independently associated with an increased risk of coronary heart disease death and myocardial infarction over 3–5 years, even after adjustment for traditional cardiovascular risk factors[41]. Although the role of CAC testing is well established in general cardiology, the specific utility of this tool in men with ED remains under investigation. Results from a prospective study involving 70 patients with vascular ED and 73 age-matched, race-matched and cardiovascular risk-matched men without ED or a history of CAD showed that CAC was more prevalent among patients with ED (75.7% versus 54.8%, $P = 0.01$)[42]. In a large cohort study including 9,150 men undergoing multidetector CT, ED was associated with CAC. However, this association lost statistical significance after multivariate adjustment[43]. Thus, the role of CAC scoring in this context remains to be established, and is currently not supported by prospective interventional evidence. Furthermore, notably, a CAC score of zero does not rule out obstructive CAD, as non-calcified plaques and stenoses might still be present[44]. Thus, CAC testing might aid in refining risk stratification, but should be interpreted cautiously and within the broader context of clinical evaluation. A similar conceptual framework might apply to ED. Early vascular or functional impairment might be present before overt ED becomes clinically apparent, with some men reporting subtle changes in erectile quality, rigidity or consistency that are not captured by standard diagnostic definitions. This notion of subclinical ED parallels that of subclinical CVD, and supports the view of ED as part of a broader spectrum of systemic vascular dysfunction, where early changes might precede clinically manifest disease.

Beyond traditional cardiovascular risk stratification tools, echocardiography has emerged as a promising modality for the early detection of cardiac dysfunction in men with ED[45]. Conventional assessment relies on surrogate markers such as blood pressure, lipid profiles and glycaemic control, but these metrics do not provide direct insight into cardiac structure or function. Conversely, transthoracic echocardiography enables non-invasive evaluation of left ventricular systolic and diastolic performance, as well as structural remodelling, offering a potential valuable adjunct in cardiovascular risk assessment for men with ED. Results from a systematic review and meta-analysis of ten studies in which echocardiography was used in men with ED, including >700 patients with ED and 350 men without ED, showed that men with ED had a statistically significantly higher E/e' ratio —the ratio of early mitral inflow velocity (E) to early diastolic mitral annular velocity (e'), which is a validated echocardiographic measure of left ventricular filling pressures and diastolic function — than men without ED (mean difference 1.17, 95% CI 0.68–1.65)[45]. These results suggest subclinical diastolic dysfunction, which is a recognized precursor of heart failure with preserved ejection fraction, and align with previous results

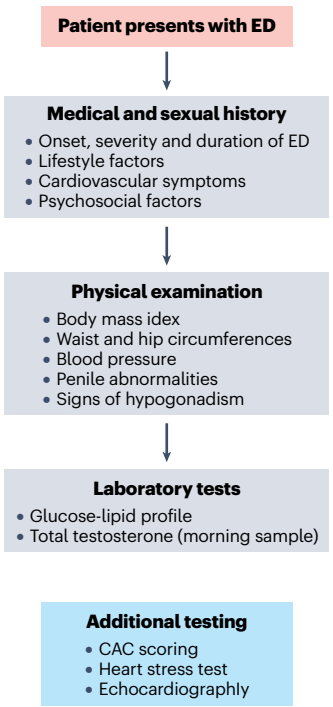

Fig. 2 | Recommended clinical evaluation pathway for patients presenting with ED. Initial assessment of patients with erectile dysfunction (ED) includes a thorough medical and sexual history focusing on ED characteristics, lifestyle, cardiovascular and psychosocial factors. This step is followed by physical examination assessing body composition, blood pressure, genital abnormalities and signs of hypogonadism. Laboratory testing typically involves evaluation of glucose-lipid profile and total testosterone levels. Additional cardiovascular testing (coronary artery calcium (CAC) scoring, heart stress test and echocardiography) might be considered based on risk factors or clinical suspicion of underlying cardiovascular disease.

in other at-risk populations[45]. Elevated echocardiographic markers such as *E*/*e*′ and left ventricular mass have previously been shown to predict cardiovascular events in both patients with diabetes and apparently healthy individuals[46,47]. Although ED might help identify men at increased cardiovascular risk, the role of additional investigations such as coronary artery calcium scoring and echocardiography remains hypothesis generating and is not yet supported by prospective interventional studies demonstrating improved clinical outcomes in this population. Accordingly, these investigations should currently be considered adjunctive rather than routine tools in the cardiovascular evaluation of men with ED.

Penile colour-Doppler ultrasound might provide additional information on penile vascular function and has been proposed as a potential tool for cardiovascular risk assessment. Abnormalities in cavernous arterial structure and flow have been associated with an increased risk of future cardiovascular event[48]. However, the use of this tool is currently limited to specialized settings, and its role in predicting future cardiovascular events remains to be established.

Management strategies

The management of ED in men with or at risk of CVD requires a comprehensive, multidisciplinary approach addressing both symptomatic relief and long-term cardiovascular health[38]. ED and CVD share pathophysiological mechanisms. Thus, the concurrent management of these two conditions is both logical and necessary. Lifestyle modification remains the cornerstone of both ED and CVD prevention and treatment. Robust evidence supports the beneficial effects of weight loss, smoking cessation, increased physical activity and dietary changes on both ED and CVD. In a randomized controlled trial, the effect of intensive lifestyle modification to improve erectile function were assessed in 110 obese men with ED[49]. Over a 2-year lifestyle intervention focusing on weight loss and increased physical activity, mean IIEF scores improved from 13.9 ± 4.0 to 17.0 ± 5.0 ($P < 0.001$), whereas no improvement was observed in men in the control group, who received general advice on healthy diet and physical activity (13.5 ± 4.0 to 13.6 ± 4.1; $P = 0.89$). These changes were paralleled by improvements in endothelial function and reductions in circulating inflammatory markers[49]. Results from a systematic review and meta-analysis of randomized controlled trials confirmed that lifestyle changes alone can improve erectile function, particularly in men with obesity, diabetes or metabolic syndrome[50].

PDE5 inhibitors have been hypothesized to also have cardiovascular benefits in addition to therapeutical effects on ED. Results from a large observational study involving 43,145 Swedish men with a first myocardial infarction showed that men receiving PDE5 inhibitors had lower risks of mortality and heart failure hospitalization than those who did not receive treatment[51]. These findings are observational, but suggest a possible cardioprotective effect of PDE5 inhibition, particularly with a dose–response pattern, although randomized trials are needed to confirm causality. PDE5 inhibition might exert a direct effect on cardiac structure and function. In the RECOGITO randomized controlled trial, daily tadalafil improved parameters of cardiac remodelling and myocardial function in patients with diabetic cardiomyopathy, accompanied by changes in inflammatory and cardiorenal biomarkers[52]. However, findings across studies remain heterogeneous, and results from large trials have not consistently showed benefit in broader cardiovascular populations. Thus, although these observations are mechanistically relevant, the role of PDE5 inhibitors in cardiovascular prevention or treatment remains to be established.

In addition to PDE5 inhibitors, statins and antihypertensives might have a dual role in the management of both ED and CVD. Statins improve endothelial function and have been shown to modestly improve erectile function. In a meta-analysis of 11 randomized trials including 713 men with ED — comprising men with hypercholesterolaemia, diabetes, CVD and men with an inadequate response to phosphodiesterase type 5 inhibitors — statins improved IIEF scores by a mean of 3.4 points (95% CI 1.7–5.0; $P = 0.0001$)[53].

Regarding antihypertensives, some conventional β-blockers and thiazide or thiazide-like diuretics have been associated with adverse effects on erectile function. Within the β-blocker class, differences between agents have also been shown. In the randomized, double-blind, crossover MR NOED trial, 48 men aged 40–55 years with stage 1 essential hypertension and normal erectile function at baseline received nebivolol 5 mg or metoprolol succinate 95 mg for 12 weeks each, separated by a 2-week washout period[54]. Despite a comparable blood pressure reduction between the two treatments, metoprolol reduced the IIEF erectile function subscore (mean change −0.92 points), whereas nebivolol had no statistically significant effect. Nebivolol was also associated with more favourable changes in orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction[54]. In the randomized TAIM trial, which included 390 overweight individuals with mild hypertension receiving thiazide or thiazide-like diuretics, erection-related problems worsened in 28% of men receiving chlorthalidone and a usual diet compared with 3% receiving placebo[55]. Similarly, in the double-blind TOMHS trial, which included 557 men with mild hypertension, erection problems at 24 months were more frequent in patients receiving chlorthalidone than placebo (17.1% versus 8.1%; $P = 0.025$)[56]. Conversely, erection-problem rates with enalapril and amlodipine were similar to that observed with placebo, supporting a largely neutral profile of ACE inhibitors and calcium channel blockers[56]. Potentially favourable effects of angiotensin receptor blockers have also been reported. For example, in a randomized 12-week trial, 124 men with type 2 diabetes and established ED were allocated to losartan, tadalafil, combination therapy or a watchful-waiting control group. Erectile function was assessed using the IIEF-5, Sexual Encounter Profile questions (SEP2 and SEP3) and the Global Assessment Question. Losartan improved all efficacy outcomes (all $P < 0.05$), although combination therapy with tadalafil resulted in greater improvements than either monotherapy[57].

Holistic management of comorbidities such as diabetes and obesity is crucial in the care of men with ED, especially when concomitant CVD is present. The Diabetes Control and Complications Trial (DCCT) and a related observational follow-up study (the Epidemiology of Diabetes Interventions and Complications (EDIC) study) provided valuable longitudinal data on the relationship between glycaemic control and erectile function in men with type 1 diabetes[58]. In this cohort, ~10 years after treatment, men who had received intensive insulin therapy during the DCCT had a statistically significantly lower prevalence of ED than those receiving conventional therapy, particularly in the secondary intervention cohort (12.8% versus 30.8%; $P < 0.001$). The risk reduction was not statistically significant in the primary prevention cohort (17.0% versus 20.3%; $P = 0.49$). In both the primary prevention and secondary intervention cohorts, higher mean HbA1c levels over time were independently associated with an increased risk of ED, with the adjusted odds increasing by 74% and 97%, respectively, for every 10% increase in time-weighted mean HbA1c (both $P < 0.0001$). These findings suggest that cumulative glycaemic exposure has a role in the pathogenesis of diabetes-related ED. However, ED was assessed at a single timepoint,

and the relatively young and healthy study population, combined with the use of a simplified ED definition, might limit the generalizability of the results. Nevertheless, these results provide important evidence supporting the early use of intensive glycaemic control to reduce the long-term risk of ED in men with type 1 diabetes[58]. Evidence also suggests that glucagon-like peptide 1 receptor agonists (GLP1 RAs), primarily used for glycaemic control and weight loss, might improve erectile function in men with type 2 diabetes mellitus. In a retrospective cohort study including 108 men with type 2 diabetes and mild-to-moderate ED, treatment with liraglutide or dulaglutide as an add-on to metformin was associated with greater improvements in erectile function than that observed with metformin alone. In multivariable analysis, treatment with GLP1 RAs plus metformin was the strongest independent predictor of improved erectile function after 12 months (estimated coefficient 2.74 ± 0.53; $P < 0.0001$)[59]. However, current data remain limited and largely observational, and randomized controlled trials are required to establish GLP1 RAs as a standard component of ED management.

Psychological comorbidities such as depression and anxiety, which frequently co-occur with ED and CVD, are also independently associated with poor outcomes. Depressive symptoms have also been associated with a substantially increased risk of both cardiovascular morbidity and ED[60]. Results from population-based studies, including the Massachusetts Male Aging Study, have shown that men with depressive symptoms are nearly twice as likely to experience moderate-to-complete ED, even after adjusting for age, physical health and cardiovascular risk factors[61]. The interplay between ED, CVD and depression is now conceptualized as a mutually reinforcing triad, where each condition can exacerbate the others, warranting integrated and multidisciplinary management[60]. This approaches consists of incorporating routine assessment of psychological well being into the evaluation of men with ED, involving mental health professionals when appropriate, and combining psychological interventions with lifestyle modification and evidence-based ED therapies. Notably, available evidence is largely derived from men aged ~40–70 years in Western populations, which might limit generalizability to other demographic and clinical settings. Specifically, the relationship between ED and CVD might differ in young men and in those with predominantly psychogenic, neurogenic or medication-induced ED, as these forms of ED are characterized by distinct underlying mechanisms and cardiovascular risk profiles. These factors should be considered when interpreting the clinical relevance of ED as a marker of cardiovascular risk.

In summary, management of ED in men at cardiovascular risk extends beyond symptomatic treatment to encompass a multifaceted, preventative framework. Targeting shared risk factors, optimizing pharmacotherapy and ensuring interdisciplinary care might improve sexual function and also reduce cardiovascular morbidity and mortality in this vulnerable population.

Future directions

The association between ED and CVD has been increasingly recognized, but several crucial evidence gaps remain. Mechanistic studies are needed to clarify the causal pathways linking ED to cardiac dysfunction, with particular focus on the role of chronic inflammation, endothelial impairment and early myocardial changes detectable through advanced imaging or biomarker profiling. In addition, most existing studies have been carried out in relatively homogeneous populations, often excluding younger men <40 years old, ethnic minorities and individuals from diverse socioeconomic backgrounds. Future research should prioritize large-scale, longitudinal studies across broader populations to ensure findings are generalizable.

Future studies should be designed to evaluate the role of coronary artery calcium scoring and the integration of ED status into cardiovascular risk calculators. Furthermore, randomized trials are warranted to determine whether targeted interventions, such as intensive lifestyle modification, pharmacological risk factor management or early cardiology referral can modify cardiovascular outcomes in men with ED. Ultimately, bridging the gap between pathophysiological understanding and clinical application will be essential to optimize prevention strategies and improve long-term outcomes in this at-risk population.

Conclusions

ED is increasingly recognized as an early clinical marker of CVD and provides an opportunity to identify men at increased cardiovascular risk before the onset of overt cardiovascular events. Epidemiological evidence consistently shows an association between ED and adverse cardiovascular outcomes, and results from different studies support shared upstream biological processes, including low-grade inflammation, endothelial dysfunction, oxidative stress and atherosclerosis. However, causal relationships remain to be established. Current evidence supports incorporating cardiovascular risk assessment into the routine evaluation of men with ED. Coronary artery calcium scoring and echocardiography show promise for identifying subclinical vascular and cardiac abnormalities in selected patients, but the routine use of these approaches in men with ED is not yet supported by prospective interventional evidence. Thus, management should focus on comprehensive cardiovascular risk reduction through lifestyle modification, optimization of cardiometabolic risk factors, appropriate pharmacotherapy and multidisciplinary care that also addresses psychological comorbidities when relevant.

Future studies should determine whether targeting these shared vascular and inflammatory pathways, incorporating ED into cardiovascular risk prediction strategies, and implementing earlier preventive interventions can reduce long-term cardiovascular morbidity and mortality in men with ED.

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Author Contributions

E.D. researched data for the article. All authors contributed substantially to discussion of the content. All authors wrote the article. All authors reviewed and/or edited the manuscript before submission.

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