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REVIEW

From bedroom to boardroom: erectile dysfunction as a window into cardiovascular health

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Erectile dysfunction (ED) has evolved from a quality-of-life concern to a recognized marker of systemic vascular disease and an early harbinger of cardiovascular events. The Princeton IV Consensus underscores that men presenting with erectile dysfunction should be presumed at increased cardiovascular risk until proven otherwise, advocating integrated risk stratification and lifestyle optimization. Beyond established risk scores, advances in omics, vascular imaging, and digital health promise precision tools for early detection and prevention. This review aims to examine erectile dysfunction as an early marker of cardiovascular disease and to summarize current and emerging approaches to cardiovascular risk stratification in men with ED.

Key Words: Erectile dysfunction, cardiovascular, risk, heart, penile

Introduction

Over the past three decades, sexual health and particularly erectile dysfunction (ED) have re-emerged as a central focus in clinical medicine. Once regarded as a taboo subject, ED gained scientific and clinical visibility following the serendipitous discovery that sildenafil, a cardiovascular (CV) drug initially developed for angina, markedly improved erectile function.[1] This breakthrough discovery not only transformed therapeutic approaches but also catalyzed a surge of research into the interplay between ED and CV health. Epidemiologic studies subsequently quantified the burden of ED, demonstrating that it affects nearly half of men older than 40 years, with prevalence increasing steadily.[2]

ED, defined as the persistent inability to attain or maintain an erection sufficient for satisfactory sexual performance, affects over 10 million men in the United States alone, and its prevalence increases with age.[2,3] NHANES data indicate that ED affects approximately 1 in 5 U.S. men overall, with prevalence rising from 5.1% of men aged 20–39 years, 17.6% of those aged 40–64 years, and over 66.1% of men aged ≥65 years.[4] While historically considered primarily a quality-of-life issue, ED is now recognized as a sentinel marker of systemic vascular disease.[5] Numerous studies have demonstrated that ED frequently precedes the onset of cardiovascular disease (CVD) by two to five years, making it an important early clinical manifestation of subclinical vascular pathology.[6,7] In NHANES, erectile dysfunction was independently associated with higher cardiovascular mortality (HR = 1.57), with effect sizes comparable to traditional cardiovascular risk factors.[4] The shared pathophysiology includes endothelial dysfunction, atherosclerosis, inflammation, and impaired smooth muscle relaxation, all of which contribute to both impaired penile perfusion and cardiovascular risk.

Screening and diagnosing ED is critical for both primary and secondary prevention of CVD. Because ED can be assessed quickly and at low cost, its assessment serves as a practical prognostic tool that

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rivals, and in some cases outperforms, investigational cardiovascular biomarkers. Evidence suggests that ED may even predict CVD risk more accurately than traditional risk factors, particularly among men whose baseline risk falls into the intermediate category, where further stratification is most clinically valuable.[8,9] This review aims to examine erectile dysfunction as an early marker of cardiovascular disease and to summarize current and emerging approaches to cardiovascular risk stratification in men with ED.

Pathophysiology

ED is governed by the same vascular processes that underlie aging and atherosclerosis in other arterial territories, including the coronary and cerebral circulation. In men with vasculogenic ED, impaired erections may result from early-stage dysfunction in endothelial-dependent or independent smooth muscle relaxation, from progressive cavernosal arterial occlusion due to atherosclerotic lesions, or from a combination of these mechanisms.[8–10]

Montorosi's artery size hypothesis (Figure 1) provides a compelling explanation for why ED often precedes CVD: given a similar atherosclerotic burden, the smaller penile arteries become obstructed earlier than the larger coronary arteries, making ED an early clinical manifestation of systemic vascular disease.[10,11] Since penile arteries are approximately 1–2 mm in diameter compared to 3–4 mm for coronary arteries, the same atherosclerotic burden produces greater obstruction in the penile circulation. Even subtle reductions in luminal diameter can lead to marked decreases in penile blood flow, as predicted by Poiseuille's law.[12] As a result, men may develop vasculogenic ED years before experiencing angina or myocardial infarction. This phenomenon might lead to thinking of ED as a "penile angina", to underscore its role as an early clinical manifestation of systemic vascular disease.[13]

While the artery size hypothesis explains much of the temporal relationship between ED and CVD, it does not capture the full spectrum of pathophysiology. Inflammation, endothelial dysfunction, and prothrombotic activation play critical roles in both conditions. This partial overlap reflects that, while not all men with ED experience overt cardiovascular events, both conditions arise from similar pathophysiological pathways (Figure 2). Men with ED demonstrate elevated levels of inflammatory biomarkers similar to those observed in patients with coronary artery disease, and the burden is additive when both are present.[14] This pro-inflammatory state may predispose individuals to rupture of unstable, non-obstructive coronary plaques, linking ED to acute coronary events even in the absence of significant stenosis. Moreover, vascular aging markers such as increased aortic stiffness and pulse pressure independently predict adverse CV outcomes in men with ED, reinforcing the concept of ED as a systemic vascular disorder.[15]

While vasculogenic ED remains the most clinically relevant subtype for cardiovascular risk stratification, ED is a heterogeneous condition that may also arise from neurogenic, psychogenic, or induced by medications, particularly antihypertensives and psychotropic agents. Neurogenic ED is commonly observed in patients with diabetes, prior pelvic surgery, often coexisting together, increasing cardiovascular risk due to its proinflammatory activity. Psychogenic ED is typically characterized by situational symptomatology, has preserved nocturnal erections, and an abrupt onset. While psychogenic ED may not directly reflect structural vascular disease, it's often associated with heightened sympathetic tone, depression, and adverse lifestyle factors that carry independent cardiometabolic implications.[16]

Additional mechanisms, including androgen deficiency and regional vascular susceptibility, further contribute to the interplay between ED and CVD.[17] Low testosterone levels are common in men with ED and have been independently associated with CV morbidity and mortality, likely through effects on vascular homeostasis and systemic inflammation.[17] Anatomically, the pre-penile vasculature is especially vulnerable to structural changes with age, including medial thickening and reduced vasodilatory capacity.[5] This vulnerability is clinically relevant, as interventions targeting the internal pudendal artery have been shown to improve erectile function in selected patients. Together, these observations highlight ED as a multifactorial condition that provides early and clinically meaningful signals of systemic CVD.[18–20]

The Princeton IV

The Princeton Consensus Conferences have been central in defining the clinical framework of managing ED in the context of cardiovascular health. As with prior conferences, a multispecialty panel of US experts in sexual medicine and CV health was assembled by the steering committee to critically evaluate the contemporary evidence linking ED and CVD.

The most recent Princeton IV (2024) recommendations emphasized that all men presenting with ED

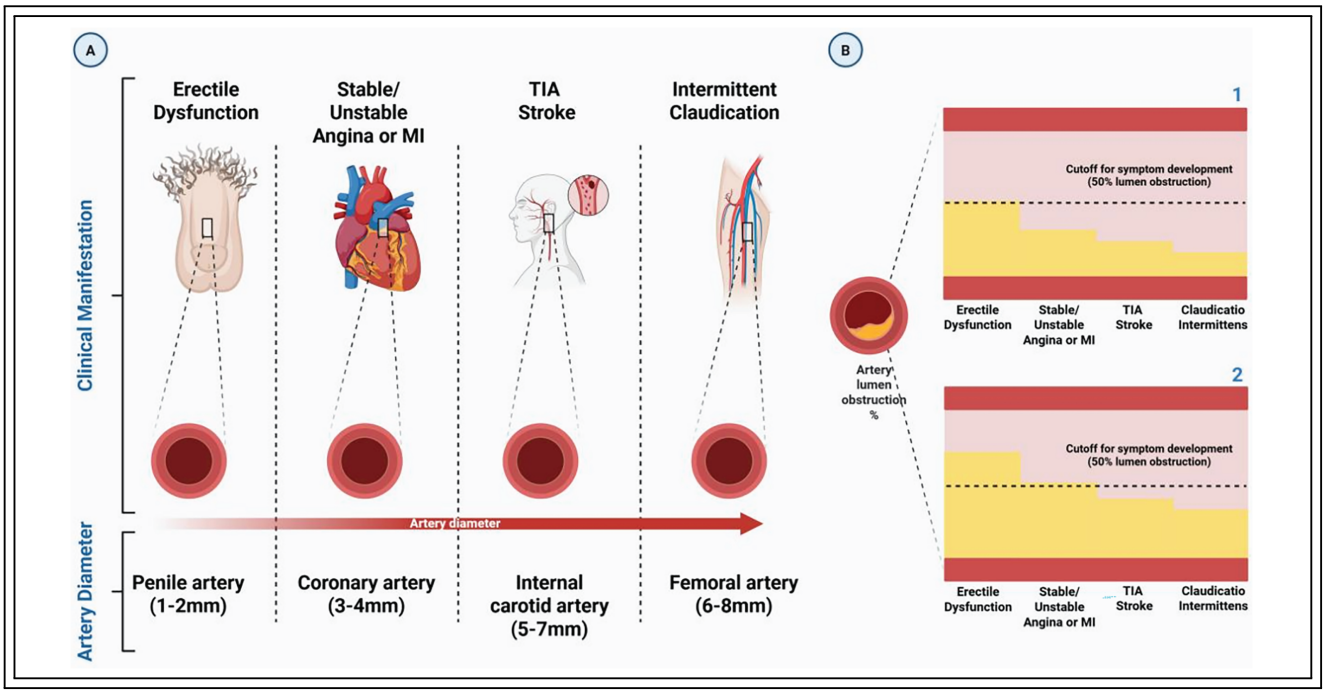

FIGURE 1. Montorsi artery size hypothesis. (A) Clinical manifestations per artery diameter. (B) Early (B1) and late stage (B2) of the atherosclerotic process. Abbreviation: TIA, transient ischemic attack

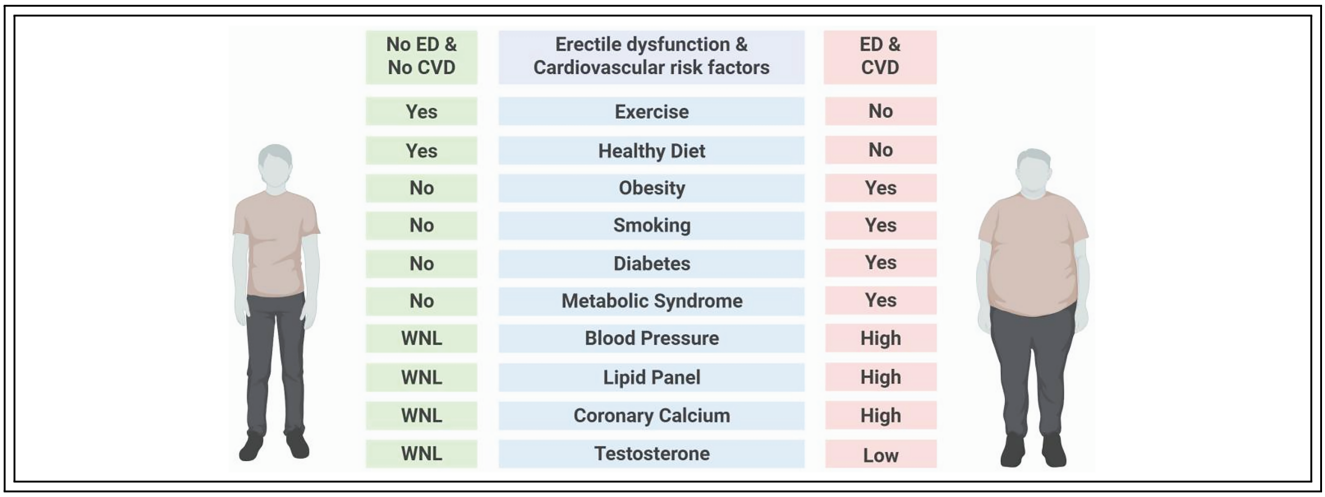

FIGURE 2. Opposite incidence and severity of shared risk of cardiovascular disease (CVD) and erectile dysfunction (ED). Abbreviation: WNL, within normal limits

should be considered at elevated cardiovascular risk until proven otherwise, advocating for comprehensive risk assessment that may include coronary artery calcium scoring and evaluation of exercise tolerance.[21–23] Importantly, phosphodiesterase 5 inhibitors (PDE5i), once used cautiously on patients with cardiovascular history, are now supported by robust safety data and emerging evidence suggesting cardioprotective effects.[24] These guidelines underscore the role of ED not only as a sexual health condition but also as a critical entry point for early cardiovascular risk stratification.

Currently, the QRISK calculator incorporates ED, but this underestimates its prognostic weight, especially since many men who present with myocardial

TABLE 1. **How to manage erectile dysfunction in men with known cardiovascular disease**

After initial sexual query, confirming ED, assess the patient's exercise ability for age.
Categorize the risk of having a cardiac event during sexual activity into low risk, intermediate or indeterminate risk, or high risk.
High risk: these are unstable cardiovascular patients who need a referral to a cardiologist. In some cases, revascularization procedures (preventive coronary intervention–angioplasty stenting) may be required before they can be reclassified. High-risk patients are unsafe for sexual activity and should be referred to a cardiologist for further evaluation. Sexual activity should be deferred until the cardiac condition has been stabilized and should be managed with a collaborative approach to primary prevention. In all cases, patient follow-up and reassessment are recommended.
Intermediate or indeterminate risk: may require additional testing to determine exercise capacity/development of ischemia with stress. This includes exercise stress testing; for those who cannot exercise, a chemical stress test (such as dobutamine echocardiogram) is appropriate. Achieving 5–6 METs (in 4 minutes on a standard Bruce protocol without ischemic chest pain, electrocardiographic changes, wall motion abnormality) suggests the patient can achieve the desired exercise tolerance required for sexual activity and is low risk. Those who have ischemia, especially at a low level of exercise, are then reclassified at high risk and require a cardiovascular consultation.
Low risk: Patient may receive therapy for ED. If the patient has a prescription for nitrates, make a determination whether nitrates are really needed. For example, some patients who have had successful coronary artery revascularization continue to carry nitrates but never need or use them. If nitrates are not needed, do not prescribe and consider PDE5i or therapy.

Note. ED, erectile dysfunction; METs, metabolic equivalents of task; PDE5i, phosphodiesterase type 5 inhibitors. Adapted from reference.[22]

infarction (MI) had ED as their only overt warning sign (Table 1).[21] Beyond vascular causes, psychogenic ED and associated mental health disorders (depression, anxiety, etc.) also elevate CVD risk, likely through sympathetic hyperactivity and increased allostatic load. Because ED and depression have a bidirectional relationship, treating one condition often improves the other, further strengthening the case for routine inquiry.[25]

It is emphasized to systemically ask about sexual health in routine practice. Sexual inquiry not only normalizes discussion of a sensitive topic but also facilitates detection of occult CVD, motivates lifestyle change, and supports adherence to preventive interventions. Lifestyle modification, including diet, weight reduction, smoking cessation, and exercise, improves both erectile and cardiovascular outcomes, while hypogonadism screening is recommended since testosterone deficiency contributes to ED and may worsen overall prognosis.[2,3,22] For men without known coronary disease (Table 2), the panel advises to calculate atherosclerotic cardiovascular disease (ASCVD) risk using pooled cohort equations, and supplementing borderline or intermediate results with coronary calcium (CAC) scoring, which offers the most sensitive marker of subclinical disease and guides tailored therapy.[21,22] For men with established CVD, exercise tolerance testing remains the cornerstone for risk stratification before initiating ED treatment, with PDE5i remaining the preferred first-line treatment alongside lifestyle optimization.[21,22]

PDE5i Interactions and Cardio-Protection

Concomitant use of PDE5i and nitrates remains contraindicated owing to the risk of synergistic vasodilation and profound hypotension. Pharmacologic studies show that short-acting nitrates can trigger hypotensive responses for up to 24 h after sildenafil or vardenafil, and for as long as 48 h after tadalafil due to its longer half-life.[26–28] Observational data on real-world literature are mixed: while two studies did not show excess adverse CV events, another study demonstrated increased risk.[29] This variability likely reflects methodological and clinical differences rather than a true biological inconsistency. Sample size, event rate, and population differ substantially across datasets, especially in underlying disease severity. These analyses rely on co-prescription data from electronic medical records and differ in dosing, PDE5 inhibitor formulation

TABLE 2. **Cardiovascular work-up of men who present with erectile dysfunction and no known cardiovascular disease**

ED is a risk marker and risk-enhancing factor for ASCVD.
Patients presenting with ED, especially vasculogenic ED, should have an assessment of their 10-year ASCVD risk based on the American College of Cardiology/American Heart Association risk score.
Borderline to intermediate risk score (5% to 20% 10-year risk of ASCVD) should have coronary artery computed tomography calcium scoring.
Score of 0 results in emphasis on lifestyle interventions.
Score of 1 to 100: Lifestyle modification plus moderate- to high-intensity statins, Control other cardiovascular risk factors (hypertension, diabetes, stop smoking). Consider referral to a preventive cardiologist.
Score of >100: Lifestyle modification plus high-intensity statins. Control other risk factors. Consider low-dose aspirin. Refer to a preventive cardiologist.

Note. ASCVD, atherosclerotic cardiovascular disease; ED, erectile dysfunction. Adapted from reference.[22]

(short vs. long-acting), nitrate regimen (continuous vs. intermittent), and exposure–outcome time windows. These findings have prompted debate over whether the current absolute contraindication might be revised to a strong precaution for carefully selected, well-informed patients; however, a definitive answer requires a prospective trial to evaluate causation. In practice, discontinuation or substitution of nitrates is often feasible, particularly after successful revascularization procedures. Severe left ventricular outflow obstruction warrants caution but is not an absolute contraindication, and riociguat remains contraindicated due to overlapping hemodynamic effects.[30–32] Caution is also advised when PDE5i are combined with alpha-blockers or sacubitril/valsartan, though these combinations are generally safe with dose adjustments.[33]

Beyond safety considerations, mounting evidence points to potential cardioprotective effects of PDE5i. Proposed mechanisms include reduction in systemic blood pressure, inflammation, fibrosis, and thrombosis, as well as protection against ischemia-reperfusion injury, oxidative stress, and endothelial activation.[34,35] Since 2005, both preclinical and clinical studies have increasingly suggested that PDE5i use may translate into improved cardiovascular outcomes.[36–43] A large nationwide Danish cohort of more than 70,000 men initiating PDE5i therapy showed reduced CV risk during the first three years of treatment with persistent benefits for myocardial infarction.[44]

Most recently, a 15-year retrospective analysis demonstrated robust associations between PDE5i exposure and reduced CV morbidity and mortality.[45] Compared with non-users, men receiving treatment had a 13% lower incidence of major adverse CV events, a 25% reduction in all-cause mortality, and significant decreases in coronary revascularization, heart failure, unstable angina, and CV death. These benefits were evident in men both with and without coronary artery disease, as well as in those with type 2 diabetes. Dose-response analyses further revealed that higher PDE5i exposure was associated with a greater risk reduction. Taken together, current evidence suggests PDE5i may hold a future role in preventive cardiology, although prospective randomized trials are essential to confirm causality.

Emerging Tools for Cardiovascular Risk Stratification in Men with ED

Beyond current established guideline-based strategies, novel biomarkers and omics-based tools emerge as promising adjuncts for CV risk assessment in men with ED. Plasma ceramides, key intermediates in sphingolipid metabolism, have shown a prognostic value for major adverse CV events independent of traditional risk factors.[46,47] The FINRISK cohort showed that ceramides were independently associated with incident major adverse cardiac events (MACE), corresponding to an approximately 20–30% relative increase in risk after adjustment for traditional cardiovascular risk factors.[48,49] Similarly, in the LURIC cohort of patients undergoing coronary angiography, elevated ceramide species and composite ceramide-based ratios were strongly associated with cardiovascular mortality, with high-risk lipidomic profiles conferring an approximately 2- to 3-fold higher risk of cardiovascular death compared with lower-risk profiles, independent of LDL-cholesterol and other conventional markers.[50] In men with ED, elevated ceramide concentrations correlate with greater symptom severity, and abnormal CV findings, suggesting a role in refining risk stratification where

conventional tools may underestimate burden. In a real-world cohort of men with erectile dysfunction, ceramide-based risk scores were independently associated with ED severity and identified a subgroup at substantially higher risk for early cerebrovascular events, supporting ceramide testing as a pragmatic adjunct for cardiovascular risk stratification in ED populations.[51] Nevertheless, these are cohort studies, and prospective trials are needed to further study this association.[51] This paradigm reflects a broader movement toward lipidomics and metabolomics as integral components of precision cardiology. Expanding further, multi-omics platforms, including proteomics, transcriptomics, and metabolomics, are being investigated to identify molecular signatures of vascular dysfunction and aging in ED populations. Although still exploratory, these approaches hold potential for individualized prediction models that complement established algorithms.[46,47,51]

In parallel, advances in non-invasive imaging and digital technologies offer additional avenues for risk stratification. Penile duplex ultrasonography, coronary CT angiography, and carotid intima-media thickness measurements can reveal early vascular pathology and provide objective markers of systemic atherosclerosis.[15,52–54] Digital health tools, including wearable devices capable of monitoring heart rate variability, sleep, and nocturnal penile tumescence, have shown early promise as adjunctive measures in detecting vascular or neurogenic contributors to ED.[25,55,56] A feasibility study of penile wearables showed 14 months of real-world data, with no complications other than 2 users with mild discomfort. The device provided objective longitudinal measurements of erectile function outside of the clinical setting, gathering metrics of the overall number of night erections, duration, rigidity, and girth expansion. This device showed the potential to reveal early functional changes related to vascular or neurogenic dysfunction before patients seek medical care. However, the study merits scalability. One of the main limitations reported by the authors was the reliance on user self-report, consistent app usage, correct placement, and the use of a non-validated algorithm.[54]

While these technologies require further validation in large, prospective cohorts, their integration into clinical practice could expand the ability of clinicians to detect high-risk individuals, motivate lifestyle change, and deliver more personalized prevention strategies. Together, these preliminary clinical data support a growing role for omics-based biomarkers, targeted imaging, and digital physiologic monitoring as secondary tools in cardiovascular risk stratification for men with ED. Larger prospective studies will be required to determine their incremental predictive value, clinical utility, and potential integration into routine practice.

Conclusion

ED is more than a quality-of-life disorder; it's a sentinel marker of systemic vascular disease and a powerful predictor of cardiovascular events. The Princeton IV consensus has reaffirmed the need to treat men with ED as at elevated CV risk until proven otherwise, emphasizing guideline-based risk stratification and safe use of pharmacologic therapies. At the same time, emerging evidence in omics, risk scores, vascular imaging, and digital health suggests that precision tools may soon complement established algorithms, enabling earlier detection and more personalized prevention strategies. As a takeaway closure, a history of erectile dysfunction obtained during routine patient evaluation provides important insight into early cardiovascular risk.

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The authors confirm contribution to the paper as follows. Study conception and design: Andres H. Guillen Lozoya, Tobias Kohler. Project administration: Tobias Kohler. Supervision: Tobias Kohler. Writing original draft: Andres H. Guillen Lozoya. Review & editing: Andres H. Guillen Lozoya, Milad Bonakdarhashemi, Sevann Helo, Matthew Ziegelmann, Tobias Kohler. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

All data analyzed are derived from the published literature and are available in the articles cited within the manuscript. No new data was generated.

Ethics Approval

Not applicable.

Conflicts of Interest

The authors declare no conflicts of interest.

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