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Research Article

# CARDIOVASCULAR DISEASE PREVENTION IN MEN WITH VASCULAR ERECTILE DYSFUNCTION: THE VIEW OF THE PREVENTIVE CARDIOLOGIST

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#### **Abstract:**

Vascular erectile dysfunction is a powerful marker of increased cardiovascular risk. However, current guidelines lack specific recommendations on the role that the evaluation of vascular erectile dysfunction should play in cardiovascular risk assessment, as well on the risk stratification strategy that men with vascular erectile dysfunction should undergo.

In the last 3 years, erectile dysfunction experts have made a call for more specific guidance and have proposed the selective use of several prognostic tests for further cardiovascular risk assessment in these patients.

Among them, stress testing has been prioritized, whereas other tests are considered second-line tools. In this review, we provide additional perspective from the viewpoint of the preventive cardiologist. We discuss the limitations of current risk scores and the potential interplay between erectile dysfunction assessment and the use of personalized prognostic tools, such as the coronary artery calcium score, in the cardiovascular risk stratification and management of men with vascular erectile dysfunction.

Finally, we present an algorithm for primary care physicians, urologists, and cardiologists to aid clinical decision-making.

**Keywords:** Atherosclerosis; Cardiovascular disease; Coronary artery calcium; Erectile dysfunction; Prevention; Risk; Vascular erectile dysfunction

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#### INTRODUCTION:

Despite reductions of cardiovascular disease mortality overall in the world in the last 40 years, cardiovascular disease remains a leading cause of death. From a prevention standpoint, sudden cardiac death often presents as the initial manifestation of cardiovascular disease in previously apparently healthy individuals, and a concerning proportion of events occur in individuals not identified as high risk by traditional scores.

Moreover, the incorporation of different lifestyles in a number of countries around the world has further increased the prevalence of cardiovascular risk factors and disease. Thus, cardiovascular disease remains a worldwide public health issue, requiring further preventive efforts.

Erectile dysfunction is a highly prevalent disorder among adult men. It can be the result of psychogenic and organic causes, or a combination of both. Among its organic forms, vascular erectile dysfunction is considered the most prevalent, with cardiovascular risk factors, atherosclerosis, and endothelial dysfunction being key contributors. Many studies have shown that vascular erectile dysfunction and cardiovascular disease are strongly linked entities that share risk factors and underlying mechanisms, and often coexist in the same individuals.

Of note, 2 key features in the relationship between vascular erectile dysfunction and cardiovascular disease make the former particularly appealing from a prevention standpoint. First, erectile dysfunction symptoms often coexist with subclinical, otherwise silent cardiovascular disease and usually antecede cardiovascular symptoms.

erectile dysfunction Second. vascular independently associated with cardiovascular disease and events beyond traditional risk factors. Thus, symptomatic vascular erectile dysfunction provides the cardiologist with a powerful independent marker of increased cardiovascular risk. Despite its potential importance, vascular erectile dysfunction has been long overlooked in cardiovascular guidelines, which lack specific recommendations regarding the role of erectile dysfunction assessment in cardiovascular risk stratification in men, as well as regarding the best risk assessment strategy for patients with vascular erectile dysfunction.

In this context, recent articles and consensus documents from erectile dysfunction experts have provided valuable insights regarding some of these questions. In this review, we provide perspective from the viewpoint of the preventive cardiologist. In particular, we focus on the role that the interplay between vascular erectile dysfunction assessment and cardiovascular risk stratification can play in clinical practice. In addition, we highlight the utility of currently available advanced cardiovascular risk assessment tools, particularly coronary artery calcium scoring, in further risk assessment of men with vascular erectile dysfunction.

## Ascertainment of a Predominant Vascular Mechanism

For erectile dysfunction symptoms to be informative from a cardiovascular disease standpoint, a key first step is to confirm the presence of an underlying vascular mechanism. Indeed, the most frequent causes of erectile dysfunction symptoms among adults aged 40 years or less are psychological rather than organic. The diagnostic strategy for patients with erectile dysfunction symptoms is beyond the scope of this review, but has been described in detail in a number of guidelines.

#### Connection between Vascular Erectile Dysfunction and Cardiovascular Disease: An Opportunity for Improving Adherence to Preventive Interventions

The pathophysiologic links between vascular erectile dysfunction and cardiovascular disease are well characterized. In brief, the 2 processes share a number of upstream risk factors (including tobacco use, obesity, sedentarism, dyslipidemia, and glucose metabolism abnormalities). These deleterious factors result in common underlying mechanisms, among which inflammation, atherosclerosis, and endothelial dysfunction are major contributors.

Consistent with this, studies have found the coexistence of vascular erectile dysfunction and silent or overt cardiovascular disease being a frequent scenario. From a prevention standpoint, the existence of common causal factors increases the potential benefits of cardiovascular preventive interventions. Indeed, lifestyle modification has the potential to affect not only the cardiovascular health but also the sexual life of the patient. This may provide motivation for the patient to adhere to lifestyle modification and pharmacologic

interventions.

## Confirmed Vascular Erectile Dysfunction as a Trigger for Cardiovascular Risk Assessment

Current cardiovascular prevention guidelines recommend that all men aged 40 years or older undergo cardiovascular risk assessment. The same guidelines recommend that risk should be reassessed every 4 to 6 years in none high-risk individuals. Unfortunately, these recommendations are often neglected.

The repercussion that erectile dvsfunction symptoms may have in an individual's sexual life may prompt a visit to a primary care doctor or urologist by patients who would otherwise be "invisible" to the medical system. Thus, this encounter provides an opportunity for assessing and reassessing cardiovascular risk, especially when there is a vascular mechanism. Thus, in accordance with the recommendations from erectile dysfunction expert groups, we support the contention that all men with vascular erectile dysfunction should undergo cardiovascular risk assessment if they have not already done so this recommendation, endorsing that a diagnosis of vascular erectile dysfunction should trigger cardiovascular risk reassessment in individuals not considered high risk in a prior evaluation.

#### Sexual Inquiry as Part of the Standard Cardiovascular Risk Evaluation in Adult Men

The present cardiovascular guidelines also do not include questions on sexual function. Nevertheless, the independent association between vascular erectile dysfunction and cardiovascular disease has resulted in the recommendation from expert groups to ask about erectile dysfunction symptoms as part of a basic cardiovascular risk assessment in all adult men, because it may provide additional prognostic information, particularly in young and middle-aged men.

Nonetheless, conclusive evidence on the prognostic value of vascular erectile dysfunction for predicting cardiovascular disease events beyond traditional risk factors is currently limited. Nevertheless, the presence of erectile dysfunction did yield a 9% net reclassification index from low to intermediate or high risk. In that study, erectile dysfunction symptoms were self-reported, and no distinction

was made between vascular erectile dysfunction and dysfunction of other causes. These limitations may partially explain some of the results

#### **METHODS:**

## Cardiovascular Risk Assessment In Patients With Vascular Erectile Dysfunction

Cardiovascular-healthy lifestyle changes have shown positive effects on the overall health and erectile function of patients with vascular erectile dysfunction and are recommended as a first-line intervention in clinical practice guidelines and consensus documents. On the other hand, those guidelines do not endorse the systematic use of statins for the treatment of erectile dysfunction of a confirmed vascular mechanism per se, provided conflicting observations on the effects of statin therapy on erectile function.

Thus, in men with vascular erectile dysfunction the decision of treating with a statin will be built on the estimated cardiovascular risk. Clinical scores estimate an individual's 10-year risk of having an event based on the rates observed in populations with similar risk factor profiles. This parsimonious strategy has been considered the cornerstone of cardiovascular risk assessment in clinical practice for decades and is also endorsed by erectile dysfunction expert groups as the first step of cardiovascular risk stratification in patients with vascular erectile dysfunction. However, current scores have important constraints that limit the accuracy of risk predictions and the adequacy of the derived management. Current scores are built on self-reported history, single day measurements, and several binary variables.

This precludes capturing the pattern of exposure to each risk factor and other relevant prognostic information. For example, regarding tobacco use, by using a yes/no variable, the number of cigarettes smoked per day, the years of duration, and the exposure to second-hand smoking are overlooked. The use of single-time measurements entails strong assumptions as well. In addition, scores ignore exposure to other risk factors, such as metabolic syndrome and the individual's genetic susceptibility. Differences in these no captured features may explain the marked heterogeneity of atherosclerotic burden and cardiovascular disease event rates observed among subjects with similar predicted risk.

Table 1 Comparison Between Competing Risk Assessment Paradigms: Risk Factor-Based Versus Disease Detection-Based		
Features	Risk Factor Model	Disease Detection Model
Measurement	Estimation of risk for developing atherosclerosis	Presence and severity of atherosclerotic disease
Approach	Population-based	Personalized
Relationship between risk factors	Separates risk elements	Integrates genetics and lifelong exposure
Role of age	Strong reliance on chronologic age	Quantifies "vascular" or "biological" age
Effect of treatment	Reduction in risk factor should reduce disease	Disease score may not measure treatment effect
Effectiveness in risk assessment	Usually mild risk-predictive value	Usually a powerful predictor of events
Role in clinical decision-making	High uncertainty, intermediate-risk group lacking specific recommendations	Reclassification, motivate patients, may help avoid unjustified treatments
Cancer analogy	High hormone levels or family history in breast cancer	Detection of suspicious nodule on mammograph

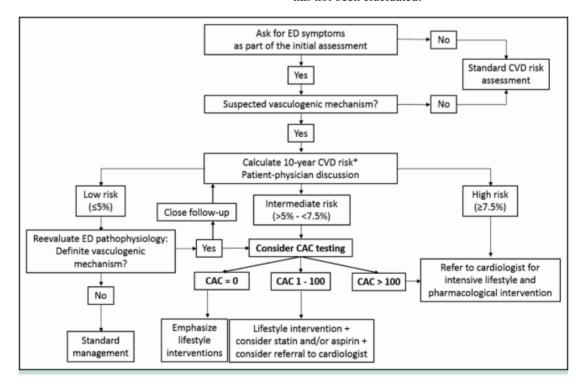
#### **RESULTS:**

#### **Ankle-brachial Index**

The prevalence of subclinical peripheral artery disease is increased in men with vascular erectile dysfunction. Given the increased cardiovascular risk faced by patients with peripheral artery disease, the ankle-brachial index also has been proposed as a tool for further risk assessment in individuals from the general population in whom management is uncertain, as well as in men with vascular erectile dysfunction. However, recent high-quality studies

have shown that the ankle-brachial index only adds modestly to traditional risk factors for cardiovascular risk prediction.

In fact, the sensitivity of the ankle-brachial index for detecting increased risk in nonelderly adults is low. Sensitivity increases in elderly individuals, but such patients are likely to be considered high risk already as a consequence of their chronologic age or traditional risk factor burden. In this context, the specific prognostic value of the ankle-brachial index in young patients with vascular erectile dysfunction has not been elucidated.



#### **DISCUSSION:**

In the same guideline, an IIb recommendation was awarded based on concerns about cost and radiation exposure. However, the associated radiation has been reduced to approximately 0.5 to 1 mSv. Also, cost-effectiveness analyses suggest that coronary artery calcium scoring may be a cost-effective strategy for statin allocation in intermediate-risk individuals. The Princeton III consensus noted that "coronary computed tomographic angiography or coronary arterycalcium scoring as the first test may be appropriate for patients (aged 60 years) with a family history of cardiovascular disease, severe erectile dysfunction, diabetes, or multiple risk factors."

The extensive evidence in the general population, together with the preliminary studies in vascular erectile dysfunction, suggests that the recommendation on coronary artery calcium may apply to most patients with vascular erectile dysfunction who are not already considered at high risk

The performance of biomarkers of inflammation such as high sensitivity C-reactive protein for risk assessment is modest in the general population, and their specific value in vascular erectile dysfunction is not well characterized. Other tests such as pulse-wave velocity and brachial artery flow-mediated dilation have also been proposed as alternative tools for cardiovascular risk stratification, yet their independent prognostic value in men with vascular erectile dysfunction remains unclear.

#### **CONCLUSION:**

Using clinical scores as a first step for risk assessment in patients with erectile dysfunction seems reasonable. However, what happens when a patient with erectile dysfunction symptoms of a confirmed vascular mechanism is stratified as low or intermediate (<7.5%) 10-year cardiovascular risk.

On the basis of currently available evidence, we recommend considering coronary artery calcium for further risk assessment in men with vascular erectile dysfunction not already stratified as high risk by scores (Figure, example case in Table 2). This strategy will be particularly informative in patients aged less than 60 years, because most men aged 60 years or more will already be considered high risk by the score.

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