Erectile Dysfunction: Patient Evaluation, Investigations

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Key Points

1. Erectile dysfunction (ED) is the inability to attain and/or maintain a penile erection sufficient for satisfactory sexual performance.
2. At a minimum, patients undergoing evaluation for ED should have a thorough psychosexual history, focused physical examination, and total testosterone laboratory testing.
3. Additional laboratory testing and imaging should be used in select cases at the discretion of the evaluating clinician if the findings may change clinical management.
4. Intracavernosal injection of an erectogenic agent combined with penile duplex doppler ultrasound is the imaging modality of choice for evaluation of penile structural abnormalities and penile hemodynamics. The findings must be interpreted carefully and in context with the overall clinical picture. (see **Figures 4-6**)

1. Definition

Erectile Dysfunction (ED) has been defined by multiple classification systems. According to the American Urological Association **Erectile Dysfunction Guideline**, ED is defined as the **inability to attain and/or maintain penile erection sufficient for satisfactory sexual performance**.[1] The DSM-5 defines erectile disorder as occurring on almost or all occasions of sexual activity and including at least one of the following symptoms: marked difficulty in obtaining an erection, marked difficulty in maintaining an erection until completion of sexual activity, or marked decrease in erectile rigidity.[2] The 4th International Consultation on Sexual Medicine in 2015 proposed a definition of ED based on clinical principle as the consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual satisfaction. [3]

2. Epidemiology

The prevalence of any degree of ED is reported as high as 52% of all men. This high level is reported in studies with a broad definition of ED using a single question self-report and includes minimal symptoms. Further,[4] this was in a fairly homogenous population of men. In a contemporary and more diverse series with a more rigorous definition of being able to achieve an erection adequate for sexual intercourse 'sometimes' or 'never' the prevalence was about 20%.[5] This rate has been supported by other studies with similar findings as well as studies using the now well established IIEF-5 with a cutoff of 'mild to moderate ED' or worse defined as a score of 16 or less.[6,7] There is a well-established increase in rates of ED with increasing age in men, increasing to over 60% for men older than 70.[7] Further, prevalence of ED is increased in men with comorbid medical conditions, particularly conditions that affect the cardiovascular system (see **Table 2**).[8]

2.1 Sexual Orientation

It is important to note the difficulties in assessing the literature with regards to ED in gay men. In general, gay men are underrepresented in research and this is thought to be due to a failure in recruiting these patients. This failure to recruit gay men is likely a combination of providers' discomfort with discussing gay sexual practices and the heteronormative nature of many sexual health questionnaires. For example,[9] the IIEF includes multiple questions that assume the patient is the one penetrating his partner,[10] which may not be true for all gay men.

2.2 Racial Disparities

Racial differences are also noteworthy when exploring ED epidemiology. It has previously been demonstrated that non-white men are less likely to seek healthcare for sexual dysfunction, even when controlling for other factors ($p< 0.05$).[11] Among patients who report ED, multiple studies show differing ED rates based on race. Data from > 3500 men in the National Health and Nutrition Examination Survey (NHANES) showed that on multivariable analysis, Hispanic men had almost 2x greater rates of ED (OR 1.89, 95% CI 1.22-2.93).[5] Interestingly, data from > 78,000 men in the California Men's Health Study did not show an increase in ED within Hispanic men compared to white men. However, this data did suggest that black men were significantly less likely to have severe ED compared to white men on multivariable analysis (OR 0.54, 95% CI 0.48-0.61).[12]

3. Diagnosis

3.1 History

3.1.1 Normal Sexual Response

The sexual response cycle in men is most commonly conceptualized in terms formulated by the sex researchers William Masters and Virginia Johnson. Masters and Johnson promulgated a linear sexual response cycle that started with the **excitement** (**arousal) phase** in response to erotic stimuli. Arousal was followed by **plateau, orgasm, and resolution phases**. It is normal for men to

experience a refractory period after the resolution phase. During the refractory period it is not possible to stimulate the penis into the erect state. The refractory period is typically brief in young men but becomes progressively longer with increasing age. Details on the events associated with these phases are detailed in **Table 1.**[13] Helen Singer Kaplan modified the Masters and Johnson model by adding a **"desire" phase** which precedes arousal and which may be spontaneous or in response to erotic stimuli.[14]

Many men have a poor understanding of the normal sexual response. This may account for the tendency of some men to state that they have ED in the setting of globally reduced libido, particularly if they are placed in a situation which was previously sexually arousing but is no longer stimulating. Conversely, men with ED may present with a complaint of low libido as their lack of confidence in their erections causes them to avoid sexual activity.

Lack of understanding about the normalcy of the refractory period is also common. Some men who report "ED" due to not being able to immediately resume sexual activity after orgasm may be experiencing the common age-related prolongation of refractory period. Rapid or premature ejaculation (PE) may also be reported by the patient as "ED". PE is defined by the **2020 AUA Guideline on Ejaculatory Disorders** as consistently poor ejaculatory control, associated bother, and ejaculation that occurs within 2 minutes of penetration since sexual debut (lifelong PE) or with a markedly reduced latency compared to prior sexual experience (acquired **PE**). It is important to note that the mean and median ejaculation latency the general population of 5 Western countries is about 5-6 minutes and there is a normally distributed variance around these values.[15,16] Men who have ejaculation latencies within the normal distribution should be reassured that they are within general population norms.[17]

Table 1: Phases of Male Sexual Response

Stage	Description
Excitement/Arousal	Tachycardia, increase in blood pressure, **penile erection**, testicular retraction, sexual excitement
Plateau	Tachycardia, increase in blood pressure, muscle contraction, **increasing sexual excitement**
Orgasm	Pelvic muscular contractions, **ejaculation, intense pleasure or satisfaction**
Resolution	Loss of penile erection, decline in heart rate and blood pressure, decreasing sexual excitement, refractory period

3.1.2 General History Taking

Table 2: Conditions Associated with ED[18]
Psychological Conditions
Traumatic sexual experiences
Conflict over cultural/religious restrictions on sexual activity
Interpersonal issues with partner
Performance anxiety
Depression
Lifestyle Factors
Stress
Sedentary lifestyle
Tobacco use
Heavy alcohol use
Illicit drug use
Vascular Disease
Hypertension
Dyslipidemia
Coronary artery disease
Peripheral arterial occlusive disease
Diabetes mellitus (types 1 and 2)

Metabolic Disorders
Renal insufficiency
Hepatic insufficiency
Respiratory Disease
Chronic obstructive pulmonary disease
Sleep apnea
Neurological Disorders
Cerebrovascular disease/stroke
Spinal cord injury
Neurodegenerative conditions (Multiple Sclerosis, Parkinson’s Disease)
Autonomic polyneuropathy
Pudendal nerve lesions
Urologic Conditions
Benign prostate hyperplasia (BPH) and lower urinary tract symptoms (LUTS)
Chronic pelvic pain syndromes
Pelvic fractures (particularly with urethral disruption)
Pelvic surgery (radical prostatectomy, cystectomy, proctectomy)
Priapism
Peyronie’s Disease
Penile Fracture

Many patients (and providers) admit to difficulty discussing sexuality. Patients avoid discussing sexual problems due to a lack of opportunity, sense of embarrassment and shame, as well as a societal taboo against the open discussion of sexuality. A systematic review of attitudes of healthcare professionals in the United Kingdom cites lack of training, lack of time, and embarrassment as the most common barriers to discussing sex with patients. [18] An international study of 27,500 men and women noted that despite half of all sexual active participants experiencing at least one sexual problem, only 19% sought medical care and only 9% reported being asked about sexual health over a 3-year period. [18] It is often necessary for the provider to initiate the conversation about sexual wellness. [19,20]

The general medical history is used to determine individual risk factors for ED (**Table 2**). Salient non-sexual portions of the patient history include assessment of age, comorbid medical (particularly vascular disease) and surgical history, family history of vascular disease, diet, weekly physical activity, and alcohol, tobacco and recreational drug use.[21] When reversible vascular issues are identified patients should be encouraged to take steps to optimize vascular health (e.g. tobacco cessation, increased physical activity, dietary modification). Optimization of vascular health may improve erectile function. [22] Improved vascular health will also slow further deterioration in erectile function and may prolong overall longevity. [23,24,8,25] Other common risk factors for ED should be evaluated including endocrinopathies, neurologic disease, psychosocial issues, medications, and medication related side effects.[1] There are many medications that can cause or contribute to ED with the most types being 5-alpha reductase inhibitors, certain antihypertensives, and psychoactive drugs including antidepressants and antipsychotics. [26]

3.1.3 ED History

Questions regarding ED include: **onset, severity, duration, rigidity during partnered relations versus masturbation, ability to attain erection sufficient for penetration, sustainability of erection, presence and rigidity of nocturnal erections, degree of bother, and use of any prior erectogenic therapies.**[19] It is also important to characterize if the symptoms are stable or worsening as this may suggest underlying comorbidities such as cardiovascular disease.[1]

There are a variety of grading systems for erectile tumescence. The **Erection Hardness Score (EHS) is a practical and useful scale which grades erection hardness on a 4-point scale**:

1. **Penis is larger but not hard**
2. **Penis is hard but not hard enough for penetration**
3. **Penis is hard enough for penetration but not completely hard**
4. **Penis is completely hard and fully rigid**[27]

Characterizing the patient's penile rigidity with erection is helpful as a means to establish baseline function and monitor response to treatment. It is important to define whether the patient has fluctuations in rigidity. ED that is situational (i.e. variable with a given partner, variable with different partners, and/or variable in the setting of masturbation versus partnered activity) may have a

psychosocial or other discrete non-medical element amenable to intervention.

The presence of nocturnal/early morning erections in a man with ED has classically been conceived as evidence for psychogenic ED, but this is no longer generally believed. Absence of nocturnal erections is associated with more severe forms of vascular disease as well as hypogonadism.[28] Some men with mild arteriogenic ED may have robust nocturnal erections.

Defining the sustainability of erections (problems with maintaining instead of gaining erection) is an essential question. Many men with ED have excellent rigidity but lose their erection with penetration or due to change in position. Loss of a rigid erection may be due to venous leak or to psychological stress leading to adrenergic tone and vasoconstriction. **It is important to differentiate between loss of erection sustaining capability and PE** so that the correct treatment plan can be put in place targeting the actual etiology of the patient's problem.

Inquiry on prior ED therapies and response is important. This will determine appropriate next steps in evaluation/treatment. The patient should also be queried on issues pertaining to **libido, ejaculation, orgasm, and penile deformity/Peyronie's Disease**.[19] Attempts should be made to determine if these other problems preceded ED, were coincident with ED, or occurred after onset of ED. It is common for secondary sexual dysfunctions to develop in response to perturbation of another phase of the sexual response cycle.

Providers should also inquire about lower urinary tract symptoms (LUTS), which are present in up to 72% of men with ED.[29,30,31,32] In addition to a medical history and physical exam, the presence of LUTS should prompt further evaluation including the American Urological Association Symptom Index and urinalysis. For patients on medical therapy for LUTS, providers should assess for sexual dysfunction side effects related to α 1-adrenergic receptor antagonists and 5α-reductase inhibitors. Patients should be counseled regarding the potential for change in ED symptoms (positive or negative) during treatment of LUTS.[33]

3.1.4 Psychosexual History

It is important to precisely clarify the circumstances and interpersonal factors of the sexual complaint before initiating further investigation.[34] When discussing sexuality with patients the **provider should be cognizant of social, cultural, religious, educational, and other factors** that may influence the man's perception of his sexual life and beliefs about sexuality. A thorough psychosexual history allows the clinician to identify or rule out the multiple psychological and interpersonal factors that affect erectile function. This can include but is not limited to anxiety, depression, external stressors (e.g. work, finances) and interpersonal conflict. [19,34]

Providers should not presume that a man is heterosexual, monogomous, or partnered. An important corollary to precise definition of the sexual complaint is **elicitation of the status of the patient's partner(s), sexuality, and sexual practices**. Characteristics of the partner(s) such as **gender, duration of relationship, legal/marital status, partner health/sexual problems, and degree of support for their partner seeking treatment for ED** are helpful. If the partner is present,

corroborating the history may be of benefit. **Sexual dysfunction is a condition that directly affects both partners**. If the partner has sexual concerns, appropriate treatment and/or referral is essential to treatment success for the index patient. These factors are important to acknowledge when determining the appropriate treatment strategy.[19,34] This includes relationship conflict that may affect a couples' intimacy and should prompt a referral to a therapist or counselor.

For patients who are not partnered, providers should assess the patient's goals of care to customize a treatment plan. Providers should be sensitive to the effect of ED on a patient's mental, emotional, and social well-being. For concerns outside the scope of urology practice, referral to an appropriate professional is warranted.

3.2 Questionnaires

The IIEF-5 Questionnaire (SHIM)

Please encircle the response that best describes you for the following five questions:

Over the past 6 months:					
1. How do you rate your confidence that you could get and keep an erection?	Very low 1	Low 2	Moderate 3	High 4	Very high 5
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never or never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always or always 5
3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?	Almost never of never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always or always 5
4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5
5. When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never or never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always or always 5

Total Score: _____

1-7: Severe ED 8-11: Moderate ED 12-16: Mild-moderate ED 17-21: Mild ED 22-25: No ED

Figure 1: The IIEF-5 Questionnaire (SHIM)

For decades assessment of ED was hampered by the absence of validated self-report scales to assess and stratify the severity of disease. The development of validated questionnaires has provided a means to quantify both the severity of ED and response to treatment as well as provide an avenue to open a discussion regarding sexual dysfunction in a patient that presents for other concerns. [1] The most widely used survey instruments are the **International Index of Erectile Function (IIEF) or its shortened version the Sexual Health Inventory For Men (SHIM or IIEF-5)** (**Figure 1**).[35,10]

The IIEF is a validated, 15 item scale that assesses five domains of male sexual experience (Sexual Desire, Erectile Function, Intercourse Satisfaction, Orgasmic Function, and Overall Sexual satisfaction).[10] Each of the six questions of the Erectile Function Domain (EFD) of the IIEF are scored 1-5, where 1 = never/almost never, 3 = about half the time and 5 = always/almost always. The maximum score is 30. Validated cut-off scores for ED severity based on EFD are: a score of 26-30 consistent with normal erectile function, 18-25 consistent with mild ED, 11-17 consistent with moderate ED, and ≤10 consistent with severe ED. [36] These questionnaires will only provide a valid result in a patient who is sexually active and will provide an artificially low result if the patient is not attempting sexual intercourse.

The Male Sexual Health Questionnaire (MSHQ) can also be utilized to provide a detailed evaluation of sexual function with a primary focus on ejaculatory disorders. This validated instrument includes 25 questions covering three domains of erection, ejaculation, and sexual satisfaction.[37] A short form of the MSHQ also may be utilized to assess ejaculatory function only.

The Sexual Encounter Profile (SEP) questions are commonly utilized as single item response questions in research on male sexual function. SEP questions 2 and 3 are the most clinically useful; SEP2 is most commonly formulated as "Were you able to insert your penis into your partner?" and SEP3 as "Did your erection last long enough for you to have successful sexual intercourse?"[38]

3.3 Physical Examination

Vital signs including pulse and resting blood pressure should be evaluated. **Waist circumference and body mass index (BMI) are independent predictors of ED**.[37,39] Progressively higher waist circumference has been clearly associated with increased ED prevalence.[40] A controlled study in obese men with BMI >30 noted that an increase of physical activity and decrease of BMI over 2 years resulted in an increase in IIEF scores.[41] Male secondary sex characteristics should be assessed for signs of testosterone deficiency syndrome (beard growth, pubic hair). **The chest should be examined for gynecomastia**. Optional vascular examinations include **abdominal palpation for abdominal aortic aneurysm** and palpation of peripheral pulses.[42]

Penile examination should include assessment of flaccid stretched length (a proxy for erect length), skin lesions, and hypospadias. The penis should be examined in the stretched flaccid state, with careful palpation of the shaft from pubic bone to coronal sulcus to elucidate any deformities or plaques consistent with Peyronie's disease. Applying side-to-side *and* dorso-ventral pressure during

palpation is the optimal means of outlining plaque and septal anatomy. Side-to-side compression beginning at the 3 and 9 o'clock position on the shaft and rolling firmly upwards (for dorsal plaque) and downwards (for ventral plaque) should be conducted meticulously along the entire penile shaft. [42]

Scrotal examination should include assessment of **testicular size, consistency, and location**. Digital rectal examination should be conducted to assess for signs of prostate pathology in patients being considered for testosterone replacement therapy or endorse LUTS. Abdominal exam should also be performed to evaluate for scars from previous abdominopelvic or inguinal surgery.

3.4 Cardiac Evaluation

As a general principle, ED is a "sentinel event" for systemic cardiovascular disease.[43,44,45] This relationship is particularly pronounced in men less than 50 years of age.[46] A 2010 study by Chew et al suggested a 7-fold increase in risk of cardiovascular events in men less than 40 years presenting with ED.[47] Data from the Prostate Cancer Prevention Trial indicated that ED was as strong a predictor of future cardiac events as cigarette smoking or family history of myocardial infarction. Per **AUA guidelines**, men should be counseled that ED is a risk factor for underlying cardiovascular disease and other health conditions that may warrant evaluation and treatment.[1,48] Consideration should be given to referring men presenting with ED to a primary care physician or cardiologist if they have not yet been evaluated for cardiac risk factors. It is reasonable for the urologist to perform basic laboratory screening for diabetes mellitus and lipid disorders. **The opportunity to address underlying risk factors and intervene early in occult vascular disease may exert a substantial benefit with respect to long-term morbidity and mortality**.[49]

Numerous studies have indicated that risk for cardiac events is increased during periods of physical exertion, including sexual activity. These risks are reduced in men who regularly engage in physical exertion (e.g. exercise, physical labor, etc).[50] Because sexual activity does pose an element of transient cardiac risk, the decision to treat ED is contingent on appropriate estimation of exercise tolerance. The standard unit for assessment of exercise activity is the metabolic equivalent task (MET). [40] One MET corresponds to the basal metabolic energy requirement of sitting quietly at rest. It is estimated that coital sexual activity in long-term couples is equivalent to 2.5-3.3 METs of exertion.[51] Non-coital sexual activity may have a correspondingly lower MET whereas sexual activity that is vigorous and/or with a novel partner will have higher MET equivalence.

A simplified approach to assessment of cardiac tolerance for sexual activity is to ask the patient if he is able to tolerate 20 minutes of walking along a flat surface or climbing two flights of stairs in 10 seconds or less; these activities require approximately 3 METs of energy expenditure and so serve as reasonable proxy measures of cardiac tolerance for sexual activity. While there is heterogeneity in energy expenditure depending on the nature of sexual activity, these proxy measures of cardiac resilience provide a general sense of cardiac health and reserve. [21,52,53]

2.4.1 Princeton III Criteria

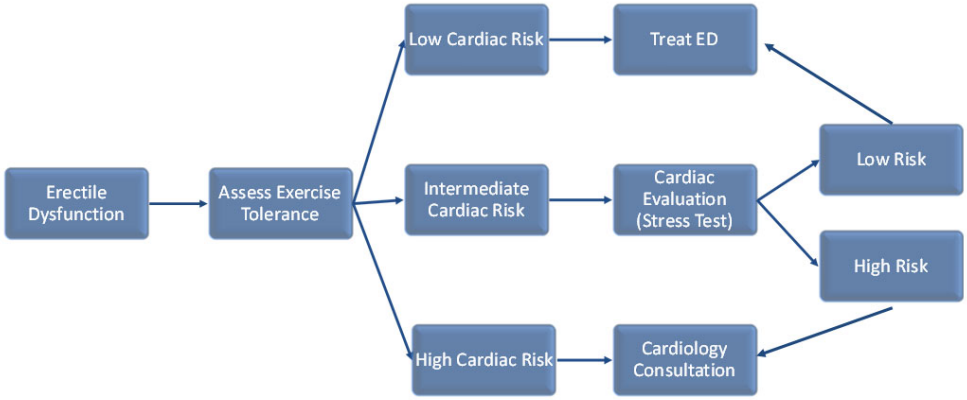

Figure 2: Princeton III Criteria

The Princeton III criteria are the most up-to-date recommendations on appropriate stratification of cardiac risk from sexual activity; use of the Princeton III criteria permits more nuanced and precise elucidation of cardiac risk profile in men with ED. Men presenting with the complaint of ED may be stratified into one of three categories depending on co-morbid cardiac and other conditions. A treatment algorithm adapted from the Princeton III criteria is presented in **Figure 2.**[21]

1. Low risk patients include all men without cardiac disease who are able to exercise with no to minimal cardiac symptoms. Low risk patients also include men with diagnosed cardiac disease who have undergone successful revascularization procedures (e.g. coronary artery stenting, coronary artery bypass graft), men with controlled asymptomatic hypertension, men with low grade heart failure (i.e. New York Heart Association (NYHA) Class I and II heart failure), and men with mild cardiac valve disease. [21]

2. Intermediate risk patients are men who have mild to moderate stable angina, myocardial infarction within the past 2-8 weeks, Class III NYHA heart failure, and history of non-cardiac evidence of vascular disease (peripheral artery disease, cerebrovascular accident, transient ischemic attack, etc). [21]

3. High risk patients are men who are at marked risk of cardiac event during sexual activity. Such men should not be treated for ED until their cardiac status has stabilized. Examples of men at high risk include those with refractory angina, poorly controlled diabetes or hypertension, Class IV NYHA heart failure, myocardial infarction within the past two weeks, high risk arrhythmia (e.g. ventricular tachycardia, uncontrolled atrial fibrillation, etc), moderate or severe cardiac valve disease, and obstructive hypertrophic cardiomyopathy.[21]

4. Investigations

4.1 Laboratory Tests

Selective laboratory studies should be considered in all patients who present with ED, particularly if organic etiologies are suspected. **Current AUA guidelines on ED recommend that early morning total testosterone should be measured in all men with ED**.[1,54] Testosterone testing may be

particularly useful to identify concurrent hypogonadism in men who report a decrease in libido.[55,42,56] Testosterone deficiency is defined as total testosterone < 300 ng/dL based on recent **AUA Guidelines**.[57] In some instances, treating symptomatic low testosterone may result in beneficial effects on erectile function, particularly in those patients with mild ED. **Other tests such as a basic metabolic panel, serum glucose, hemoglobin A1C, and serum lipids are unlikely to change the management options for ED but may unmask undiagnosed chronic medical conditions that warrant further risk mitigation.**[1] These serum studies are optional but should be considered if they have not been ordered already by a primary care provider.[21,42,58,59] **Assaying for thyroid function and prostate specific antigen (PSA) screening may be considered in certain populations**.[1,54]

4.2 Neurological Testing

4.2.1 Biothesiometry

Biothesiometry is a general term used to describe office-based tests for assess neuropathic changes in the penis. A device that produces vibrations of standardized intensity is the most commonly utilized biothesiometer for evaluation of penile sensitivity. Vibration sensation is transmitted by mechanoreceptors. As an alternative to vibration assessment, the neural integrity of light touch/nociceptive nerve fibers of the penis may be accomplished by application of graded degrees of heat or cold or performing a genital pinprick testing.[60]

To date there is no standardized protocol when performing penile biothesiometry or interpreting results. Terrier et al described one approach using a biothesiometer to assess penile sensation after plaque incision and grafting surgery for Peyronie's Disease.[61] In this protocol, baseline vibratory stimulation thresholds is measured along several sites on the penis including the dorsal and ventral glans and areas on the penile shaft. The device is then turned off and vibrations of progressively greater intensity are applied in a gradual fashion. The patient is asked to report the first sensation of vibration; this is marked as the threshold for sensation, and the results are compared against "normal" threshold levels.

While biothesiometry may be informative with respect to ED etiology (i.e. sensory neuropathy such as can be seen with various neurologic conditions or diabetic neuropathy), there are few data to suggest that it substantially changes management of the ED patient.[1,62]

4.2.2 Other Historical Neurologic Testing

There are several other specialized neurologic testing modalities available including pudendal somatosensory evoked potentials (SSEP), cavernous electromyography (EMG), bulbocavernous reflex time (BCRT), and sympathetic skin response (SSR).[63,64,65,66,67,68,69] These tests are purported to be useful for evaluation of somatic and autonomic neuropathy, which may impact genital function and sensation. These tests are occasionally used by neurologists and physical medicine and rehabilitation specialists, but in modern urologic practice are rarely if ever recommended due to a lack of specificity. Moreover, in the current treatment era these tests do not impact our treatment pathways. As such, these specialized neurologic tests are not recommended for routine use in the

evaluation of men presenting with ED.

4.3 Vascular Testing

4.3.1 Office Injection Test

Intracavernosal Injection (ICI) for ED was developed in the early 1980s.[70] The office injection test provides a simple albeit non-specific way to evaluate vascular integrity of the penis. An erectogenic agent such as prostaglandin E1, papaverine, or combination of similar vasodilating agents is administered to the patient by injection into the corpora cavernosa of the penis. The erectile response is then assessed several minutes later, often after sexual stimulation. Maintenance of a rigid erection indicates adequate venocclusive function (i.e. absence of venous leak). Failure to obtain a rigid erection does not always signal the presence of true organic ED; sympathetic response and adrenaline release may occur in response to stress from the injection itself. This may overwhelm the vasodilatory effects of the injection. Repeat dosing may be necessary to overcome this sympathetic nervous system response. Risks of in-office injection include penile pain (especially when alprostadil is used), ecchymosis, and the development of a prolonged erection requiring pharmacological detumescence (priapism), particularly in the setting of repeated injections. [71]

4.3.2 Penile Duplex Doppler Ultrasound (DDUS)

DDUS was developed in the mid-1980s for real-time assessment of penile blood flow.[72] The ability to simultaneously assess for arterial insufficiency and venous leak in real time was a notable advance in the diagnostic workup of the ED patient. DDUS is currently the gold standard in evaluation of erectile hemodynamics. Its accuracy is dependent on complete cavernosal smooth muscle relaxation.[73] ICI of vasoactive agents is used to achieve this smooth muscle relaxation and an experienced sonographer is important for accurate results. The dose of the vasoactive agent is less important than the actual erectile response. Failure to achieve a good erection lowers the accuracy of this test. [73]

With the advent of phosphodiesterase type 5 inhibitors (PDE5i), some experts have questioned the utility of DDUS in routine ED management.[57] **DDUS is thought to remain useful in the case of (i) patients with a high likelihood of psychogenic ED, to establish the absence of an organic etiology and provide reassurance to the patient, (ii) men with the possibility of arteriogenic ED, where cardiology evaluation may be indicated, (iii) young men with a history of pelvic trauma who might be candidates for surgical revascularization, (iv) men with Peyronie's disease who are considering invasive intervention, and (v) identification of men with severe venocclusive dysfunction who are unlikely to respond to medical therapy and should consider surgical intervention.** [1,74]

In addition to providing vascular information, DDUS permits real time assessment of intracorporal pathology (corporal fibrosis, septal calcification, septal hematoma, Peyronie's Disease plaques). [73] Identification of plaque calcification has utility as calcification predicts reduced response to clostridium collagenase in men with Peyronie’s Disease.[75,76]

Standard operating procedures for DDUS support the use of a 7.5–12 MHz linear array ultrasound probe.[73] The entire penis should be scanned to identify abnormal anatomy, ideally in the flaccid state prior to intracavernosal injection of an erectogenic medication and again with the penis fully erect. Key hemodynamic parameters on DDUS include peak systolic velocity (PSV, cavernosal blood velocity at the start of systole) and end diastolic velocity (EDV, blood velocity at the end of diastole). The velocities are measured in cm/sec.

Some authorities advocate for the PSV and EDV to be assessed prior to penile injection of a vasoactive agent, and all authorities support measurement after the penile injection.[73] PSV values in the flaccid state prior to injection are correlated to post-ICI PSV values. However, a 50-patient study indicated that there is no clear association between PSV in the flaccid state and attaining a rigid erection post-ICI. Furthermore, flaccid PSV was a relatively poor predictor of post-ICI PSV.[77]

Evidence supports the use of audio-visual sexual stimulation to augment erectile response and minimizing false arterial insufficiency and venous leak.[73,78] Redosing of vasoactive agent in an effort to ensure good erectile response has also been shown to reduce errors in PSV and EDV measurements.[73]

PSV and EDV cut-offs are used to define arterial insufficiency and venous leak, respectively. The cut-off points by the interpreting clinician selected dictate the sensitivity and specificity of the testing and diagnosis. There is significant variation in defining abnormal penile hemodynamics based on DDUS findings, even amongst sexual medicine experts.[79,80]

A review of 86 papers on DDUS for ED demonstrated that there was no consensus on normal results. However, the most common definition of *arterial insufficiency* (in 39% of papers) was a **PSV < 30 cm/sec. There was more consensus on EDV, with 57% of papers using a definition venous leak being an EDV > 5 cm/sec.**[80] Negative EDV values occur due to retrograde blood flow at the end of diastole, when intracorporal pressure exceeds cavernosal artery pressure (**Figure 3**). This is actually a normal finding and is indicative of excellent smooth muscle relaxation.

Some experts advocate the use of resistive index [RI, defined as (PSV+EDV)/PSV] as an adjunctive assessment of venous leak. **RI values >0.80 has been cited as indicative of normal venocclusive function.**[73] **Figure 4** and **Figure 5** represent images of arterial insufficiency and venous leak, respectively.

While the primary utility of DDUS is in evaluation of ED, a recent study in 298 hypertensive men indicated that men in the lowest tertile of PSV (<25 cm/s in this study) had a greater than 3-fold higher risk of major adverse cardiac event compared to men with PSV > 35 cm/s with a median follow-up of almost 5 years.[81] When extrapolated, these findings support the utility of DDUS to further characterize cardiac risk in patients presenting for evaluation and management of ED, particularly in the setting of early onset symptoms.

The future of DDUS lies in the application of novel technologies. One example is penile ultrasound vibro-elastography or shear wave elastography. With this approach a specialized handheld device on the surface of the penis is used to generate a low frequency harmonic vibration. The resulting shear

wave is propagated through the penile tissues to an ultrasound probe that can assess information on wave speed dynamics. In a pilot study from Zhang et al, penile elasticity and viscosity based on this assessment was positively correlated with PSV, and negatively correlated with cardiovascular risk for patients undergoing assessment for ED and Peyronie's Disease. [82] Further work is needed to expand upon and corroborate these findings; in the future this may be a useful tool for ED evaluation.

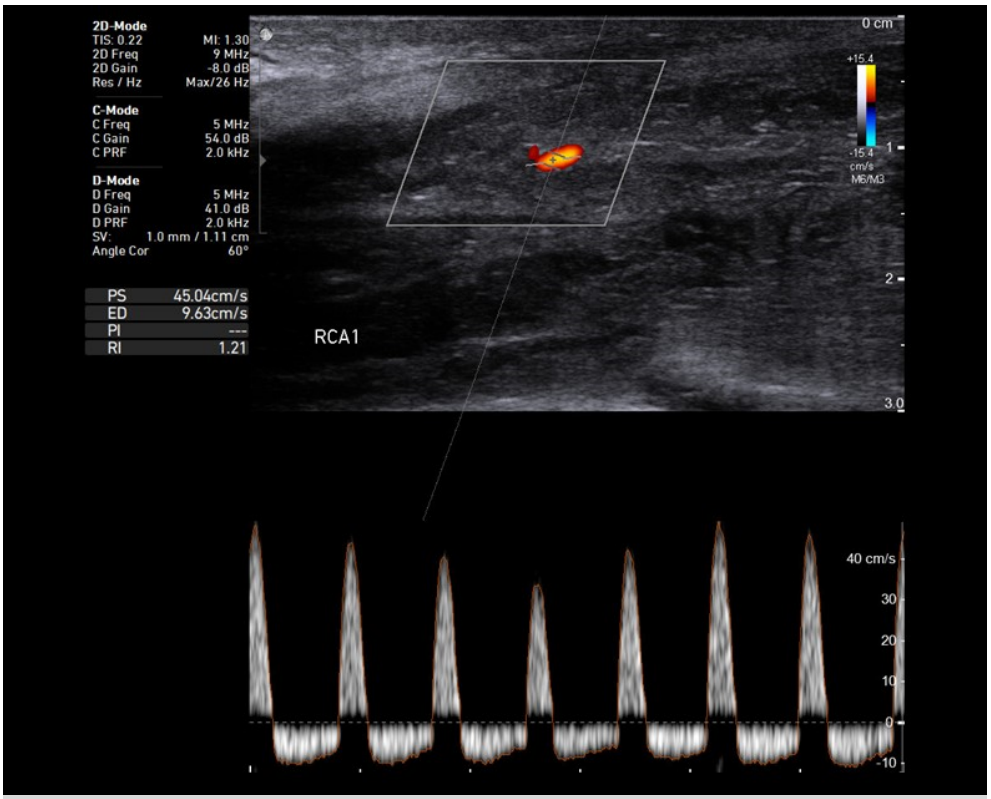

Figure 3: Normal penile hemodynamics. Note the presence of negative end-diastolic velocity secondary to retrograde blood flow with diastole.

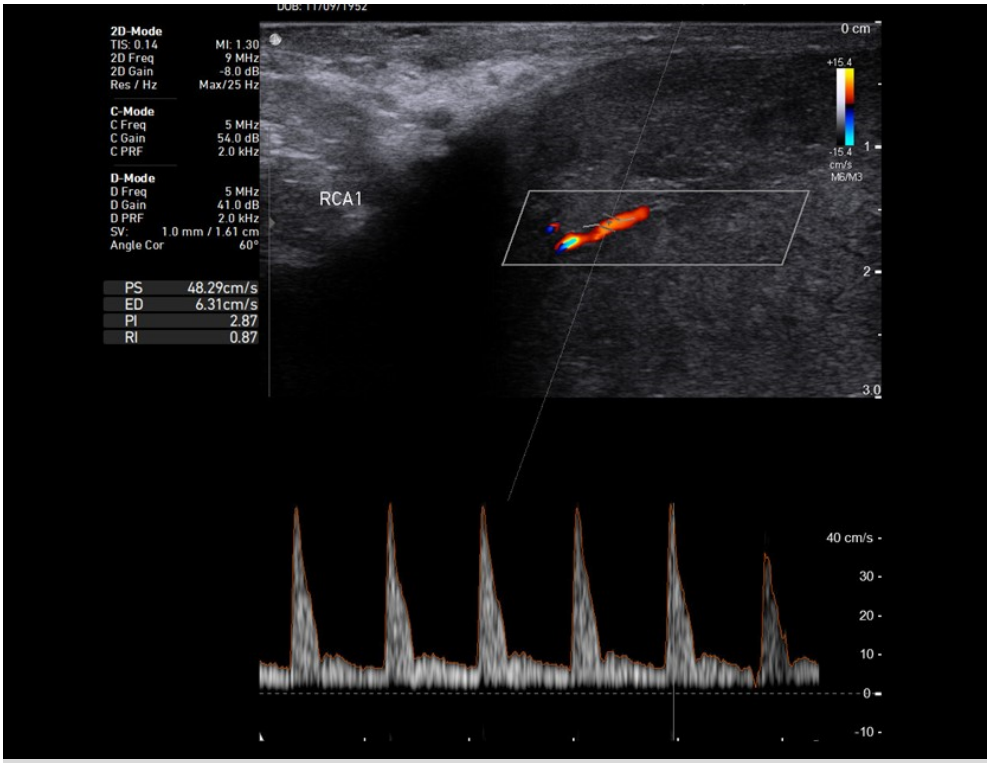

Figure 4: Venous Leak

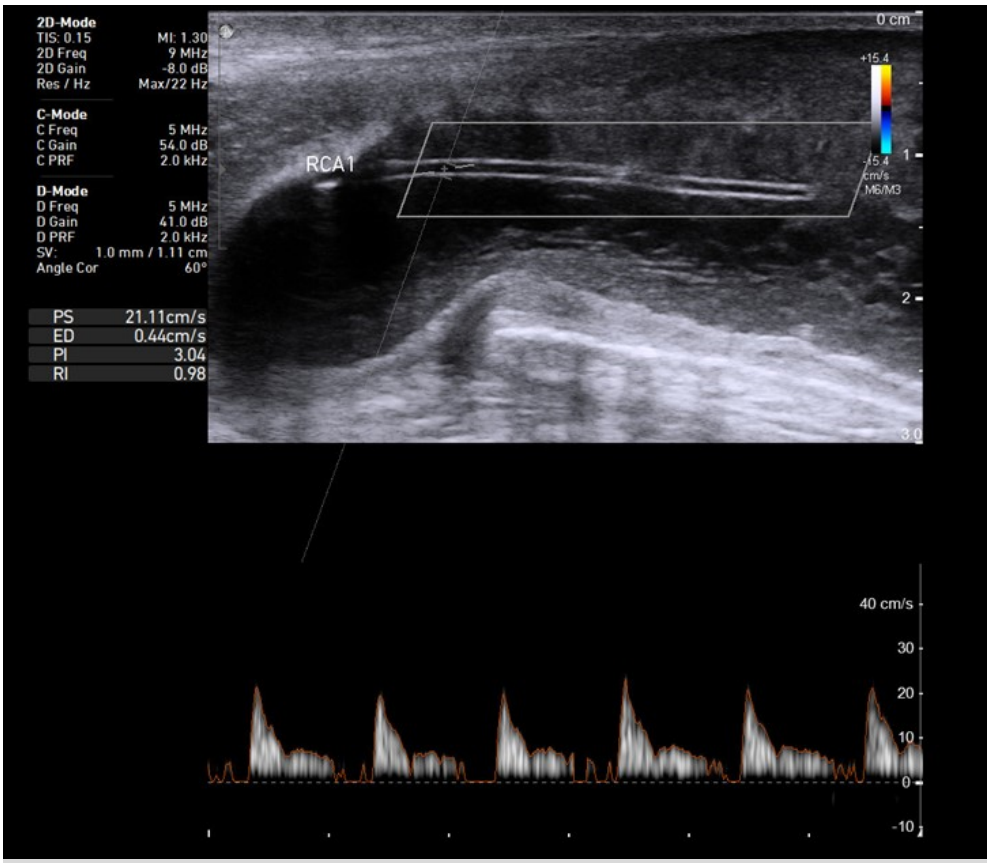

Figure 5: Arterial insufficiency

4.3.3 Cavernosometry/Cavernosography

The diagnosis of venocclusive dysfunction as the etiology of ED can be confirmed with cavernosometry and the site of “leakage” can be assessed through cavernosography. These are some of the most reliable tests for assessing for venous leak, but are infrequently performed in the modern era due to the increased invasiveness and limited utility with respect to treatment decision-making over DDUS and clinical history.[83] One suggested role is in young men undergoing evaluation for possible penile arterial reconstruction, in order to rule out venous leak prior to surgery. This test induces an artificial erection and measures the pressures within the corpora.

During cavernosometry, high dose vasoactive agents are injected into the penis through one of two intracorporal butterfly needles. **Equilibrium pressure** is that pressure achieved 10 minutes after injection of vasoactive agent. Equilibrium pressure > 60 mmHg is indicative of normal venocclusive function. Saline infusion is achieved using a pump. The amount of saline required to keep the intracorporal pressure at a fixed value is known as the **flow-to-maintain (FTM) value**. FTM > 3-5 mls/min is considered abnormal. **Arterial inflow gradients** (brachial artery systolic pressure - cavernosal artery pressure) is an assessment of arterial inflow. Arterial Inflow gradient values > 30 mmHg indicates arterial insufficiency. **Pressure decay** is measured when the intracorporal pressure is raised to 150 mmHg using the saline infusion pump. The pump is turned off and the drop in pressure over a 30 second period is recorded. This pressure decay is another indicator of venocclusive function. Pressure decay values > 45 mmHg/30 seconds is abnormal and suggests the presence of venous leak.[83]

Cavernosography, the infusion of contrast agent into the corporal bodies at an intracorporal pressure of 90 mmHg, is rarely used. It may be indicated to identify the venous outflow channels involved in patients with venous leak. **Figure 6** and **Figure 7** demonstrate a normal cavernosogram and one with florid diffuse venous leak, respectively.[83] Isolated crural leakage is a rare finding, present primarily in young men with lifelong ED. If such a discrete area of corporal leakage is identified, ligation of the crura has been shown in two small series to improve erectile function; care must be taken to avoid occlusion of the cavernous arteries in such a circumstance.[84,85,86] Since **current guidelines** recommend against penile venous surgery for men with ED, there is scant indication for cavernosography in contemporary practice.[1]

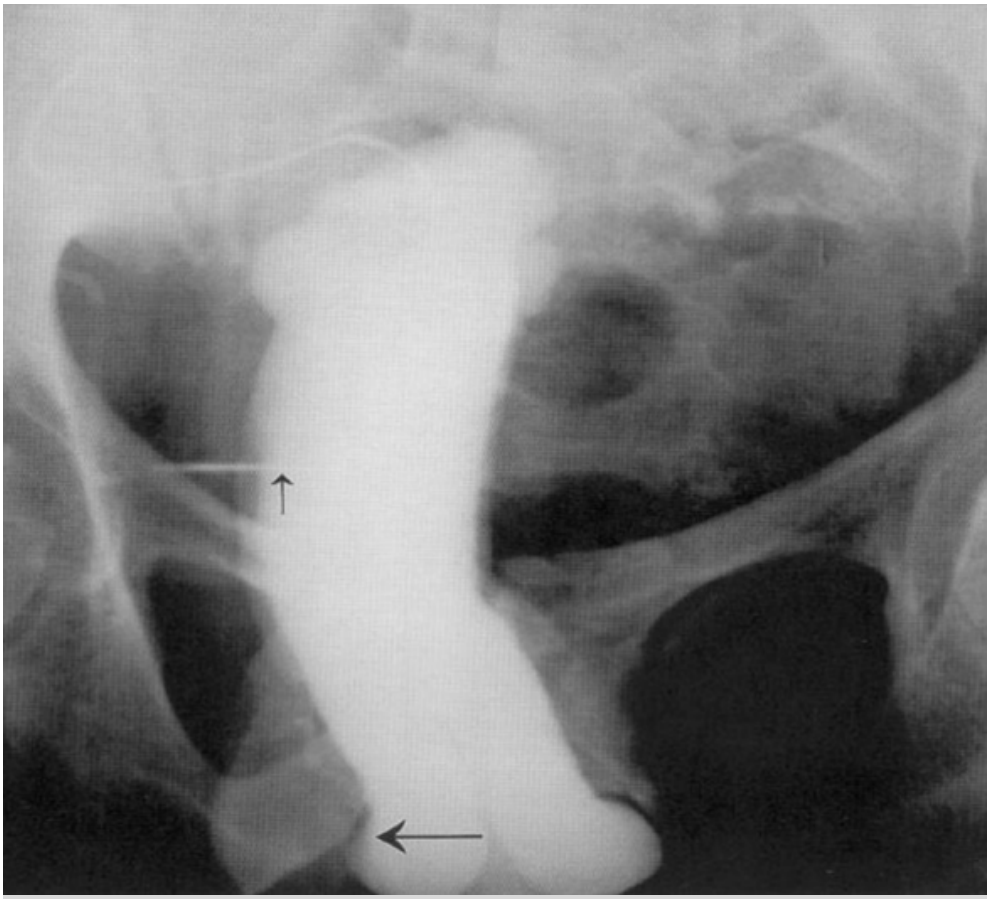

Figure 6: Normal Cavernosogram

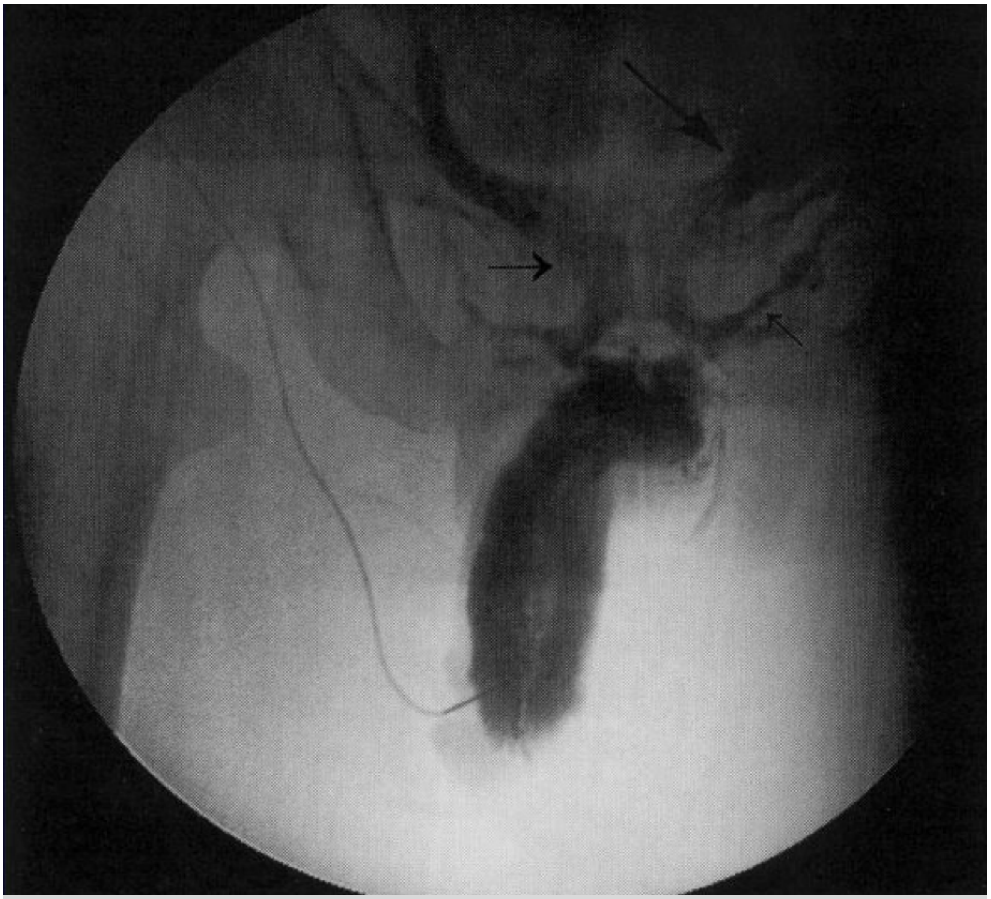

Figure 7: Florid Diffuse Venous Leak

4.3.4 Pudendal Angiography

Selective internal pudendal arteriography (SIPA) is an anatomic rather than functional study, indicated only in the setting of patients with suspected focal arterial insufficiency (diagnosed on DDUS), who are considering penile revascularization surgery.[73] In the modern era, this is limited to young men without venocclusive dysfunction or evidence of generalized vascular who may have vascular disruption related to pelvic trauma. [1] It is the most invasive diagnostic test for vasculogenic ED and it is not indicated in men who are not candidates for operative revascularization.[73] Arteriography is performed with the patient in the erect state. The test is technically challenging to perform and should be done only by an interventional radiologist experienced in SIPA.[87] Intra-arterial vasodilators should be administered to avoid arterial vasospasm. **Figure 8a** and **Figure 8b** represent a normal SIPA and stenotic cavernosal artery respectively.

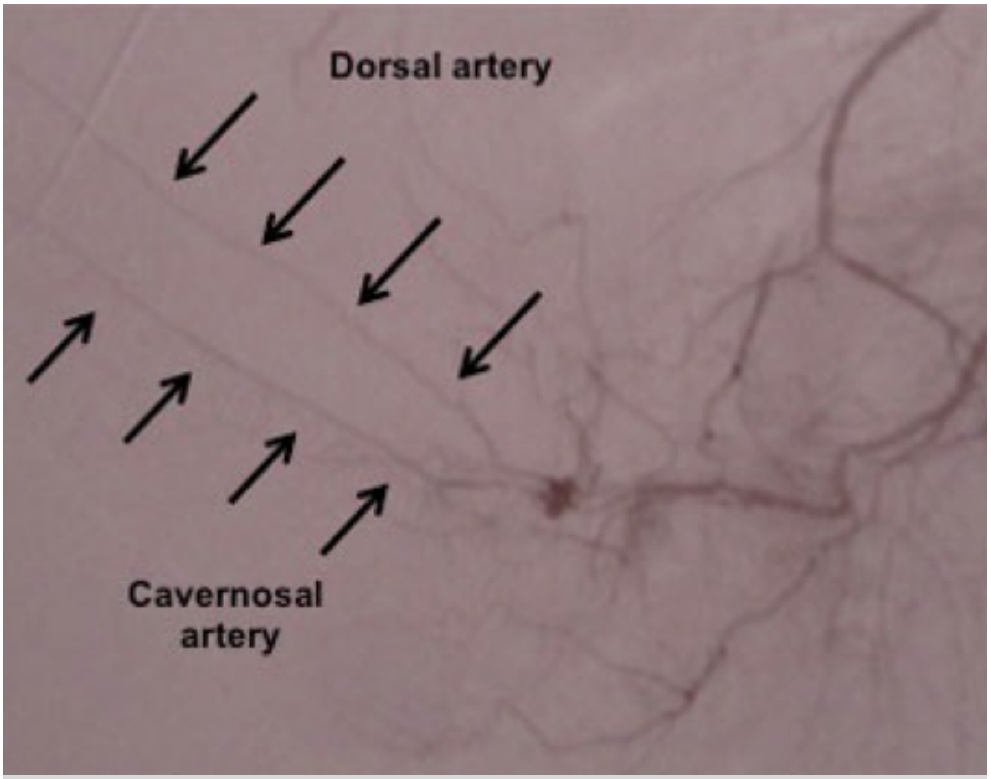

Figure 8a: Normal SIPA

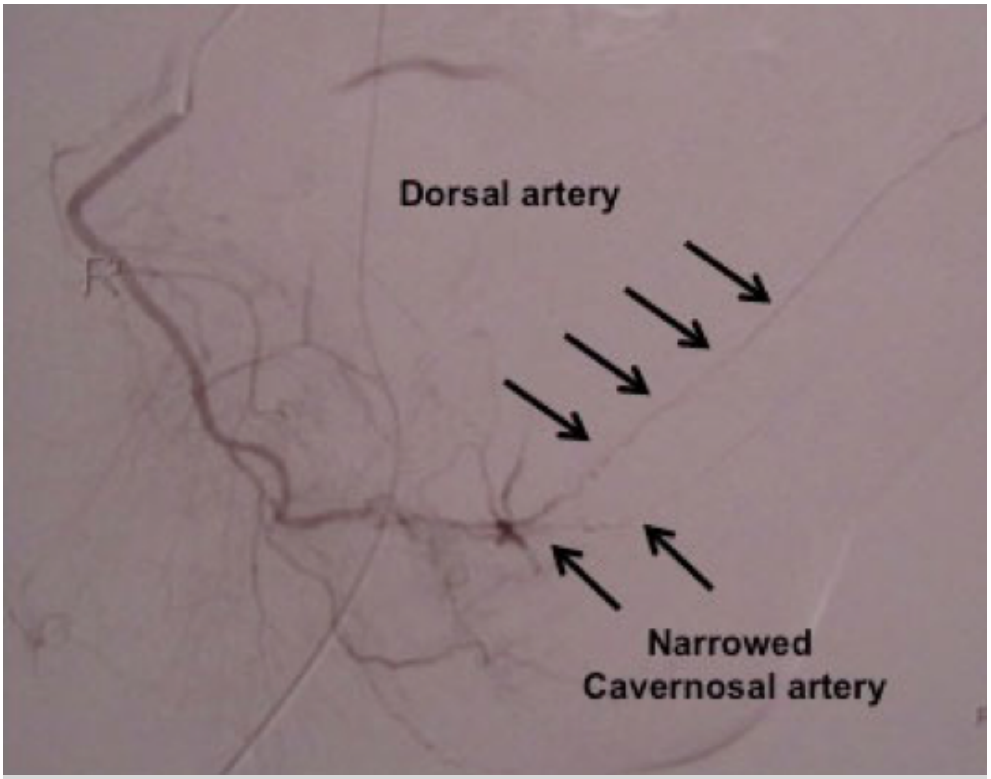

Figure 8b: Stenosed Cavernosal Artery

4.4 Miscellaneous Testing

4.4.1 Nocturnal Penile Tumescence and Rigidity (NPTR) Assessment

NPTR testing (commercially known as Rigiscan™) is based on assessment of nocturnal erections that occur in healthy men nightly during rapid eye movement (REM) associated sleep. The test involves placement of two strain gauges on the penile shaft (one at the base and other at mid-shaft). The strain gauges contract periodically and measure the radial rigidity of the penis at both locations. This device is used overnight (on 2-3 consecutive nights) and its purpose is to measure the number, rigidity, and duration of erections.[88]

NPTR has traditionally been used to differentiate psychogenic from organic ED.[89] Unfortunately, there is a high false negative rate (i.e. abnormal scan in men with normal erectile function). Many factors can impair nocturnal REM sleep (e.g. irregular sleep schedules, sleep apnea, restless leg syndrome, post-traumatic stress disorder, depression)[90] and hence disrupt erectile activity and NPTR analysis. The study is generally believed to be accurate only when it is completely normal (≥3 erections, ≥60% rigidity, ≥10-minute duration). When erections are completely absent, the possibility of complete neurogenic ED (severe diabetes, post-radical prostatectomy) or profound hypogonadism should also be considered.[91] A study of men with hypogonadism indicated that NPTR parameters (specifically erection frequency and duration) tend to improve with androgen replacement in appropriately selected men; this was associated with improvements in self-reported erectile function.[91] Most NPTR studies demonstrate some erectile activity but not enough to meet normal criteria. Thus, this test is of limited clinical utility.

4.4.2 Thermographic Imaging

Vascular flow has long been associated with temperature changes in the affected area. Because of the substantial change in vascular flow, there are reliably measured changes in surface temperature of the penis during arousal and erection.[92] For this reason, thermography has been used as marker for sexual arousal in research. Thermographic measurements have recently been investigated as a diagnostic tool for erectile dysfunction and showed a significant correlation with changes in PSV as measured on DUS. [93] The potential benefit of this technique is its ease of use as a 'point and shoot' device as compared to DUS which provides a wealth of data but is technically challenging. With further study this may prove to be a useful screening tool that can be performed by the general urologist to rule out arteriogenic erectile dysfunction. Currently the use of this for diagnostic purposes continues to be experimental and under investigation.

5. Conclusions

Contemporary evaluation of ED relies on a detailed history and physical examination. Adjunctive serum and laboratory studies may helpful in elucidating etiologies and comorbidities and may be helpful for counseling men with regards to treatment options. Advanced testing may have a role to play in some select cases.

Presentations

Erectile Dysfunction Patient Evaluation, Investigations Presentation 1

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