# Doppler Blood Flow Analysis of Erectile Function: Who, When, and How

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## OVERVIEW

Since the introduction of several effective oral treatments for erectile dysfunction (ED), primary care physicians and midlevel providers manage most patients wishing treatment of male sexual dysfunction. ED is defined as the consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual performance.[1] ED constitutes an evolving public health concern. Studies from the 1990s estimated that half of men older than 40 years had ED.[2] Public awareness, pharmaceutical marketing, and new areas of research, such as cancer survivorship, are also increasing. In aggregate, this research and awareness is increasing the demand for treatment to the primary provider. Failure or poor efficacy of first-line treatments often leads to specialty referral. Other reasons for specialty referral may be trauma, uncertainty of diagnoses, or simply, the wish of the patient or provider.

Broadly categorized, there are 3 types of ED: neurogenic, psychogenic, and vasculogenic. Neurogenic and psychogenic causes are discussed by Altof and Needle elsewhere in this issue. Vasculogenic causes can be arterial, venoocclusive, or some combination of the two. Vasculogenic ED may account for up to 60% to 80% of all cases reported.[3]

There has been considerable research into diagnostic techniques over the past few decades. Without invasive testing, the urologist was limited to inferences made from physical examination and patient-based questionnaires. More data were often required to make solid clinical and surgical decisions. This requirement of data prompted several different types of investigations. The first-line diagnostic test for vasculogenic ED has been combined intracavernous injection and stimulation (CIS) and direct assessment by an observer.[4] This test is used to bypass both neurologic and hormonal influences and allow the provider to directly evaluate the vascular status of the penis. A normal response from CIS is associated with appropriate venous occlusion. False-negative results are found in as many as 20% of patients with intermediate arterial inflow. False-positive result could also commonly occur.

If more testing is thought to be needed or an operative intervention is being considered, such as for Peyronie's disease or for pelvic trauma, a second-line study is warranted. The pharmaco-penile Doppler ultrasonography (PDDU) is a diagnostic modality useful in determining the subtype of vasculogenic ED as well as the magnitude of its severity. PDDU involves injecting a vasoactive penile stimulant followed by genital self-stimulation, audiovisual stimulation, or in some cases, repeat injection during which blood flow is assessed by color duplex Doppler ultrasonography. This procedure allows for both a direct and a quantifiable evaluation of ED. Ultrasonography is also able to provide information on the

underlying soft tissue abnormalities such as a Peyronie's plaque.

## PENILE ANATOMY

Three cylindrical structures, the corpus spongiosum, ventrally containing the urethra, and the paired corpora cavernosa, form the penis. The corpora cavernosa are covered by a 2-layer tunica with outer longitudinal fibers and inner circular fibers. There are also fibrous struts that help add support to the erect penis. The intracavernosal septum incompletely divides the 2 cylinders. Clinically, this anatomy is advantageous because only a single injection to the corporal body is required. The medication will circulate to the contralateral side. The tunica albuginea itself is also covered with a more superficial Buck fascia and a loose connective tissue and skin (**Fig. 1**). On ultrasonography, the corpora cavernosa appears hypoechoic and encased in a hyperechoic tunica.

Arterial supply to the penis is from the branches of the common penile artery, which is the direct continuation of the internal pudendal artery bilaterally. This artery branches into 3 named arteries. The cavernosal artery pierces the corporal body and travels in the center of the erectile tissue. These arteries are evaluated during the ultrasonographic study as discussed later. The bulbourethral artery enters the spongiosum superiorly and supplies the urethra, the spongiosum, and the glans penis. The third artery is the dorsal artery of the penis that courses between the dorsal vein and penile nerves. It gives off branches to the cavernous bodies and circumferential branches to the spongiosum. As with much of the pelvic vasculature, considerable variations have been found in the arterial supply to the penis.[5,6] On ultrasonography, the arteries can be found in several imaging planes and are easily seen as bright parallel lines because the arterial walls are hyperechoic (**Fig. 2**). The venous drainage of the corpora begin with the intersinusoidal and subtunical venous plexuses. This venous drainage continues to the emissary veins and then to larger channels such as the dorsal vein of the penis. The venous function in ED is described later.

## PHYSIOLOGY OF ERECTION

In a flaccid state, the subtunical and intersinusoidal veins freely flow to the emissary veins. The arterioles and sinusoids maintain a high resting tone, which limits the inflow into the corpora. When combined, these yield a flaccid penis. After appropriate neural stimulation, a cascade of neurotransmitters, such as nitric oxide, affect the vascular supply to the penis. This starts with relaxation of the smooth muscle in the cavernosal arteries and then proceeds to the sinusoids. This
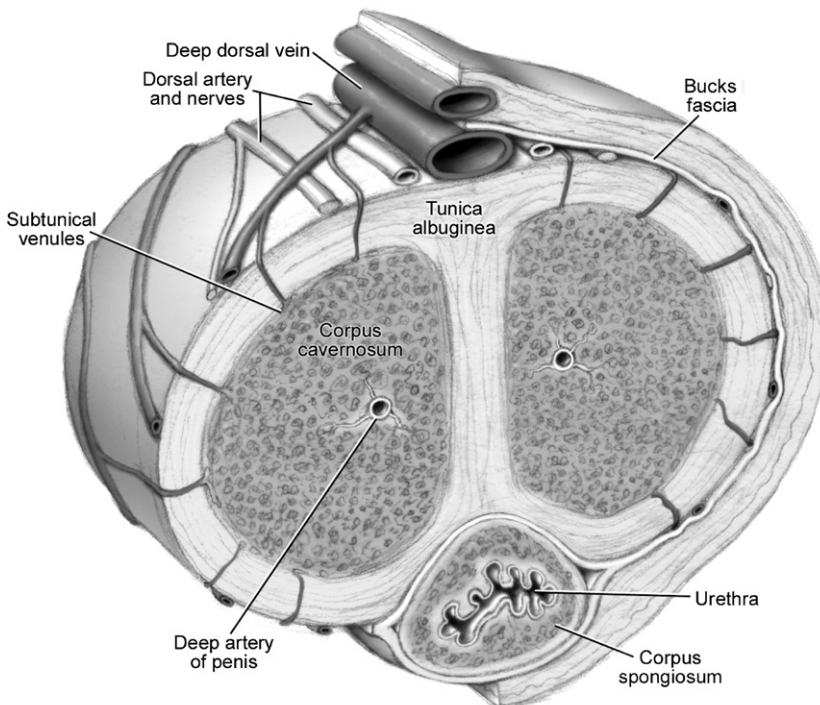


**Fig. 1.** Cross section of the penis demonstrating the visual anatomy noted on a typical study.
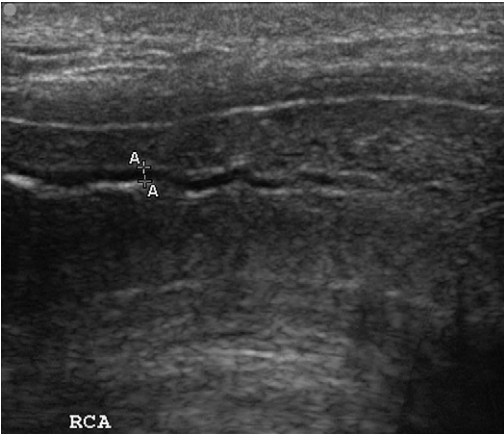
**Fig. 2.** A cavernous artery is seen in this sagittal ultrasonography. The appearance of the arterial walls is consistent with arthrosclerosis and/or calcification. RCA, right cavernous artery.

relaxation promotes a high inflow to the corporal bodies. Tumescence continues as the sinusoids fill with blood and begin to engorge. As the tunica elongates and expands, it begins to occlude the emissary veins between the inner circular and outer longitudinal layers described earlier. (**Fig. 3**) The occlusion propagates the erection because inflow is high and vascular outflow is at a minimum. Eventually, the intracorporal pressure increases to systemic levels and the inflow becomes reduced as well. Initially, the glans penis and corpora spongiosum react similarly in regard to flow. The major difference is the lack of tunical coverings and thus minimal venous occlusion. These structures continue to have high arterial inflow and function similar to an arteriovenous shunt. Just as tumescence proceeds step-wise, detumescence does so as well, with several separate stages proceeding according to penile pressure as the penis returns to its normal state.

## PATIENT SELECTION

As with most diagnostic interventions, the patient selection process begins only after a satisfactory evaluation has been performed. A full patient history should be obtained, including a medical, surgical, sexual, and psychosocial history. The use of a patient self-assessment such as the International Index of Erectile Function or the Sexual Health Inventory for Men is also helpful in the


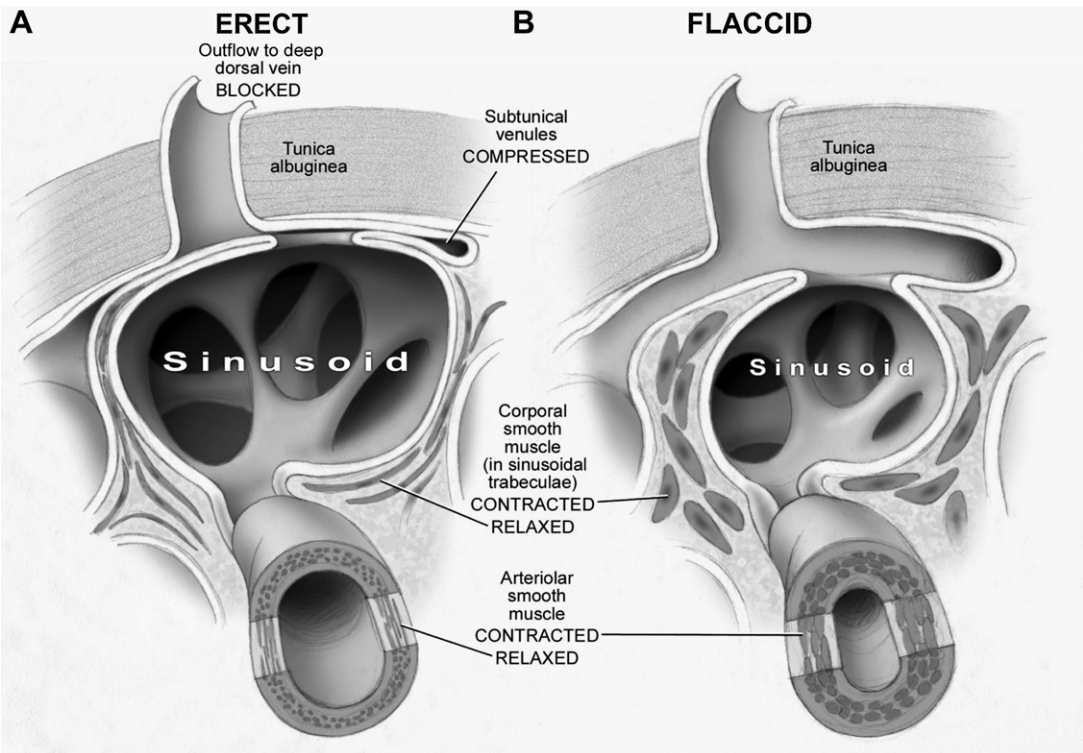
**Fig. 3.** Physiology of erection revealing the changes in the corporal smooth muscle and the accompanying vasculature. (*A*) The normal anatomy and physiology in the erect phallus, (*B*) the normal anatomy and physiology in the flaccid phallus.

standard evaluation. Given the considerable patient, and potentially even physician awkwardness of this type of interaction, the authors recommend an attitude of comfort and adaptability throughout the evaluation process.[7] Physical examination should include a broad screening for medical comorbid conditions relevant to ED, such as body habitus and blood pressure measurements. Urologic evaluation may reveal physical findings such as Peyronie's plaques, and neurologic evaluation may yield clues to neurogenic causes including presence of the bulbocavernosus reflex or peripheral neuropathy suggesting diabetes. Laboratory studies to identify or confirm a specific cause, such as hypogonadism, may be used as appropriate.

Many patients have an obvious and often severe cause of ED, such as Peyronie's disease, pelvic surgery, or metabolic syndrome. Another large subset of patients would have tried and failed oral treatments with phosphodiesterase 5 inhibitors. Further testing to confirm the cause is not mandatory for the urologist. First and foremost, the provider should review the medications tried and their doses to ensure that first-line trials have been appropriate. The provider may then pursue other empirical treatments such as intracavernosal injections, but the patient should have an option of undergoing more definitive studies. Some patients who have undergone CIS report that even though they had an appropriate response in the clinic, it does not correlate with their "home" experience. This report might be an indication of venous leak, and PDDU may be helpful to better understand the cause of the patient's ED.[4] Another indication for PDDU is operative planning. If, for example, the urologist is deciding between plaque excision and grafting and a penile implant for Peyronie's disease, a quantifiable examination of penile blood flow may provide the data needed for the decision.

## TECHNIQUE OF PENILE DOPPLER ULTRASONOGRAPHY

As with any invasive procedure, a proper informed consent should be undertaken with the patient outlining the purpose, alternatives, risks, and benefits of the testing process. The examination room should be comfortable, safe from intrusion and distraction. False-positive test results (a partial erection when there is no underlying vascular abnormality) may ensue secondary to patient anxiety, needle phobia, and/or inadequate medication dosage. Although penile sonography is noninvasive to the patient, intracavernous injections (ICI) have morbidity that both the examiner and patient should be informed of. It is reported

that 1 in 5 neurologically intact men complain of an ache in the penis after prostaglandin $E_1$ injections. Prolonged erection is another well-known risk and must be pharmacologically reversed with subsequent injections to avoid priapism and its subsequent morbidity. Equipment needed includes a 5/8-in needle (27–29 gauge) and syringe for injection and the vasoactive medication chosen by the examiner for the study. A high-resolution ultrasonographic probe (7–10 MHz) is able to perform real-time ultrasonography and color pulsed Doppler. This technique allows the examiner to evaluate penile blood flow changes throughout the various phases of erection. In color-coded duplex sonography, the direction of blood flow is designated with red (toward the probe) or blue (away from the probe), making the identification of the small cavernous vessels and recording of blood flow easier.[8,9]

Attempts have been made to lessen the invasiveness of PDDU by substituting an oral medication such as sildenafil for injectable medications. These studies did show an increase in the peak flow velocities that were comparable to those seen with ICI, but the time frame was considerably longer. Testing may begin in 1 to 20 minutes with injectables versus in 30 to 90 minutes after an oral medication.[10] Other similar studies found that oral medications did not provide as strong an efficacy or any response when compared with injectable medications.[11,12] Further complicating oral medications such as sildenafil is that often the patient selected for PDDU has already had poor efficacy with that treatment type.

An example protocol of study would include an injection of 10 μg of prostaglandin $E_1$ (alprostadil). Direct pressure may be applied to the injection site for 2 to 3 minutes to prevent hematoma formation. If the examiner suspects a robust response given the patient's history and physical examination, this dose may be decreased by half. If necessary, the dose may be escalated up to 20 μg. This is only one of several possible medication protocols that have been described. Other agents that have been used include papaverine (7.5–60 mg), papaverine with the addition of phentolamine (0.1–1 mg), and papaverine + phentolamine + alprostadil. Some protocols use redosing of alprostadil, 10 μg, + phentolamine, 1 mg, + papaverine, 30 mg, (Trimix) to help predict arterial dysfunction if the initial dose of alprostadil fails. This protocol has been shown to have a higher risk of prolonged erections and priapism (10% with Trimix vs 1% with alprostadil alone).[13] The initial flows should be measured 5 to 10 minutes after injection. Some investigators recommend measurements every 5 minutes for the first 20 to 30 minutes, but

this is often not practical in a busy practice. It is not unusual for the initial response time to be changed based on the patient's mental state and medical conditions. For example, a delayed response can be found in the hypertensive patient as well as the anxious patient. A rapid and robust response can be expected in the young man with psychogenic ED and patients with a neurogenic cause (including after prostatectomy and colorectal surgery). The examiner should record the erection hardness and correlate this with the PDDU measurements. A recent validated scale, the Erection Hardness Score (scale 1–4) can be used to standardize responses.[14] As first described by Donatucci and Lue,[4] the combination of injection plus manual self-stimulation leads to higher rates of rigid erections compared with injection alone. As such, the patient should be reexamined after self-stimulation. Other investigators suggest repeat pharmacostimulation as an adjuvant if self-stimulation is not preformed.[15] When there is full tumescence (or best achieved rigidity), gray-scale imaging for the presence of nonvascular abnormalities such as plaques and fibrosis should be performed and noted. Doppler evaluations should include samples at the penoscrotal junction for the evaluation of blood flow at intervals described earlier and any physical deformity noted (such as a Peyronie's plaque). Evaluating the blood flow at the base of the penis limits the effect of penile pressure on arterial inflow.[15] Both arteries should be evaluated in a typical study.

At then end of the testing period, it is important to ensure a complete detumescence. The patient should not leave the office until the penis returns to a normally flaccid state. This will sometimes require injecting a diluted phenylephrine (an $\alpha$-adrenergic agonist) solution of 200 $\mu$g /mL, given 1 mL every 3 to 5 minutes until detumescence. The patient should be monitored for symptoms such as acute hypertension, tachycardia, arrhythmias, and palpitations. Some providers choose to use a cardiac monitor during this process.

## NORMAL STUDY

The PDDU should be preformed as described earlier. Measurements and rigidity should be recorded. **Fig. 4** demonstrates the normal Doppler waveform of a PDDU over time. Initially, the penile flow is elevated, both systolic and diastolic, because of smooth muscle relaxation. As the penile pressure increases the diastolic flow decreases and eventually reverses direction. At peak pressures, the arterial flow is dampened and no diastolic flow is noted. There are several possible parameters that might be measured, but the most common ones are peak systolic velocity (PSV), arterial diameter, end-diastolic velocity (EDV), and resistive index (RI). These variables are described in context with the pathologic condition they best elucidate. Performing an evaluation as described earlier should allow the examiner to understand the cause of a vasculogenic ED, if present in the patient.

## ARTERIAL INSUFFICIENCY

Sufficient arterial inflow is of paramount importance to the study because without it, adequate



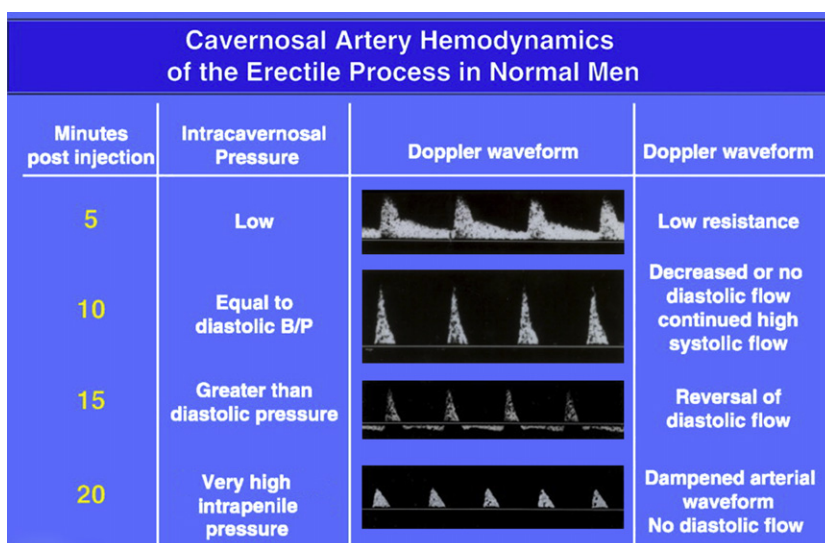| Minutes post injection | Intracavernosal Pressure | Doppler waveform | Doppler waveform |
|:---:|:---:|:---:|:---:|
| 5 | Low | | Low resistance |
| 10 | Equal to diastolic B/P | | Decreased or no diastolic flow continued high systolic flow |
| 15 | Greater than diastolic pressure | | Reversal of diastolic flow |
| 20 | Very high intrapenile pressure | | Dampened arterial waveform No diastolic flow |

**Fig. 4.** The normal Doppler waveform changes over time in the normal subject. As the penile pressure increases the waveform initially shows a diastolic flow. This then stops and even reverses direction. B/P, blood pressure.

erectile rigidity is unlikely to be obtained. Inflow is directly related to both arterial diameter as well as blood flow velocity. Whereas diameter can be useful, it is many variables such as location of examination (distal vs proximal), compression with the probe, and normal anatomic differences that make it difficult to use arterial inflow as the sole standard. The finding typically used is the PSV. PSV represents the highest recoded blood flow in the artery during systole. In the historical literature, in patients with abnormal pudendal arteriography, PSV less than 25 cm/s has a sensitivity of 100% and a specificity of 95%.[16] Severe unilateral cavernous arterial insufficiencies (AIs) are manifested by an asymmetry of PSV greater than 10 cm/s from the contralateral side. Many investigators conclude that a normal PSV should be greater than 35 cm/s. An example of a Doppler waveform of AI is shown in **Fig. 5**.

## VENOOCCLUSIVE DYSFUNCTION OR VENOUS LEAKAGE

The trapping of blood within the corpora cavernous limits the venous outflow and is necessary for tumescence to occur. Cavernous venous occlusive disease (CVOD) is defined as the inability to achieve and maintain adequate erections despite appropriate arterial inflow. On PDDU, if the Doppler waveform continues to manifest high systolic flows and persistent EDV greater than 5 to 7 cm/s, the patient is considered to have CVOD. As seen in **Fig. 4**, the only time one expects to see elevated diastolic flow is at the beginning of tumescence. A continually high EDV is typically evident in CVOD. EDV alone looses specificity for venous leakage if it is associated with AI.[17] As such,



**Fig. 6.** This PDDU shows sufficient arterial inflow at 51.4 cm/s poststimulation but an RI consistent with CVOD. A/B, points A & B; ACC, acceleration index; ET, elapsed time; RCA, right cavernous artery.

many investigators include another value that takes PSV into account. This value is the RI. The formula for RI is as follows:

$$RI = (PSV - EDV)/PSV$$

As the penile pressure equals or exceeds the diastolic pressure, the diastolic flow in the corpora approaches zero and the value for RI approaches 1. During tumescence as well as in partial erections, the diastolic flow remains and the RI value is less than 1.0. Naroda and colleagues[18] concluded that an RI of less than 0.75 predicts CVOD in nearly 95% of patients and that an RI greater than 0.9 to 1 is normal. RI is typically recorded at the 20-minute mark of the study. **Fig. 6** shows the typical waveform noted in CVOD.
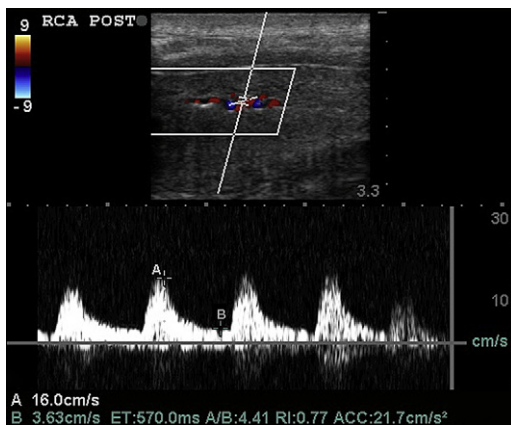


**Fig. 5.** PDDU showing a peak PSV of 16.0 cm/s poststimulation revealing that the patient has arterial insufficiency. A/B, points A & B; ACC, acceleration index; ET, elapsed time; RCA, right cavernous artery.
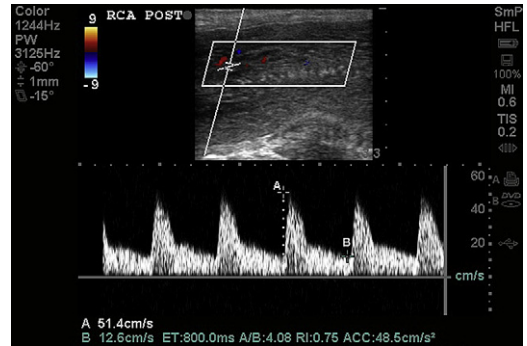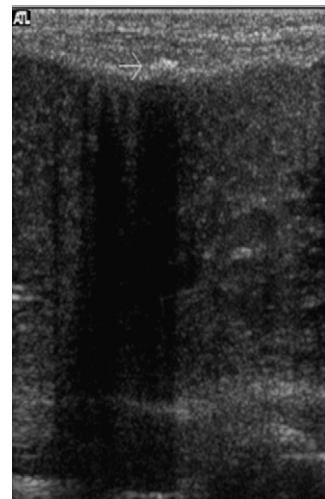


**Fig. 7.** Doppler ultrasonography of a Peyronie's plaque. The plaque often manifests as a hyperechoic to isoechoic finding with through shadowing.
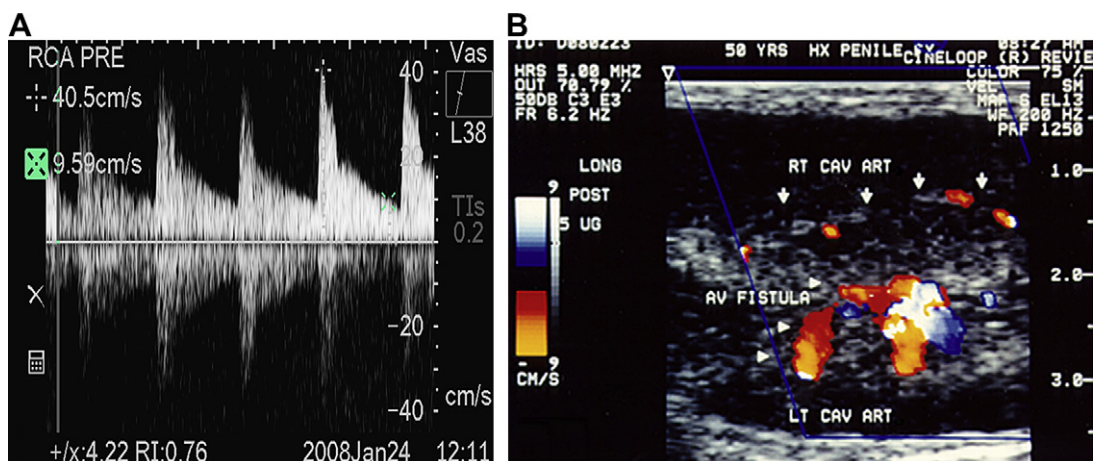
**Fig. 8.** PDDU of an arteriolar-sinusoidal fistula as is seen in nonischemic priapism. (*A*) PDDU waveform, note the elements of both a high PSV (in this study 40 cm/s) and elevated diastolic flow. (*B*) Color Doppler view over the fistula showing high flows of the left cavernous artery (LT CAV ART). RT CAV ART, right cavernous artery.

## COMBINED DISEASE

As expected, combined disease manifests features of both AI and CVOD. The extent of each component may not be as severe when present in combination. The typical findings include a lower PSV, greater than 25 cm/s but not higher than 35 cm/s. In addition to this finding, there will be evidence of CVOD. As discussed earlier, the specificity of EDV is blunted in the presence of low arterial inflow. Therefore, the authors use RI and expect to see a value less than 0.9 in a combined disease picture.

## PEYRONIE'S DISEASE

Peyronie's disease is a male sexual disorder that may be associated with ED and pain on erection. It is a condition of the tunica albuginea characterized by the formation of plaques of fibrous tissue that results in various severities of penile curvature. The authors do not recommend PDDU as a first-line evaluation of Peyronie's disease. A significant proportion of patients with this condition never require medical or surgical intervention. The discussion of the cause and medical/surgical interventions in Peyronie's disease is outside the scope of this discussion. However, if there is significant ED or severe curvature precluding sexual intercourse, the PDDU can be invaluable for surgical planning and patient counseling. Plaque length and characteristics can be readily demonstrated on Doppler ultrasonography. The PDDU is performed as described for the normal study. The pharmacologically produced erection also gives the examiner an idea of the severity and direction of penile curvature during tumescence. These plaques often manifest as hyperechoic or isoechoic lesions with through shadowing (**Fig. 7**). A careful examination of the patient's erectile quality is also paramount because it can determine if the patient is ultimately a candidate for a penile implant or one of the various incision/plication/grafting techniques available.

## PRIAPISM

Priapism is defined as a full or partial erection that continues more that 4 hours beyond sexual stimulation or is unrelated to sexual stimulation. The 2 broad categories are ischemic (low flow, venocclusive) and nonischemic (high flow, arterial) priapism. The dysregulated arterial inflows with or without a fistula can best be distinguished from a persistent ischemic priapism with PDDU. In the setting of priapism, no injectable medications should be used as part of the study. Doppler examination should include the cavernosal arteries from the base of the corpora (ie, below the penoscrotal junction) proceeding distally in an attempt to find a potential fistula. On PDDU, an ischemic priapism simply shows no or very minimal arterial flow through the corpora. In high flow priapism, the examiner often finds a high PSV consistent with increased arterial inflow. There is often a high diastolic flow accompanying this observation if examining the arteriolar-sinusoidal fistula (**Fig. 8**).

## SUMMARY

In the appropriately selected patient, PDDU can be extremely valuable to the urology practitioner. Use of PDDU does require an understanding of the

relevant penile anatomy and physiology of erection as well as their clinical correlations to ED. It also requires that the practitioner have access to the Doppler equipment and pharmacotherapy for injection. Following the steps outlined in this article to perform the study, and by applying the basic understanding of the main vascular causes of ED, PDDU can be used to diagnose and guide the patient and practitioner to the best treatment options.

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