



A Review on Penile Doppler and Ultrasonography for Erectile Dysfunction

Kareem Elgendi¹ · Nicholas Zulia² · Jonathan Beilan² 

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Abstract

Purpose of Review Herein, we seek to review the clinical applications of penile duplex Doppler ultrasound (PDDU) in sexual medicine practices and discuss the indications, protocols, advantages, and limitations of this diagnostic modality. Other more outdated diagnostic tests, such as cavernosometry, are briefly discussed to provide the reader a background of understanding on the evolution of diagnostic testing within the realm of sexual medicine.

Recent Findings PDDU has become a key diagnostic tool in the clinical evaluation of both erectile dysfunction (ED) and Peyronie's disease (PD). With the assistance of intracavernosal injections such as alprostadil, clinicians can utilize ultrasound technology to produce a detailed description of the hemodynamics of the patient's erection cycle. This information plays a pivotal role in establishing an accurate diagnosis and creating a sensible management plan for the patient.

Summary This review aims to provide a better understanding regarding the technique and interpretation of PDDU as it pertains to male sexual function.

Keywords Erectile dysfunction · Peyronie's disease · Sexual function · Penile ultrasound · Duplex Doppler ultrasound · Clinical evaluation

Introduction

Erectile dysfunction (ED) is defined by the National Institute of Health as a condition regarding the inability to achieve an erection sufficient for satisfactory sexual activity [1]. The prevalence of ED is relatively common among men, particularly those over the age of 50, although estimates can vary widely. According to a 2019 review, the prevalence of erectile dysfunction globally ranges from 3 to 76.5% [2]. As the general population continues to grow, and average life expectancy increases, the incidence and prevalence of this condition similarly increases. Modern medicine has seen the development of several diagnostic methods which have been used to detect and ultimately treat ED.

The causes of erectile dysfunction are divided into multiple categories including psychogenic, anatomic, neurogenic, vasculogenic, and drug-induced. To properly diagnose and treat ED, a full medical history and physical exam are necessary. Among the various etiologies of ED, vascular pathology has gained a particular interest within the clinical field due to its high association with cardiovascular events (CVEs) and other comorbid conditions.

The first proposed method to diagnose vascular ED involved penile intracavernosal injection (ICI) with a vasoactive medication such as alprostadil [3]. The injection aims to induce an immediate erection by increasing arterial inflow and reducing venous outflow. In early studies, the length and circumference of the penis were measured after injection to determine if there was a vascular abnormality [3]. The use of ICI was a therapeutic approach for ED before oral PDE-5 inhibitors (PDE5i's) were introduced. However, since this method alone fails to detect the difference between arterial and venous ED, penile duplex Doppler ultrasound (PDDU) has become a popular adjunct to determine a more accurate diagnosis. This review focuses on the clinical applications of PDDU in diagnosing erectile dysfunction and Peyronie's disease (PD) and discusses recent studies regarding the advantages and limitations of this diagnostic modality.

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✉ Jonathan Beilan
Jonathan.Beilan@auhealth.com

¹ Nova Southeastern University College of Osteopathic Medicine, Fort Lauderdale, FL, USA

² Advanced Urology Institute, Largo, FL, USA

Clinical Evaluation/Patient History

Collecting a detailed past medical history is paramount in the initial clinical assessment of erectile dysfunction. Important variables within the past medical history include age, a history of smoking, diabetes, hypertension, obesity, dyslipidemia, coronary artery disease, and CVEs such as heart attack and stroke. Psychosocial history and a history of hypogonadism should also be elucidated [4•]. Further basic medical testing consists of a review of the patient's medication list, a focused physical exam, an analysis of contributing psychosocial factors, and subjective questionnaires. The 2018 AUA guidelines on ED recommend the use of validated questionnaires to assess and qualify the severity of ED, as well as provide a platform from which to discuss future management options (expert opinion) [4•]. Many patients will respond to initial conservative therapy such as lifestyle maneuvers or oral medications and may not require an additional medical workup; however, patients suffering from moderate to more severe ED often require a more in-depth workup. Severe erectile dysfunction may indicate an improper arterial and venous response to PDE5i's or other vasoactive medications. In such situations, PDDU can clarify the inadequate vascular response.

Standardized Questionnaires

There are multiple subjective questionnaires to help aid in the diagnosis of patients with erectile dysfunction. Two of the most commonly questionnaires in modern urology practices include the International Index of Erectile Function (IIEF-5) and the Sexual Health Inventory for Men (SHIM) [5–7]. IIEF-5 is a five qualitative-based questionnaire that places patients into five separate categories based on their cumulative score from 1 to 24: none (22–24), mild (17–21), moderate to mild (12–16), moderate (8–11), and severe (1–7). The more abbreviated version of the IIEF-5 is the SHIM, an effective diagnostic tool for patients experiencing ED. Moreover, higher scores are negatively correlated with the severity of erectile dysfunction. Other popular questionnaires include the Erection Hardness Score (EHS) and the Male Sexual Health Questionnaire (MSHQ) [8, 9]. As mentioned, per American Urological Association guidelines, all patients suffering from ED should undergo validated questionnaires to assess their ED [4•, 10].

Other Diagnostic Modalities

A more outdated model to evaluate erectile function is the nocturnal penile tumescence rigidity test, which bases erectile function on spontaneous/nocturnal erections at home.

Testing involves two loops, one at the distal aspect of the penis and one at the base. The pressure exerted on the penis by two opposing loops can gauge the rigidity of a patient's nocturnal erections. Typically, testing will occur over several consecutive nights for 8–10 h at a time [11]. Through separate contractions, the loops can measure the penile circumference and penile hardness. The circumference is measured in centimeters, and rigidity is measured in percentages relative to a standard hard-rubber cylinder [12]. In the past, nocturnal penile tumescence rigidity testing has been used to decipher between men suffering from psychogenic ED versus organic etiologies. The benchmark for psychogenic ED was a patient gaining 60% rigidity on the tip of his penis relative to a standard hard-rubber cylinder, lasting equal to or greater than 10 min [11]. The differentiation between psychogenic and organic ED relied upon the assumption that men with psychogenic ED preserve nocturnal erections. In recent years, this has been debunked, as the testing is susceptible to false negatives. Per AUA guidelines, it is also noted that testing may be less useful in men with impaired sleep schedules [4•].

Biothesiometry is a rapid in-office test introduced during the 1990s to assess erectile function. It measures the sensory capacity of mechanoreceptors by administering vibrations at a controlled and consistent intensity to a patient's penis. After being applied to multiple locations on the penile shaft, the minimal amount of vibration intensity is quantified and compared to other parts of the body. In comparing the two different body parts, a lower threshold detection of the penis implies intact peripheral nerves. This testing is considered faulty due to testers' inconsistent methodology, which has led to an inability to set a universal range for biothesiometry [13].

Another outdated method, cavernosometry, measures the pressure of cavernous bodies following ICI to diagnose venous occlusive disease. After an alprostadil injection through a contrast injection pump, a baseline pressure is measured until 150 mmHg is reached. The pump is later removed, and the pressure decrease is measured. Venous occlusion is diagnosed in a patient with a pressure decrease greater than 45 mmHg over 30 s [14]. Often, this was used in conjunction with cavernosography to detect the areas of venous leakage [15]. This practice has been discontinued due to the invasiveness and high expense. Often, the method induced a high degree of anxiety in patients leading to false negatives and inaccurate results. Current AUA guidelines do not recommend surgery on venous occlusive disease, and results concluded by this diagnostic method are not of significant clinical use [4•].

History of Doppler Testing in ED

The advancements in ultrasound (US) technology in the 1990s enabled the modern practice of penile Doppler ultrasound in urology and sexual medicine clinics across

the nation. PDDU has become a critical tool to help evaluate the organic causes for men whose erectile dysfunction does not respond to PDE5i's [16]. The introduction of the first PDE5i's in 1998 led to a paradigm shift with respect to the use of PDDU. Assuming no contra-indication exists, PDE5i's are typically considered first-line maneuvers for patients experiencing ED and are often used prior to considering Doppler testing [17]. It is noteworthy that as the survival rates of patients undergoing treatment (such as surgical resection or pelvic radiation) for prostate, bladder, and rectal cancer have improved, the clinical field of cancer survivorship has similarly grown. The need for post-operative ED treatments has become essential to improve the quality of life of these men, and their partners. Penile Dopplers have become a crucial tool to help patients better understand the nature of their erectile dysfunction and help clinicians find an appropriate therapy for their disease [16].

ED is one of the better-known side effects of radical prostatectomies and cystoprostatectomies. Although nerve-sparing techniques have become more advanced with robotic procedures, the nerve plexuses to the penis are often affected or can become removed in some instances. The cavernous nerve (CN) is the most prominent nerve that controls erectile function; the CN originates from the pelvic plexus and joins multiple arteriovenous branches to form the neurovascular bundle (NVB). The NVB is easily damaged during prostatectomies, and in many cases, some degree of cavernous nerve injury to bound to happen. Despite the promotion of cavernous nerve-sparing surgeries and the introduction of robotic-assisted radical prostatectomies, the rate of erectile dysfunction is estimated to be as high as 84.6% [18]. Up to 70% of radical prostatectomy patients have erectile dysfunction at the 12-month postoperative mark. Histopathology studies of post-surgical patients have shown that the cavernous bodies of the penis are severely fibrotic, exacerbating ED in the postoperative setting [19]. Furthermore, sexual dysfunction is a common side effect of deep pelvic surgery, such as abdominoperineal resection for rectal cancer patients. ED results directly from an anatomical or neural disruption or indirectly from either loss of continence or altered cosmesis [20].

Penile pathology, as detected by ultrasound, can help aid in the discovery of men who have silent coronary artery disease (CAD). ED is often an early indicator for patients with endothelial dysfunction and vascular disease. PDDUs have aided in the discovery of men needing further cardiac testing [16]. Patients with poor vascular response on ultrasound are more likely to have increased fasting lipids, serum glucose levels, BMI, homocysteine, and C-reactive protein, all of which are considered cardiovascular risk factors. Compared to men without ED, patients with ED showed more severe

CAD and higher mortality rates associated with cardiovascular disease [21, 22].

ED is also highly associated with DM. Worsening erectile function positively correlates to the duration of time a patient has suffered from DM. Patients are 7.2 times more likely to be diagnosed with ED when suffering from DM for > 35 years. More than 50% of patients with a < 10-year history of DM will experience ED. When patients suffer from DM for > 10 years, they have a 38-fold increase in the risk of suffering from ED [23•]. PDE5i's are typically the first-line treatment for patients, although it is shown that about 50% of patients with DM do not respond to oral therapies [24]. Patients diagnosed with ED and type II DM may have associated CAD that is undetectable by stress tests. Although patients may be asymptomatic, some experts advocate for these patients to undergo further cardiac testing [25].

Color Duplex Doppler Ultrasound

Aside from a thorough history and physical exam, color duplex Doppler ultrasound (CDDU), in combination with intracavernosal injection, is considered a first-line method for the diagnosis of vascular ED [3]. Initially, a gray-scale ultrasound is used on the penis to exclude any morphological or anatomic abnormalities. After an erection is induced, typically by administration of a prostaglandin-E1 analog, dynamic assessment can take place via CDDU. The cavernosal arteries are assessed at intervals of 5 min until PSV and EDV values are obtained [26••]. CDDU can detect penile blood flow and is used to isolate vascular from non-vascular ED, as well as identify the type of vasculogenic cause.

Although first line, CDDU has some limitations that must be accounted for. As with many advanced imaging techniques, CDDU is very operator-dependent and requires proficiency to receive accurate results. More importantly, it requires the smooth muscle to be completely relaxed for proper measurements, and anxiety or insufficient ICI dosing may hinder complete relaxation. These factors must be accounted for when evaluating a patient in the clinic setting—an “artificial” environment for sexual arousal. Additionally, the different anatomic locations assessed while using Doppler imaging can create variability in the results of the PSV and EDV. It has been shown that measurements of the PSV and EDV are variable depending on if it is measuring the proximal versus distal cavernous artery [3]. Regardless of these limitations, CDDU is still accepted as a useful diagnostic tool for vascular ED among most sexual medicine experts.

Erectile Dysfunction Pathologies and Vascular Assessments from Doppler

As mentioned, erectile dysfunction (ED) is a common medical condition with a high prevalence in men older than 40 years old. Multiple known etiologies, both physiological and psychological, can explain the cause of ED and aid in the diagnosis and treatment of this condition. Among these etiologies, organic ED, such as vasculogenic, hormonal, or neurogenic causes, are the most prevalent [3]. The association among ED and cardiovascular disease is relatively high, which has led to vasculogenic etiologies becoming a focused area of study in an effort prevent future cardiovascular events and improve patient outcomes [3]. These vascular causes include endothelial dysfunction, arterial insufficiency, venous leak, and mixed arterial and venous insufficiency (indeterminate). In order to isolate vascular from nonvascular causes of ED, PDDU has been proven to be an effective diagnostic tool to measure penile blood flow.

Arterial Insufficiency

Arterial insufficiency is any condition that stops or slows the inflow of blood to a particular organ. This can be secondary to peripheral vascular disease or other conditions, such as diabetes, chronic hypertension, or coronary artery disease. Atherosclerosis is an most important disease linked to arteriogenic ED [27••]. Peak systolic velocity (PSV) is a parameter measured by PDDU that is suggested for the diagnosis of arteriogenic ED. PSV, measured in cm/s, indicates the maximum flow rate in systole and how fast blood is reaching the penis during an erection [27••]. During PDDU measurements, normal PSV is > 30 cm/s and any value < 25 cm/s is indicative of arterial dysfunction. In addition, a difference of greater than 10 cm/s PSV between both cavernosal arteries on the right versus left sides suggest arteriogenic ED [26••]. This PSV threshold has been shown to be highly accurate (> 90%) in the diagnosis of arterial insufficiency [26••].

Venous Leak (Veno-occlusive Insufficiency)

Veno-occlusive insufficiency, commonly referred to as venous leak, is another vasculogenic cause of ED, resulting from insufficient penile blood retention during the erectile process. In a normal erectile state, the veins are compressed to prevent blood from escaping. In men with venous leak, there is insufficient sinusoidal relaxation and expansion leading to improper closure and compression of the veins [28]. Multiple causes of venous leak are known, such as congenital anomalies, Peyronie's disease, trauma, and arterial insufficiency [28]. Penile Doppler US can be used to help detect

venous leak leading to ED. The parameters used for venous leak are end diastolic velocity (EDV) and resistive index (RI); EDV is defined as the residual blood flow at the end of diastole, and RI is the peripheral resistance to blood flow [26••]. Normal EDV is < 5 cm/s and RI is > 0.9 cm/s. An EDV of > 5 cm/s and RI of < 0.8 cm/s is indicative of venous leak and inadequate blood retention in the penis [26••]. It is important to note that when detecting venous leak with PDDU, the presence of significant arterial insufficiency will create unreliable results since there is less blood reaching the penis to accurately measure EDV and RI [28]. In addition to PDDU, other techniques, such as dynamic infusion cavernosography and cavernosometry (DICC), have been used to identify veno-occlusive dysfunction; however, the poor specificity and invasiveness of these modalities have hindered their use [28].

Indeterminate Result

An indeterminate result or a mixed arterial and venous ED is seen when arterial inflow is normal, but there is still a poor erectile response. The use of penile Doppler ultrasound is inefficient in diagnosing indeterminate ED because venous competence cannot be measured in a patient with significant arterial insufficiency [29]. Outside factors such as ICI dose and patient comfort/anxiety levels can falsely create these borderline or indeterminate situations. This author's experience has found that adequate patient education and an accurate description of the testing protocols and has helped reduce the level of anxiety patients may have going into PDDU testing.

Peyronie's Disease

Peyronie's disease (PD) is a chronic fibrotic alteration of the penis characterized by fibrous plaques developing within the tunica albuginea, causing penile deformity and often a painful penile erection [30, 31]. Penile US can be a useful tool for diagnosis and surveillance of PD. On gray-scale US, plaques can be visualized as focal hyperechoic thickening of the tunica albuginea [26••]. Plaques may also be seen as hypoechoic lesions in the initial stages of PD as well or visualized within the penile septum if the plaque is more mature. An increased Doppler signal demonstrating hyperperfusion of the plaques may be indicative of inflammation surrounding this disease process [26••]. Clinicians can utilize this information, together with the patient's history and physical exam, to consider therapies such as oral non-steroidal anti-inflammatory medications for pain management [31].

Coding and Billing

Both private insurances and Medicare recognize the use of penile Doppler as an effective when diagnosing erectile dysfunction. The appropriate CPT code for PDDU is 93980 “Duplex scan of arterial inflow and venous outflow of penile vessels; complete study” [32]. Other associated codes, such as 54,234 “Penile Injection” can be found in Appendix 1.

An important concept for practitioners to understand is the credentialing necessary to ensure that not only has an adequate study been performed, but that the test will be billed, coded, and reimbursed appropriately. Per the Local Coverage Determination guidelines from the Centers for Medicare & Medicaid Services, “all non-invasive vascular diagnostic studies must be performed under at least one of the following settings: (1) performed by a physician who is competent in diagnostic vascular studies or under the general supervision of physicians who have demonstrated minimum entry level competency by being credentialed in vascular technology, or (2) performed by a technician who is certified in vascular technology, or (3) performed in facilities with laboratories accredited in vascular technology” [33]. Furthermore, “examples of appropriate personnel certification include, but are not limited to the Registered Physician in Vascular Interpretation (RPVI), Registered Vascular Technologist (RVT), the Registered Cardiovascular Technologist (RCVT), Registered Vascular Specialist (RVS), and the American Registry of Radiologic Technologists (ARRT) credentials in vascular sonography. Appropriate laboratory accreditation includes the American College of Radiology (ACR) Vascular Ultrasound Program, and the Intersocietal Commission for the Accreditation of Vascular Laboratories (ICAVL)” [33].

Regarding ED treatment options, Medicare and most private insurances are selective on what modalities may be covered. Presently, brand name PDE5i’s, including Viagra, Cialis, and Levitra, are often not covered by insurance providers. However, generic versions such as sildenafil, tadalafil, and vardenafil may be covered. The advancement of compounding pharmacies, and companies like GoodRx, has helped many patients save money on prescription PDE5i’s not covered by their insurance.

Other modalities such as vacuum erection devices (VED), intracavernosal injections (ICI), intraurethral suppositories, and low-intensity shock wave therapy (LiSWT) are not covered by insurance or Medicare. Patients wanting to use these modalities are subject to personal out-of-pocket costs. Finally, for end-stage erectile dysfunction, penile prosthesis surgery is considered the gold standard. Medicare and many private insurance plans typically cover this procedure; however, large disparities of coverage still exist [34].

Conclusion

Among the various diagnostic modalities used in the management of male sexual dysfunction, PDDU has proven to be an essential tool in the diagnosis and treatment of both ED and PD. In addition to intracavernosal drugs, PDDU plays an important role in identifying and illustrating vascular ED, as well as quantifying the hemodynamic patterns seen in penile erection response to vasoactive injections. Being familiar with the technique, limitations, and interpretation of PDDU is an important step toward an accurate diagnosis and determining the best management plan for the patient.

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Compliance with Ethical Standards

Conflict of Interest KE and NZ have no conflicts of interest to report. JB is a paid consultant to Boston Scientific Corporation, menMD, In., and Bastion Health. The authors received no financial benefit from the planning, implementation, writing, peer review, editing, and publication of this scientific work.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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