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Organic Causes of Erectile Dysfunction in Men Under 40

Key Words
Erectile dysfunction · Peyronie's disease · Sexual dysfunction · Trauma · Young men · Organic etiology

Abstract
There are a significant number of men under 40 who experience erectile dysfunction (ED). In the past, the vast majority of cases were thought to be psychogenic in nature. Studies have identified organic etiologies in 15–72% of men with ED under 40. Organic etiologies include vascular, neurogenic, Peyronie's disease (PD), medication side effects and endocrinologic sources. Vascular causes are commonly due to focal arterial occlusive disease. Young men with multiple sclerosis, epilepsy and trauma in close proximity to the spinal cord are at increased risk of ED. It is estimated that 8% of men with PD are under 40, with 21% of these individuals experiencing ED. Medications causing ED include antidepressants, NSAIDs and finasteride (Propecia), antiepileptics and neuroleptics. Hormonal sources are uncommon in the young population, however possible etiologies include Klinefelter's syndrome, congenital hypogonadotropic hypogonadism, and acquired hypogonadotropic hypogonadism. The workup of young men with ED should include a thorough history and physical examination. The significant prevalence of vascular etiologies of ED in young men should prompt consideration of nocturnal penile tumescence testing and penile Doppler ultrasound. Treatment options that may improve ED include exercise and oral PDE-5 inhibitors.

Introduction

Our understanding of erectile dysfunction (ED), defined as the inability to achieve or maintain an erection sufficient for sexual performance, has changed drastically over the last 50 years [1]. Once assumed to be a problem primarily rooted in the psyche, ED is now understood to frequently have a physiological basis [2]. Organic sources including vascular, neurologic and hormonal abnormalities, with occasional psychogenic overlay, are often the causes attributed to ED in older men, while men under the age of 40 are often thought to have only psychogenic factors contributing to their ED. However, a review of the literature reveals that many cases of ED are organic in origin, including vascular, neurogenic, hormonal or due to medication side effects. Assuming that ED is psychogenic may miss significant underlying disease, a correction of which could lead to considerable improvement in many men's lives.

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Prevalence

52% of men aged 40–70 have some degree of ED and moderate to severe cases increase sharply with age [2]. The percentage of men under 40 with ED varies greatly according to the study and methods used to determine the cause of ED, as shown in table 1. A Turkish study of 948 men with an IIEF5 score <21 were evaluated with a psychiatric evaluation, nocturnal penile tumescence (NPT) with RigiScan and penile Doppler ultrasound found that 14.8% of men under 40 had ED due to organic causes. This was identified as a number of different factors including arteriogenic 32, venogenic 16.6, neurogenic 12.8, endocrinologic 2.5, drug-induced 7.6, mixed type 11.5, and unknown 16.6% [3].

Another Turkish study, in which ED was diagnosed with a thorough physical examination, employed a more extensive diagnostic workup, including color Doppler ultrasound, dynamic pharmacocavernosometry, selective pudendal pharmacoarteriography and NPT with RigiScan and found an organic cause in 45% of cases [4]. In an American study, 100 men with ED under 40 were evaluated, 72 were found to have vasculogenic ED, 12 neurogenic ED and only 13% had psychogenic ED [5].

Honeymoon impotence has long been regarded as psychogenic in nature, but of 90 men presenting with honeymoon impotence and evaluated with intracavernous injection of papaverine and self-stimulation (CIS), NPT and color Doppler ultrasound, sequentially with negative CIS response, 27.7 were vascular and 4.4% were neurogenic in etiology.

Table 1. Prevalence of ED found in men under 40 in a variety of studies looking at men within different age ranges

Age range	Number in study	Prevalence of ED
18–24	1,475	3 [48]
20–24	20,055	12 [49]
20–29	1,410	7 [50]
25–34	1,475, 20,055	2 [48], 14 [49]
25–39	1,857	4 [51]
30–39	1,410, 4,883	9 [50], 2 [52]

Table 2. Overview of possible etiologies of ED in men under 40

Vascular disorders
Focal arterial occlusive disease
Subclinical endothelial dysfunction
Peyronie's disease
Neurogenic disorders
Multiple sclerosis
Epilepsy
Intramedullary nailing of femoral fractures
Surgical procedures of lumbar spine
Medication side effects
Neuroleptics
Antiepileptics
Finasteride
NSAIDs
Endocrine disorders
HIV-induced decrease in testosterone
Klinefelter's syndrome
Congenital hypogonadotropic hypogonadism
Acquired hypogonadotropic hypogonadism
High soy diet
Diabetes mellitus
Hyper-/hypothyroidism

Etiology of Erectile Dysfunction

An overview of possible etiologies of ED in men under 40 is shown in table 2.

Vascular Disorders

There has been a great deal of speculation that young men with vascular ED may be due to subclinical perineal trauma. This was supported by a study that looked at 91 men with ED and without a history of perineal trauma who underwent penile angiography – younger men were found to more frequently have focal arterial occlusive disease and exposure to subclinical trauma [6]. This concept has been supported by the association between bicycling and ED. This relationship was first noted in a number of case reports, but later cross-sectional studies found that young men who bicycle more than 3 hours a week have an increased risk of developing ED [7]. Bicycling has been shown to reduce the peak cavernosal artery systolic velocity to 0 due to perineal pressure from bicycle seats, and is thought to temporarily occlude penile vessels and lead to focal arterial occlusive disease [7].

Interestingly, young men with no identifiable cause of ED have evidence of subclinical endothelial dysfunction, as determined by blood pressure, C-reactive protein level, total cholesterol and triglyceride levels, and carotid intima-media thickness. When young men at low risk for coronary artery disease with ED were compared to young men without ED, they were found to have lower flow-

mediated brachial vasodilatation, higher systolic blood pressures, C-reactive protein levels, cholesterol and triglycerides, carotid intima-media thickness and Framingham risk scores, however all of these values were within the normal range [8]. This study indicates that many cases of ED with no identifiable source are associated with subclinical cardiovascular factors.

Neurogenic Disorders

There are a number of known neurogenic risk factors for ED in young men. A study of men with multiple sclerosis, of whom 28.4% were younger than 40, showed multiple sclerosis increases the risk of ED by 2.2 times [9]. There is a high prevalence of ED among men with epilepsy – in a study of 80 men between the ages of 22 and 50, 42.5% had ED [10]. Young men with epilepsy are 1.8–3 times more likely to have ED than men without epilepsy [11].

Trauma can cause both vascular and neurogenic ED. While usually caused by perineal trauma, it can also be due to trauma to nearby structures, such as femoral fractures. When men under 40 experienced femoral shaft fractures treated with intramedullary nailing, there was an increased risk of ED compared to men with tibial fractures. This is thought to be due to pudendal nerve damage caused by countertraction on the femoral head. Following intramedullary nailing of the femoral head, 40.5% of men experienced mild to moderate ED [12]. A case series of 4 men with an age range of 19–37 suffered from ED after a femoral fracture was corrected with femoral nailing. In all 4 cases the ED resolved after 1–2 years of treatment with a PDE-5 inhibitor [13].

Neurological damage can be sustained during surgical procedures of the lumbar spine. 34.3% of men under 50 who underwent surgical decompression of the lumbar spine experienced ED after surgery [14].

Peyronie's Disease

The precise mechanism of ED in men with Peyronie's disease (PD) is unclear. PD is thought to arise from repeated trauma to the tunica albuginea with the eventual formation of a plaque that causes penile curvature and concomitant ED. Plaque formation is thought to require a significant amount of time and thus the prevalence of PD increases as men age. However, 8.2% of patients with PD are under the age of 40, and 21% of these men have ED. The onset of PD in men under 40 is often much more acute and can usually be treated successfully with intracavernosal injections [15]. Occasionally, PD occurs in teenaged individuals. A study of 32 teenagers with PD showed that 37% of these individuals had ED, none had hemodynamic abnormalities and they were more likely than older men with PD to have multiple plaques [16].

Medication Side Effects

A variety of medications commonly taken by young individuals are associated with ED including antidepressants, finasteride, anxiolytics, neuroleptics, NSAIDs and muscle relaxants.

SSRIs have been notoriously associated with sexual dysfunction but they may not cause ED specifically. In a randomized, double-blinded study of men using citalopram (Celexa) or fluoxetine (Prozac) compared to placebo, there was no effect on erectile function as measured objectively with RigiScan, while subjective measures of erectile function were negatively affected [17]. 5-HT may affect and be a predictor of other aspects of sexual dysfunction in young men, such as premature ejaculation [18].

Finasteride is commonly used in the young male population to prevent and reverse male pattern baldness. 1.4% of men taking finasteride, with an average age of 31, experienced ED, compared to.9% of men taking placebo [19]. A recent case report of 71 individuals aged 21–46 have shown that finasteride use for MPB caused irreversible sexual side effects, including 92% who reported ED [20]. Regular NSAID usage is associated with an odds ratio of 2.4 for ED [21].

Neuroleptics of all varieties are well known to cause ED, due to increased prolactin levels [22]. Antiepileptic medications are associated with ED and may be due to vasogenic effects [23].

Endocrine Disorders

Hormonal sources of ED are uncommon in the young population. ED due to low testosterone is mainly seen in older men. When men with ED under 50 had testosterone and prolactin levels measured, 4% of men had low testosterone, however it is unclear that this was a contributor to ED in this population. There are populations of young men, such as those infected with HIV that experience a premature decrease in testosterone [24].

When present, hormonal etiologies of ED can include Klinefelter's syndrome (KS), congenital hypogonadotropic hypogonadism (CHH), acquired hypogonadotropic hypogonadism (AHH) and cryptorchidism. KS has a prevalence of 1:500–1,000. Importantly, many men with KS do not have the textbook appearance of a eunuchoid body habitus, micropenis and microorchidism, however there is a broad phenotypic spectrum with many men appearing essentially normal. Men with KS often present to

urologists with infertility, ED or poor libido. Individuals with KS will have low testosterone and elevated LH, FSH and often estradiol [25]. Most recently, a 2010 study looked at 1,386 consecutive patients presenting with sexual dysfunction. Karyotype analysis was performed on all men with a testis volume <6 ml. 23 (1.7%) men with an average age of 40 years had KS. 22.7% of men with KS experienced severe ED [26]. In a prior study on men with KS with a mean age of 32.2 years, severe ED was found in 2.5% [27].

CHH, which includes Kallmann syndrome, is rare with a probable prevalence of 1/4,000–10,000. Patients typically present with pubertal failure [28]. In a study of 39 men with CHH treated with testosterone replacement therapy (TRT), prior to treatment, 100% experienced sexual dysfunction (erectile function was addressed as part of the Arizona Sexual Experience Scale questionnaire, but was not specifically mentioned). TRT improved sexual function in this cohort of men [29]. However, the presence of micropenis is frequently the primary sexual impediment [30].

AHH can be due to a variety of causes, such as head trauma, prolactinoma, sellar or infundibular cysts, pituitary surgery, alcohol and drug abuse, as well as infiltrative conditions such as hemochromatosis and sarcoidosis [31]. ED and loss of libido frequently accompany this condition. Diagnosis can be made LH, FSH and testosterone levels and an MRI of the sella can be considered in cases with high clinical suspicion [32].

Cryptorchidism can lead to low testosterone levels as well. A study of 49 patients with cryptorchidism who underwent orchiopexy between 10 months and 13 years were on average less sexually active than controls [33].

Although very rare, a connection between high soy diets and ED has been postulated. The effects of daidzein, a soy isoflavone, have been studied in animal models. Relatively large amounts cause histological changes in the penile structure of rats, including an increase in collagen and a reduction in smooth muscle and elastic fiber content [34]. When juvenile rats were exposed to daidzein, erectile function was impaired when the rats matured into adults in a dose-dependent manner [35]. Apart from animal models, there has been a case report of an 18-year-old who developed hypogonadal ED due to a high soy vegan diet that was reversible with diet cessation [36].

Individuals with endocrine disorders, such as diabetes and hyper- and hypothyroidism, have significantly poorer erectile function than disease-free men [37]. While metabolic syndrome is associated with ED in older men, no association has been found in with men under 50 [38].

Risk Factors for ED in Young Men

Studies investigating risk factors for ED have failed to find an association between many factors that are often related to ED in older men. Interestingly, in men aged 18–40, lower educational levels, psychosocial problems, lack of information about sex and no history of masturbation were correlated with ED, while smoking, alcoholism, sedentary lifestyle, obesity, diabetes, hypertension, CV disease, hyperlipidemia, depression and anxiety were not found to be correlated to ED [39]. In men under 40 with known organic ED, only smoking and recreational drug use were found to be associated with ED, and no association was found with obesity, dyslipidemia, obesity, diabetes mellitus, hypertension, coronary heart disease and chronic pain syndrome [40].

Conclusion

Diagnosis

For men under 40 with ED, the diversity of etiologies mentioned above should prompt a thorough history. This should include developmental history, psychosocial and relationship history, trauma, amount of time spent cycling, surgical procedures to the spine or femur, penile curvature, review of medications, smoking status, recreational drug use, and past medical history including diabetes neurological disorders, and hyper- and hypothyroidism. A physical examination should be performed with special attention to eunuchoid body habitus, secondary sexual characteristics, anosmia, testicular volume, penile length, blood pressure and a focused genital examination for the presence of penile curvature.

The low incidence of hormonal abnormalities may lead a clinician to include testosterone in the initial evaluation only if secondary sexual characteristics are abnormal. Frequently, a comprehensive metabolic workup is initiated for older men, however as there is no associated metabolic component in young men with ED, a metabolic workup may not offer any additional information. The large percentage of vascular anomalies should encourage physicians to consider a workup with NPT and penile Doppler studies if no other etiologies are clearly identified. The combination of intracavernous injection and audiovisual sexual stimulation may improve the recording of physiologic erectile response during the Doppler study [41].

Treatment

For men with organic ED, there are a number of behavioral modifications that may be considered before

pursuing medical or surgical treatments. Although obesity appears not to be a risk factor for ED in young men, weight loss has been found to improve erectile function in men aged 35–55 [42]. Interestingly, exercise also is associated with better erectile function in men under 40 [43]. Smoking and recreational drug use should be discontinued, as they are modifiable behaviors associated with ED in younger men. For ED due a medication side effect, the offending medication should be discontinued. For men taking an SSRI, 20 mg of tadalafil has been shown to significantly improve erectile function, with tolerable side effects [44]. Trazodone has also proven to be effective in treating ED in men taking SSRIs [45].

Regardless of etiology, treatment almost always begins with oral PDE-5 inhibitors. For ED due to KS, CHH, AHH hypogonadism, TRT will often lead to improvements in EF. Failure of PDE-5 should prompt a trial of treatments of increasing invasiveness, alprostadil urethral suppositories, intracavernosal injections of papaverine, Bimix or Trimix, and finally penile prosthesis. In general, previous attempts at the use of surgery to improve EF in men with vasculogenic ED has not achieved good long-term outcomes and has not been suggested for routine use [46]. However, for men with who are found to have focal arterial occlusive disease, penile microvascular arterial surgery is a possibility [47].

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