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Non-invasive vascular imaging for erectile dysfunction

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ABSTRACT. In the era of orally active agents the clinical context of the diagnosis and treatment of erectile dysfunction (ED) has radically changed. There is a general trend oriented towards choosing invasive diagnostic testing and surgical treatment solutions. Along this view, penile pharmacotesting (PPT) may represent a inexpensive and easy diagnostic procedure to be performed in the office setting. However, this procedure provides no direct vascular imaging, has a high percentage of false diagnoses and its accuracy for subsequent treatment decisions remains quite limited. Hence, home testing with orally active agents may provide better information for the patient's goals. In the diagnostic work-up of ED, the combination of PPT plus colour-duplex Doppler ultrasonography (CDDU) has gained more credit because of a higher diagnostic accuracy than PPT alone, so that it should be always performed when possible. It represents an accurate mean to predict cavernous artery inflow and venous leakage when compared to more invasive diagnostic techniques; in fact it allows the measurement of the resistive index when maximal response to vasodilator challenge has occurred. In conclusion, we recommend CDDU to all ED patients with a significant risk of cardiovascular disease, as well as in the presence of penile plaques whereas a frequent involvement of neuro-anatomical structures occurs. Other vascular testing - *i.e.* natural penile tumescence, cavernosometry/graphy, angiography are reserved to selected patients in whom CDDU alone has provided inconsistent information.

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INTRODUCTION

Numerous diagnostic tests have been employed to evaluate penile blood flow: these include plethysmography, penile blood pressures, penile/brachial pressure index, penile pharmaco-angiography, duplex Doppler sonography, dynamic infusion cavernosometry/graphy, nuclear washout radiography, color duplex doppler ultrasonography (CDDU), penile near-infrared spectrophotometry and magnetic resonance angiography. In the late 90's, penile pharmacotesting (PPT) was the most commonly used diagnostic approach for erectile dysfunction (ED) for a long time. It was simple, minimally invasive, and performed without equipment. It consisted of intracavernous injection of vasoactive drug/s and visual rating of erection. The choice of the vasoactive agent is important. A variety of intracavernous drugs can induce erection, but the two most common agents are alprostadil (PGE^1) or papaverine. Phentolamine can be used in conjunction with these agents allowing a reduction in the dose of stimulant required and in the potential penile ache that was sometimes associated with PGE^1 use (1). If a sustained and rigid erection is achieved within 10 minutes of injection, venous and arterial insufficiency are unlikely to happen. Men with moderate to severe venous insufficiency will have difficulty in achieving a pharmacological erection. The failure of corporeal smooth muscle to fully relax after a dose-test (negative response) may be frequently determined by the presence of stress-induced changes related to the procedure (2), so that a combination of vasoactive agents is often required. If a full erection is not seen, or if the erection lasts only a short period, the patient is asked to stimulate himself in an attempt at improving the response (3). Again, if a good quality sustained erection is achieved, then a severe arterial or venous insufficiency is unlikely (4).

Key-words: Penile pharmacotesting, duplex ultrasound, cavernous artery, venous leakage.

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PENILE BLOOD FLOW IMAGING

In the new millennium, CDDU after intracavernous injection with vasoactive drugs is an important tool to evaluate vasculogenic impotence. Penile blood flow

studies with CDDU have been found to be more specific and accurate, correlate well with dynamic infusion cavernosometry/graphy results and allow a diagnostic categorization of impotent patients (5). By using CDDU, it has been demonstrated that a positive injection test is not necessarily associated with a normal arterial function (4). Also, it has been suggested that, despite the presence of an erection valid for intromission after injection test, veno-occlusive dysfunction may be present due to either compensated borderline arterial inflow or microcirculation integrity as showed by power Doppler studies. Based on the results of this studies, patients requiring more invasive testing can be selected.

CDDU is performed by high-frequency linear array transducers (7.5-13 MHz) which produces the best images of the penis and emits an ultrasound pulse that is then returned. When the returning echo has a different frequency to that emitted, a Doppler shift has occurred. The blood flowing in a vessel that is approaching the transducer will produce echoes of a higher frequency than those that were emitted; blood flowing away produces a lower frequency. As blood flow velocities increase, the Doppler shift, displayed as a 2-dimensional color image, increases. The angle between the Doppler beam and blood vessel is important, and attention should be made to maintaining the same angle in multiple recordings (usually between 50 and 60). For example, arterial velocity in the same vessel will be calculated as 20 cm/sec, 25 cm/sec or 203 cm/sec as the probe-vessel angle changes from 30 to 45 to 85 (6). The test itself should be conducted in comfortable, calm and private surroundings in order to alleviate anxiety and to allow cavernous smooth muscle tone relaxation. The penis can be scanned by a dorsal or ventral approach at the base, with the probe held transversally or in an oblique-longitudinal position. The dorsal arteries are not scanned since they are not subject to intracorporal pressure changes at each progressive erection phase; therefore, even in well-sustained rigidity, antegrade diastolic flow persists. The velocity of blood should be recorded at the peno-scrotal junction in the cavernous artery during systolic and diastolic phases within 5-10 minutes of injection (alprostadil 10 μg) and repeated frequently until a stepwise evaluation of the entire erectile cycle has been accomplished (usually for 20 minutes) (Table 1).

Table 1 - *Reference values (mean of two determinations for each corpora) for Color Duplex Doppler Ultrasonography studies.*

Peak systolic velocity	>30 cm/sec
Systolic rise time	<110 cm/sec
End diastolic velocity	<5 cm/sec
Resistive Index (RI= PSV-EDV/PSV)	>0.85

EDV: End Diastolic Velocity, PSV: Peak Systolic Velocity

If full erection is not achieved after a period of privacy and self-stimulation, a second injection (alprostadil 10 μg) should be given in order to achieve the best erection for the patient. A low resistance tissue bed, as in the relaxed cavernosal sinusoids in early erection, will allow forward flow with high diastolic velocity. A high resistance bed, such as the engorged sinusoids of the erect penis or tonic cavernosal sinusoids in the flaccid penis, will only allow flow during the high pressure systolic portion of the cardiac cycle. During diastole, the pressure will be insufficient to overcome the peripheral vascular resistance and the diastolic flow (and velocity) will be low (6). The patterns produced by a normal patient and a patient with arteriogenic ED are shown in Figure 1. The vascular

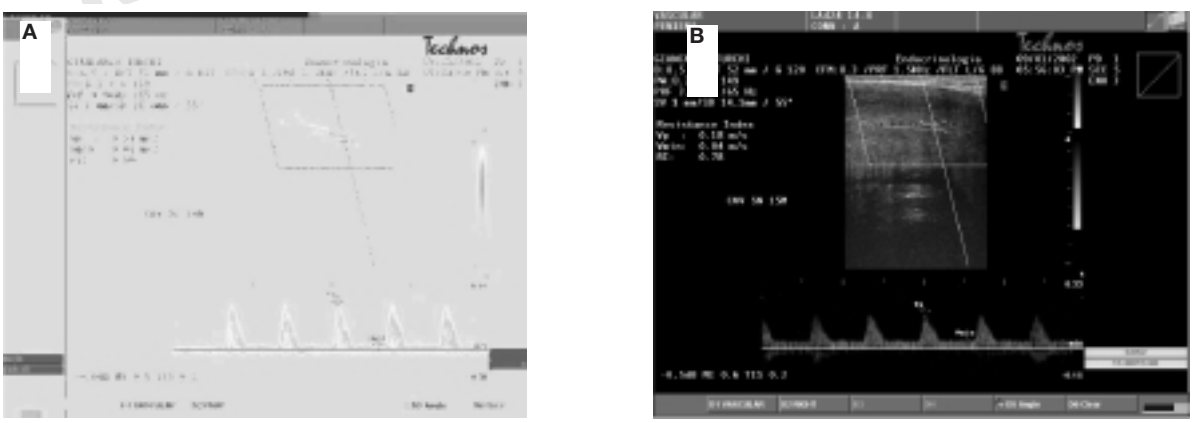

Fig. 1 - *Results of CDDU imaging. A) Normal response; B) attenuated response.*

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response in a normal patient shows high systolic peaks and negative or near zero diastolic pressure troughs. By comparison, the patient with ED presents with low systolic and/or positive diastolic pressure.
Characteristic patterns can be produced for different vascular-related EDs, such as:
- failure of initiation (inadequate cavernosal smooth muscle relaxation);
- failure of inflow augmentation;
- defective veno-occlusion.

With failure of sinusoidal relaxation, there will be no velocity increase. With insufficient cavernosal artery flow, the sinusoids fail to become engorged and the venous occlusive mechanism is not activated. Hence, the wave pattern shows low systolic velocity and elevated diastolic velocity. In comparison, with defective veno-occlusion, both systolic and diastolic velocities will remain high. It should be noted, however, that patients with minimal organic ED do not always show low systolic and high diastolic pressure. Gradations of the two are common and the test cannot be reliably used to discriminate these patient types (6).
In the next future, non-invasive vascular testing are recommended in all impotent men presenting with vascular risk factors, especially in those not responding to first-line orally active drugs and seeking for an explanation to why these agents failed in their cases.

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