

Sexual Dysfunction and Infertility

Preoperative Corporal Biopsy as a Predictor of Postoperative Results in Venocclusive Erectile Dysfunction

Mohammadreza Nikoobakht,* Ali Saraji, Alimohammad Meysamie

Urology Research Center, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

Introduction: Our aim was to investigate the association of corporeal cavernosal pathology with venocclusive erectile dysfunction (ED) and whether preoperative corporeal biopsy can help predict postoperative results.

Materials and Methods: Thirty-six patients with venocclusive ED underwent corporeal cavernosal biopsy and venous ligation. Preoperative assessment included complete physical examination, international index of erectile dysfunction (IIEF) scoring, nocturnal penile tumescence, penile Doppler ultrasonography, cavernosography, and, if needed, cavernosometry. Three months postoperatively, all patient parameters were reevaluated and compared with the preoperative results. Biopsy results of 43 patients with penile fracture were used for controls.

Results: The mean age of the patients with ED was 32.1 ± 8.6 years. The IIEF score and peak systolic velocity of the cavernosal artery in the patients did not differ postoperatively. The mean end diastolic velocity, however, decreased from 11.0 cm/s to 5.1 cm/s ($P = .023$). Only 2 patients had satisfactory penile rigidity after venous ligation. Pathologically, 23 patients had a slight decrease of cavernosal smooth muscle cells, while in 9 patients, the cavernosal smooth muscles were markedly decreased and replaced by collagen fibers. Four patients had normal histologies, and all responded either partially or completely to surgical therapy. In the control group, 41 of 43 patients had normal histologies, and 2 had a slight decrease of smooth muscle cell mass.

Conclusion: Decreased cavernosal smooth muscle mass may impair erectile function. Its association with venocclusive ED may be a poor prognostic factor of the outcome of surgical therapy. For the preoperative evaluation of patients, we propose cavernosal biopsy.

KEY WORDS: erectile dysfunction, venous leakage, biopsy, smooth muscles

Introduction

Erectile dysfunction (ED) is a common medical problem in men that can destroy the family bonds if neglected or improperly managed. By

Received December 2004

Accepted May 2005

**Corresponding author: Urology Research Center,
Sina Hospital, Hassanabad Sq, Tehran 19953 45432
Tel: ++98 21 66701041-9, Fax: ++98 21 66717447
E-mail: nikoobakht_m@hotmail.com*

definition, ED is the inability to establish enough penile rigidity for acceptable intercourse, or an inability to maintain full penile rigidity enough for complete intercourse. Generally, the etiology of ED can be either organic or psychogenic; most EDs are organic, which is more common in older men. Vasculogenic causes are the most common form of organic ED. Venocclusive dysfunction (venous leakage) is an important form of

vasculogenic ED. Different surgical procedures are used to manage venoocclusive ED, including dorsal and circumflex penile vein ligation or rearterialization, unfortunately however, they have high postoperative failure rates. In the current study, we compared the preoperative corporeal pathology with the postoperative outcome in patients with venoocclusive ED after venous ligation and with patients without ED.

Materials and Methods

Between 1996 and 2003, 36 patients presented with venoocclusive ED to our andrology clinic. None had comorbid diseases (hypertension, diabetes mellitus, or neurologic disorders). Their histories were negative for previous urogenital trauma, urogenital surgery, and medical treatment. Preoperative assessment included complete physical examination, international index of erectile dysfunction (IIEF) scoring, hormonal study (follicle-stimulating hormone, luteinizing hormone, prolactin, and testosterone), biochemical tests (fasting plasma glucose and serum urea, creatinine, triglyceride, and cholesterol), nocturnal penile tumescence, penile Doppler ultrasonography, cavernosography, and, if needed, cavernosometry. Informed consent was obtained from all patients. All patients underwent circumflex, superficial, and deep dorsal vein ligation. At the same time, intraoperative cavernosal wedge biopsies were taken for pathologic examination. At 3 and 12 months after surgery, all patients were reevaluated, and the clinical results were compared with the pathological findings. Biopsy results from 43 patients with penile fracture were used as controls.

Histologic slides were prepared using hematoxylin-eosin and trichrome staining for each specimen. One pathologist, blinded to the study objectives, reviewed all slides in 3 sessions. The degree of smooth muscle reduction was graded as *slight reduction* or *marked reduction*; the latter was accompanied by replacement with collagen fibers.

Data analyses were performed using SPSS software (Statistical Package for the Social Sciences, version 11.5, SSPS Inc, Chicago, Ill, USA), with chi-square test, Kolmogorov-Smirnov test, paired *t* test, and Wilcoxon signed rank test, as appropriate. Values for *P* less than .05 were considered statistically significant.

Results

The demographic and clinical characteristics of the patients with venoocclusive ED are shown in Table 1. In all of the patients, venous leakage was clearly demonstrated by cavernosography, before ligation. Postoperatively, the mean IIEF and peak systolic velocity (PSV) of the cavernosal artery did not differ significantly (Table 1). The mean end diastolic velocity (EDV), however, decreased from 11.0 cm/s to 5.1 cm/s (*P* = .023). In 7 patients, the EDV was more than 7 cm/s, and cavernosography demonstrated venous leakage. Twelve months after surgery, no venous leakage was demonstrated by cavernosography.

Clinically, only 2 patients recovered full penile erection (at 3 months' follow-up), while 2 other patients required intracorporeal injection of prostaglandin E1, and 1 required sildenafil administration to recover penile rigidity.

Figures 1 through 4 show the changes in smooth muscle mass in a patient with ED and the normal pathologies in a patient in the control group. Pathologically, 23 patients showed slight decreases in cavernosal smooth muscle mass, while in 9 patients, the cavernosal smooth muscles were completely replaced with collagen

TABLE 1. Demographic characteristics and pre- and postoperative parameters in patients with venoocclusive ED

Number of patients	36	
Mean age (years)	32.1 ± 8.6	
Mean follow-up (months)	49.0 ± 24.1	
Preoperative assessments		
IIEF	11.0 ± 3.1	
PSV (cm/s)	38.0 ± 3.2	
EDV (cm/s)	11.0 ± 2.6	
Postoperative assessments (3 months)		
IIEF	10.9 ± 2.6	<i>P</i> = .31
PSV (cm/s)	39.2 ± 3.8	<i>P</i> = .30
EDV (cm/s)	5.1 ± 2.4	<i>P</i> = .023
Outcome		
Full erection	2 (3.4%)	
Erection with intracorporeal injection.	2 (3.4%)	
Erection with sildenafil	1 (2.7%)	

IIEF: international index of erectile dysfunction, PSV: peak systolic velocity of the cavernosal artery, EDV: end diastolic velocity of the cavernosal artery

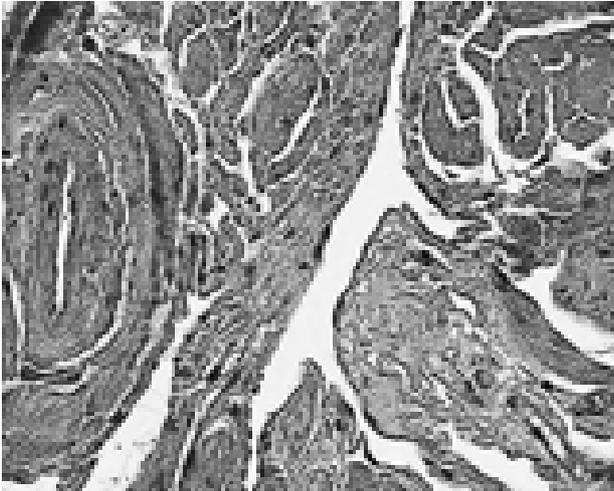


FIG. 1. Normal cavernosal histology of a young man with penile fracture (hematoxylin-eosin $\times 40$)

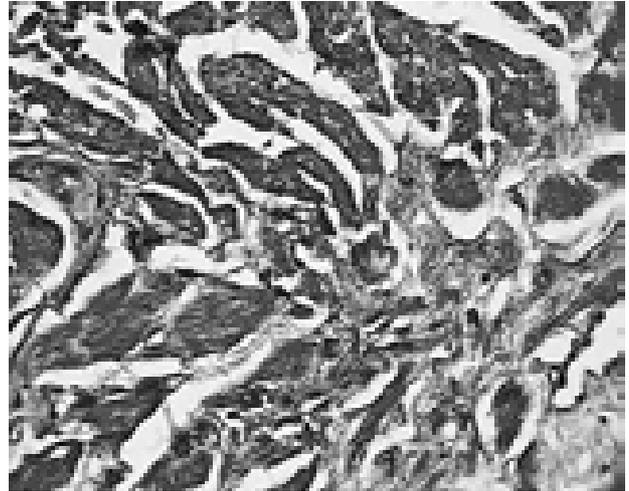


FIG. 3. Trichrome staining of a normal cavernosal specimen of a patient with penile fracture ($\times 40$)

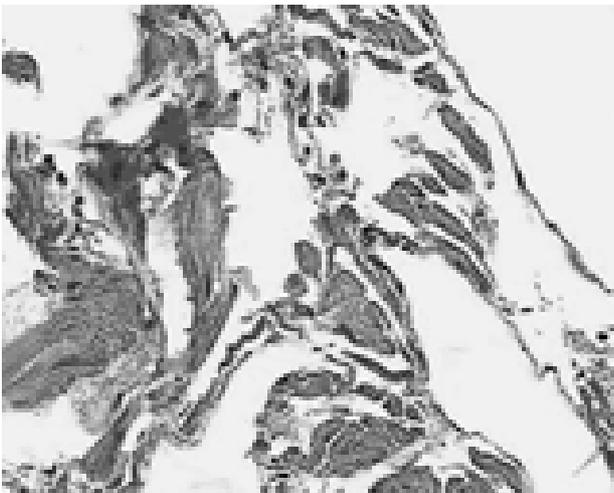


FIG. 2. Cavernosal pathology of an impotent man with venooclusive ED showing a significant decrease of smooth muscle fibers (hematoxylin-eosin, $\times 40$)

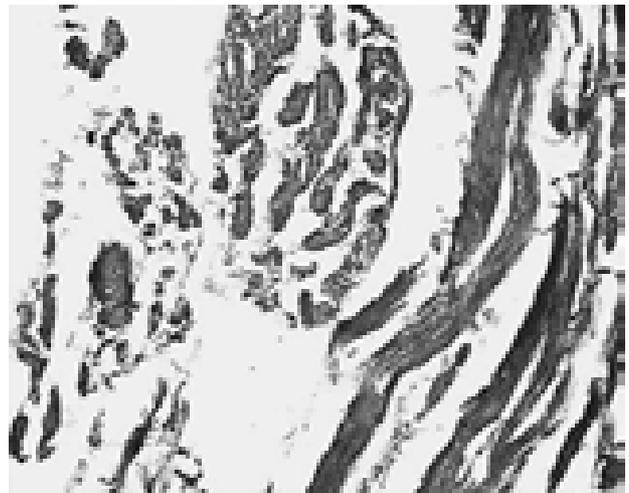


FIG. 4. Trichrome staining of cavernosal specimen of a patient with venooclusive ED ($\times 40$)

tissue (marked reduction). Only 4 patients had normal cavernosal smooth muscle mass, all of whom were among the recovered patients (Table 2). On the other hand, 41 of 43 patients in the control group had normal results on pathological study, and only 2 patients had a slight decrease in cavernosal smooth muscle mass ($P < .001$).

TABLE 2. Histologic examination results in patients with venooclusive ED and in controls

Pathology	Patients with venooclusive ED (%)	Controls (%)
Normal	4 (11.2)	41 (95.3)
Slight reduction of smooth muscle mass	23 (63.9)	2 (4.7)
Marked reduction of smooth muscle mass	9 (25)	0 (0)
		$P < .001$

Three patients in the control group developed venooclusive ED, postoperatively, documented with penile Doppler study and cavernosography.

The main postoperative complications in the patients with venooclusive ED were numbness in 2 patients and penile edema in 4, which spontaneously resolved after 3 weeks.

Discussion

Vasculogenic impotence is the most common form of ED, and venooclusive ED disease is a peculiar form of it, which imposes a major challenge for andrologists. Unfortunately, no known medical therapy for this form of the disease currently exists, and surgical therapy (venous ligation) is associated with a high failure rate. During detumescence phase, sinusoidal smooth muscles contract to expel the

intracavernosal blood at low pressure through the emissary veins, while during tumescence phase, there is complete sinusoidal smooth muscle relaxation and cavernosal arterial dilation. To rapidly fill the corpora cavernosal spaces, the emissary veins compress between the internal and external layers of the tunica albuginea. This abolishes blood leakage from the corporal bodies and maintains full rigidity.^(1,2) Cavernosal smooth muscle damage precludes proper sinusoidal expansion, the albuginea layers do not tightly compress, the emissary veins improperly close, and venous leakage ensues. This leads to early detumescence and ED.

Jevtich and colleagues have compared cavernosal biopsy results of patients with ED and healthy individuals. They have shown that 42% of patients with ED had marked decreases of cavernosal smooth muscles and increases of collagen, while only 5% of controls had decreases of smooth muscles or collagen.⁽³⁾ In a similar study, Karadeniz and coworkers demonstrated that significant decreases in smooth muscles and increases of interstitial fibrous tissue occur in patients with venoocclusive ED.⁽⁴⁾ Although Mersdorf and coworkers have not defined the specific pathological forms for every type of ED, they have reported a decrease of cavernosal smooth muscles and an increase of collagen tissue in patients with ED when compared with controls.⁽⁵⁾ Wespes and colleagues have demonstrated that when computerized morphometry was used in young patients with a curved penis but one that can maintain a hemodynamically adequate erection, that the corpora cavernosa was composed of 40% to 52% smooth muscle compared with 19% to 36% in elderly men with corporeal venoocclusive dysfunction and 10% to 25% in those with arterial impotence. In addition, collagen was correspondingly increased.⁽⁶⁾

Until now, there has been no accurate index to assess the normal values of cavernosal tissue components. However, several studies have demonstrated that there is an association between the percentage of cavernosal smooth muscle and venous leakage, which is considered a significant postoperative prognostic factor. Sattar and coworkers have compared the biopsy results of 5 potent patients with 17 impotent ones. They showed that the average cavernosal elastic tissue in potent patients was 9%, while it was 5% and 4% in those with the venoocclusive and arterial

insufficiency types of ED, respectively. No association between age and cavernosal elastin ratio was observed. They also showed that a 29% cavernosal smooth muscle is the cutoff for a good postoperative prognosis.⁽⁷⁾

In the abovementioned studies, no association between cavernosal pathology and specific type of ED was found. In the present study, of 36 patients with venoocclusive ED, 23 had a slight decrease of cavernosal smooth muscles, and 9 had a marked decrease in smooth muscle and an increase collagen tissue. Only 4 patients had normal histologies, all of whom had favorable postoperative responses (partial or complete). Unfortunately, because of technical shortages and the unavailability of highly specialized pathological facilities, we were unable to assess the ultrastructural characteristics of the smooth muscles or the different types of collagens. Further studies of the cavernosal smooth muscle and collagen ultrastructures are needed.

The current study demonstrates that venous leakage is secondary to primary cavernosal muscle pathology, and that penile Doppler and cavernosography can be used to assess the final manifestations of this pathology. In a study of penile biopsies in 50 patients, Malovrouvas and coworkers reported that biopsy gun specimens were as representative as were open biopsy specimens.⁽⁸⁾ Accordingly, in preoperative evaluation of patients with ED, needle biopsy may be useful in avoiding unsuccessful surgery.

Conclusion

Surgical intervention in venoocclusive ED is disappointing. However, preoperative cavernosal needle biopsy may be helpful in patient selection and surgical decision making.

References

1. Lue TF, Tanagho EA. Physiology of erection and pharmacological management of impotence. *J Urol.* 1987;137:829-36.
2. Krane RJ, Goldstein I, Saenz de Tejada I. Impotence. *N Engl J Med.* 1989;321:1648-59.
3. Jevtich MJ, Khawand NY, Vidic B. Clinical significance of ultrastructural findings in the corpora cavernosa of normal and impotent men. *J Urol.* 1990;143:289-93.
4. Karadeniz T, Topsakal M, Aydogmus A, Gulgun C, Aytakin Y, Basak D. Correlation of ultrastructural alterations in cavernous tissue with the clinical diagnosis vasculogenic impotence. *Urol Int.* 1996;57:58-61.
5. Mersdorf A, Goldsmith PC, Diederichs W, et al.

- Ultrastructural changes in impotent penile tissue: a comparison of 65 patients. *J Urol.* 1991;145:749-58.
6. Wespes E, Goes PM, Schiffmann S, et al. Computerized analysis of smooth muscle fibers in potent and impotent patients. *J Urol.* 1991;146:1015-7.
 7. Sattar AA, Wespes E, Schulman CC. Computerized measurement of penile elastic fibres in potent and impotent men. *Eur Urol.* 1994;25:142-4.
 8. Malovrouvas D, Petraki C, Constantinidis E, et al. The contribution of cavernous body biopsy in the diagnosis and treatment of male impotence. *Histol Histopathol.* 1994;9:427-31.