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# Alterations of Intracorporeal Structures in Patients with Erectile Dysfunction

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**Key Words**
Impotence · Smooth muscle cells · Endothelium · Elastic fibres

**Abstract**
***Objective:*** We sought to quantify intracavernosal smooth muscle content (SMC), endothelial cells (EC) and elastic fibres (EF) in both potent and impotent men. We compare the results in impotent men with regard to patient age, aetiology of impotence, presence or absence of diabetes mellitus and smoking. ***Patients and Methods:*** Seventy penile biopsies were taken from 10 potent patients with congenital penile curvature (age 17–24 years, mean: 21 ± 1.16) and from 60 impotent patients (age 28–64 years, mean: 46 ± 7.64). Biopsies were stained immunohistochemically to quantify the percentage of SMC by anti-desmin and anti-SMA, anti-CD-34 for EC and Verhoeff's histochemical staining for EF. Statistical analyses were performed by using one-way Anova after square root transformation. ***Results:*** We observed a statistically significant difference in the amounts of corporeal SMC, EC and EF with regard to the following subgroups: potent versus impotent men; men with arterial aetiology versus veno-occlusive aetiology; men under the age of 45 versus men over the age of 45; patients with diabetes mellitus versus non-diabetes mellitus, and smokers versus non-smokers. ***Conclusion:*** Quantification of intracavernosal structures appears to be important for either understanding the mechanism of impotence or deciding the appropriate treatment.



## Introduction

Penile erection results from increased arterial flow, sinusoidal smooth muscle relaxation and decreased venous return [1]. Failure of any of these vascular mechanisms may lead to erectile dysfunction. Previous studies have shown that intracavernosal smooth muscle cells (SMC) form the structural basis for sinusoidal relaxation which is locally neurally controlled by the active corporeal lacuna endothelium (EC) [2–4]. In addition, elastic fibres (EF) are important elements for rigid erection [5]. The short- and long-term success of penile revascularization procedures may ultimately depend on these endothelial-associated structures. Thus, SMC, EC or EF could be regarded as fundamental to the erection process and demonstration of their parcity pre-operatively, might prevent some candidates with a poor prognosis from undergoing surgery for veno-occlusive or arteriogenic disease because of end-organ failure.

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In this study we attempted to quantify the SMC, EF and EC of the corpus cavernosum of both potent and impotent men and compared the results with regard to patient age, vascular aetiology of impotence, presence or absence of diabetes mellitus, and smoking.

## Patients and Methods

The study included 60 impotent patients aged 28–64 years (mean 46 ± 7.64 years) who had erectile dysfunction of organic aetiology. Pre-operative evaluation included complete medical history, physical examination, routine serum biochemical analyses, serum testosterone and prolactin levels, sleep tumescence and rigidity monitoring by Rigiscan device (Dacomed, Minneapolis, Minn., USA). Both colour-flow Doppler sonography of the penis and pharmacocavernosometry-cavernosography and neurologic tests were carried out in selected cases when organic factors were suspected. Colour-flow Doppler sonography of the penile arteries which revealed at least a 75% increase in the diameter of the cavernous arteries after 60 mg papaverine administration intracorporeally and a peak flow of >40 cm/s, indicated a normal arterial erectile mechanism, but end-diastolic velocities of ≥5 cm/s suggested the possibility of an excessive venous leakage [1, 6]. Patients suspected of having venous impotence underwent dynamic cavernosometry and cavernosography. Subjects who required either more than 150 ml/min of fluid inflow to initiate or more than 30 ml/min to maintain an erection during cavernosometry were suspected of having venous incompetence and they underwent cavernosography [1, 7]. For this purpose, 50–100 ml of non-ionic contrast material were injected continuously at a rate that maintained the intracorporeal pressure at 90 mm Hg. Pathological visible contrast outflow in the dorsal vein and pelvic veins was consistent with corporeal veno-occlusive dysfunction.

The study also included 10 potent men, 17–24 years (mean 21 ± 1.16 years) with congenital penile curvature who were regarded as control group.

Cavernous biopsies were obtained from the mid shaft of the corpus cavernosum just under the tunica albuginea during correction of congenital penile curvature, or a venous operation or at implantation of a penile prosthesis. Biopsy specimens were fixed in formalin, processed routinely and stained with HE for histologic evaluation. Immunohistochemistry was performed by using a Zymed Histostein™-Plus Bulk kit with the monoclonal antibodies CD34 (Zymed; 1/20; 1 h) for demonstrating EC; SMA (Y lem; 1/75; 3 h) and desmin (Immunon; 1/75; 30 min) for SMC. Myometrium sections served as positive control for monoclonal antibody SMA, desmin and CD 34. Verhoeff's elastic histochemical stain was used for demonstrating EF. Skin sections were used as positive control for elastic stain. Monoclonal antibodies were omitted for negative controls. The average percentage of the positively of anti-SMA, anti-desmin, elastic stains and also the average number of the EC were evaluated in a minimum 20 high power fields (HPF: 10× ocular; 40× objective) for each case.

The content of SMC, EC and EF were compared between potent and impotent men; arterial disease and veno-occlusive dysfunction; patients with diabetes mellitus and who smoke regularly (more than 15 cigarettes daily), and lastly between patients above and below 45 years.

**Table 1.** Percentage of corporeal SMC (both stained with anti-actin and anti-desmin), endothelial cells and elastic fibres with regard to potent control group and impotent patients with various sub-groups ($\bar{x}$ ± SD)

| | Potent, control group (n = 10) | Impotent men with various sub-groups (n = 60) |
|---|---|---|
| SMC | 51.33 ± 3.66 | 21.71 ± 22.10 |
| Desmin | 41.05 ± 6.62 | 20.28 ± 13.00 |
| Endothelial cells | 4.34 ± 1.67 | 1.69 ± 2.52 |
| Elastic fibres | 7.81 ± 1.97 | 3.00 ± 4.39 |

Statistical analyses were performed by using the one-way Anova test initially, then to find out the differences of the groups we used the Duncan test.

## Results

The mean percentage of cavernous SMC, EC and EF in tissues from each group of patients is given in tables 1 and 2. We observed a statistically significant difference of corporeal SMC, EC and EF with regard to the potent control group versus the impotent men (table 1) ($p < 0.05$). When we analysed those impotent men into the various subgroups such as arterial versus veno-occlusive aetiology, men under the age of 45 versus men over the age of 45, patients with diabetes mellitus versus non-diabetes mellitus, and smokers versus non-smokers, we observed that impotent men with arterial disease, men older than 45 years old, smokers and diabetics had significantly lower concentrations of intracorporeal structures. All of the patients diagnosed with arterial disease or veno-occlusive dysfunction had pathological nocturnal penile tumescence at testing. Nocturnal penile tumescence and rigidity with at least 1 erectile episode of tip penile rigidity greater than 60% and 10 min in duration may be associated with potency [15].

## Discussion

Revascularization procedures for the treatment of impotence are well established. However, more than 50% of the patients who undergo these procedures do not attain improved erectile capability, indicating that other factors may also have an important role in the pathophysiology of

**Table 2.** Percentage of corporeal SMC (both stained with anti-actin and anti-desmin), endothelial cells and elastic fibres with regard to potent control group, impotent patients with and without diabetes mellitus, smokers versus non-smokers, patients with arterial disease, veno-occlusive dysfunction and above/below 45 years old ($\bar{x} \pm SD$)

| | Control group (n = 10) (age 17–24) (mean age 21 ± 1.16) | DM(+) group (n = 16) (age 28–64) (mean age 48.6 ± 10.96) | DM(–) group (n = 44) (age 28–64) (mean age 42.4 ± 2.77) | Smokers (n = 42) (age 28–58) (mean age 41.6 ± 7.68) | Non-smokers (n = 18) (age 30–64) (mean age 49.5 ± 11.25) | Age | | ED etiology | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | <45 years old (n = 24) (age 28–45) (mean age 38.7 ± 5.38) | >45 years old (n = 36) (age 46–64) (mean age 51.2 ± 6.58) | arterial disease (n = 38) (age 39–64) (mean age 47.3 ± 5.92) | veno-occlusive dysfunction (n = 22) (age 28–56) (mean age 43.5 ± 9.64) |
| SMC | 51.33 ± 3.66 | 21.96 ± 6.87 | 35.35 ± 7.65 | 31.97 ± 5.68 | 36.64 ± 6.30 | 31.28 ± 7.78 | 27.25 ± 6.83 | 21.71 ± 7.10 | 30.66 ± 7.44 |
| Desmin | 41.05 ± 6.62 | 20.28 ± 2.51 | 29.38 ± 3.82 | 24.97 ± 5.74 | 28.11 ± 3.34 | 31.76 ± 3.06 | 23.39 ± 3.62 | 23.66 ± 2.13 | 28.10 ± 2.50 |
| Endothelial cells | 4.34 ± 1.67 | 1.96 ± 1.00 | 2.30 ± 1.26 | 1.69 ± 0.78 | 2.10 ± 1.93 | 2.93 ± 1.11 | 2.13 ± 1.52 | 2.00 ± 1.33 | 3.10 ± 1.00 |
| Elastic fibres | 7.81 ± 1.97 | 3.00 ± 2.60 | 3.86 ± 2.44 | 3.07 ± 2.48 | 3.84 ± 1.63 | 4.84 ± 2.59 | 3.04 ± 2.48 | 3.05 ± 2.62 | 3.96 ± 2.41 |

impotence [6, 7]. It is generally accepted that the elevation of intracorporeal pressure leads to erection and this is achieved by the relaxing-contractile action of the smooth muscle cells, so their degeneration may be an important factor in erectile dysfunction. Such a process may limit restoration of erectile capability by revascularization and eventually lead to organ failure. Penile corporeal lacunar endothelium is active in the local neural control of the corporeal smooth muscle relaxation by producing nitric oxide, a potent vasodilator neurotransmitter [8]. The third important corporeal structures that are important for restoring erection are EF which play a role in human erectile tissue compliance and elasticity. Understanding the importance of the above-mentioned structures and analysing our revascularization results in 1996 (which revealed only 25% improvement in erectly potency for patients with veno-occlusive dysfunction) [8, 9], we began in this study to try and quantify those above-mentioned intracorporeal structures.

We observed that the content of corporeal smooth muscle cells of potent and impotent men is statistically different. On the other hand, we tried to group those impotent patients with regard to aetiology (arterial versus veno-occlusive), age (below and over 45 years, which can be used for cut-off age of penile revascularization procedures) and risk factors of erectile dysfunction (diabetes mellitus and smoking, which might both be regarded as prognostic factors for the success of revascularization procedures). With regard to aetiology, our patients with arterial disease tend to have lower levels of SMC than the patients with veno-occlusive disease. Those results are consistent with the already published studies of Wespes et al. [2] and Sattar et al. [10] which also showed decreased SMC in patients with arterial disease. Wespes et al. [2] recommended that one should not operative on impotent men who have less than 29% SMC on penile biopsy, since the outcome of the surgery was unlikely to be successful. It has been suggested that chronic vascular insufficiency leads to ischemic injury by free oxygen radicals [11]. Hence, merely increasing the blood supply may not reverse all types of ischemic cellular damage. This might explain the failure of revascularization in such a high percentage of cases. On the other hand, other factors such as patient age, smoking and chronic disease (e.g. diabetes mellitus) may also contribute to damage of muscular cells [6, 12]. Our results were in concordance with those hypotheses that we observed lower levels of SMC at older ages, patients with diabetes mellitus (DM) and smokers.

We observed an almost similar correlation in the amounts of corporeal EC and EF. Both were present in higher concentrations in potent versus impotent, younger versus older, arterial versus veno-occlusive, DM(–) versus DM(+), and non-smokers versus smokers. It has been demonstrated that relaxation of the human corpus cavernosum requires an intact endothelium. Thus, endothelial cell dysfunction would result in failure of the local neural control and impairment of endothelium-dependent relaxation of the corporeal smooth muscles which could produce erectile dysfunction [13]. It can be speculated that all the above-mentioned parameters can alter endothelial cell function.

EF probably also play an important part in achieving firmness of the corpora cavernosa during erection [5, 14]. Changes in EF content may play a role in decreased relaxation of erectile tissue in impotent patients, which may interfere with the normal filling of the vascular spaces. Our study also supports the importance of EF for erectile activity.

## Conclusion

We think that definition and quantification of intracavernosal structures preoperatively (by penile biopsy, especially in patients resistant to medical treatment, e.g. sildenafil non-responders) will assist the clinician in deciding the appropriate treatment especially on the benefits of surgical reconstruction, and thus may prevent some from non-feasible operations. Perhaps in the future, the use of immunohistochemical staining and more sophisticated techniques will allow the study of neurotransmitters present in the cavernous tissues and help in the decision as to whether medication or surgery is most appropriate for the impotent patient.

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