SEXUAL MEDICINE REVIEWS REVIEW

Cardiometabolic Risk and Female Sexuality—Part I. Risk Factors and Potential Pathophysiological Underpinnings for Female Vasculogenic Sexual Dysfunction Syndromes

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ABSTRACT

Introduction: Erectile dysfunction is recognized as an opportunity for preventing cardiovascular (CV) events, and assessing the impairment of penile vascular flow by Doppler ultrasound is an important tool to ascertain CV risk. Conversely, the role of genital vascular impairment in the pathophysiology of female sexual dysfunction (FSD) remains contentious.

Aim: To focus on the current scientific support for an association between CV risk factors and female sexual health in the 1st part of a 2-part review.

Methods: A thorough literature search of peer-reviewed publications on the associations between CV risk factors and FSD and their underlying mechanisms was performed using the PubMed database.

Main Outcome Measures: We present a summary of the evidence from clinical studies and discuss the possible mechanisms providing the pathophysiologic bases of vasculogenic FSD syndromes.

Results: The peripheral sexual response in women is a vascular-dependent event, and evidence suggests that cardiometabolic-related perturbations in endothelial function can determine vascular insufficiency in female genital tissues. Although epidemiologic and observational studies demonstrate that the prevalence of FSD is higher in women with diabetes mellitus, a cause-effect relation between these clinical conditions cannot be assumed. Evidence on the effect of obesity, metabolic syndrome, and polycystic ovary syndrome on sexual function in women is controversial. Data on the associations of dyslipidemia and hypertension with FSD are limited.

Conclusion: Common cardiometabolic alterations could affect vascular function in the female genital tract. Based on limited data, there is an association between CV risk factors and female sexual health in women; however, this association appears milder than in men. **Maseroli E, Scavello I, Vignozzi L. Cardiometabolic Risk and Female Sexuality—Part I. Risk Factors and Potential Pathophysiological Underpinnings for Female Vasculogenic Sexual Dysfunction Syndromes. Sex Med Rev 2018;X:XXX–XXX.**

Key Words: Cardiovascular Diseases; Female Sexual Dysfunction; Sexual Response; Methodology; Gender Differences; Doppler Ultrasound

INTRODUCTION

Despite increasing attention to the topic, female sexual dysfunction (FSD) remains a poorly studied and underdiagnosed condition. The multidimensionality of the disorder, the lack of universally accepted diagnostic procedures, the ever-changing definitions, and the different populations from which samples for epidemiologic studies are drawn result in a poor number of data establishing worldwide prevalence and risk factors for FSD. According to the Fourth International Consultation on Sexual Medicine 2015, there appears to be reasonable consensus that the prevalence of women who report at least 1 manifest FSD is approximately 40% to 50%, irrespective of age.[1]

For risk factors, the debate on the relative influences of sociocultural, psychological, relational, and biologic parameters on female sexuality continues. Compared with male sexuality, biologic determinants of female sexual response, in particular cardiovascular (CV) risk factors, have received scant attention.

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Erectile dysfunction (ED) is considered a harbinger for CV disease (CVD) and has been claimed as providing a "window of curability" in men to perform the requisite CV risk assessment. This stems from clinical and preclinical evidence that ED is predominantly a disease of vascular origin, with endothelial dysfunction as the unifying link. In contrast, although preclinical data and many sexual similarities suggest a close link between sexuality and CVD in women, definitive clinical evidence of this association is lacking. More importantly, the role of CVD-related genital vascular impairment in the pathophysiology of FSD remains contentious. A still unanswered question is whether sexual health can be a proxy for CV health in women.

This is the 1st part of a state-of-the-art review that focuses on the current scientific support for an association between CV risk factors and female sexual health. In the 2nd part, the potential reasons for the apparent sexual dimorphism in vasculogenic sexual dysfunction are reviewed, with a focus on available assessment techniques and suggested areas and methods for future investigation.

DO COMMON CARDIOMETABOLIC ALTERATIONS INCREASE THE RISK FOR FSD? EVIDENCE FROM CLINICAL STUDIES

Diabetes Mellitus

Diabetes mellitus (DM) is the most-studied metabolic risk factor for FSD in women. Its prevalence has reached epidemic proportions: in 2013, the number of patients with DM was estimated to be roughly 382 million worldwide, with numbers predicted to reach approximately 600 million by 2035.[2] In men, DM has long been recognized as a major risk factor not only for ED but also for ejaculatory, orgasmic, and desire problems.[3–5] Interestingly, DM affects more women than men, and they share similar risks for complications.[4] However, it has not been elucidated whether DM is a determinant of FSD and whether 1 DM parameter above others can predict FSD in women with DM.

Table 1 presents the most important clinical studies that have reported data on the prevalence of FSD in women with type 1 DM (T1DM) and type 2 DM (T2DM) since the 1980s.[6–51] The different definitions used for FSD in recent decades, reflecting changes in the conceptualization of sexual disorders, contribute to the challenges of comparing data across clinical studies on FSD in women with DM.[52] Since the development of the Female Sexual Function Index (FSFI)[53] and its clinical cutoff scores,[54] most studies have complied with this approach in the evaluation of sexual function. The FSFI is brief multidimensional scale for assessing all phases of the female sexual cycle (desire, arousal, and orgasm) and sexual satisfaction and dyspareunia; women with a total score no higher than 26.55 are classified as being at risk for FSD.[54] Trials investigating the prevalence of FSD in T1DM report a range of 18% to 71%; the frequency of FSD in T2DM is even more heterogeneous, ranging from 12% to 88% (Table 1). Therefore, the prevalence of women with DM reporting at least 1 sexual dysfunction appears to be higher than that of the general population, which is 40% to 50%[1]; this gap seems more pronounced when considering only women with T2DM. Indeed, the vast majority of studies that performed a statistical comparison of FSD prevalence or overall sexual functioning in women with DM vs controls detected a significant difference (Table 1). The only published meta-analysis on the topic, including records up to 2012, consistently highlighted a higher risk for FSD in T1DM, T2DM, and in "any diabetes" vs controls (odds ratio = 2.27, 2.49 and 2.02, respectively).[55] Notably, in the "any diabetes" group, the risk was significant in premenopausal, but not in menopausal, women.[55]

Data on the specific effect of different types of DM on female sexual function are conflicting. Nowosielski et al[27] reported a higher prevalence of FSD in women with T2DM than in those with T1DM. In contrast, Mazzilli et al[41] found a significant decrease in FSFI total score and in most of its domains in women with T1DM compared with controls, but not in those with T2DM, except for the FSFI desire domain; however, they attributed the discrepancy to the duration of disease in their sample, because it was significantly longer for T1DM. Similar results were obtained in 2 other studies.[17,48] A possible explanation for the more severe sexual impairment in T1DM is the longstanding complications, which have more time to exert their effects, and the development of a negative attitude toward sexuality, which is typical of chronic progressive diseases.[48] Much of the variation across types of DM can include age or age-related factors, such as an increasing burden of diseases or menopause.[52] In particular, most studies on women with DM fail to adjust for menopause and treatment status with local or systemic estrogens, which could modulate the association between DM and FSD in postmenopausal women. This is of special relevance because clinicians might be more reluctant to prescribe estrogen treatment in diabetic than in healthy women because of the fear of CV side effects.[52] Although this topic is beyond the scope of this review, it is worth emphasizing that this fear has been recently undermined. A recent analysis of the 18-year follow-up of the Women's Health Initiative (WHI) demonstrated that hormone therapy with conjugated equine estrogens plus medroxyprogesterone acetate for a median of 5.6 years or with conjugated equine estrogens alone for a median of 7.2 years was not associated with risk of all-cause, CV, or cancer mortality.[56] Other possible confounders modulating the effect of diabetes on FSD within the T1DM and T2DM groups are psychological comorbidities.[57] Indeed, it should be considered that although the earlier onset of T1DM allows for an easier psychosocial and sexual adjustment, the occurrence of T2DM later in life might undermine an established female self-image and require adaptive changes in relationship patterns.[10] In addition, the presence of DM doubles the odds of depression in women,[58] and although comorbid depression is more common in T2DM, anxiety is more typical of T1DM.[59] However, no studies thus far have been designed to evaluate the role of depression as a possible