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آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Penile Revascularization for Erectile Dysfunction
A Systematic Review and Meta-Analysis of Effectiveness and Complications

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Introduction: Patients with arteriogenic erectile dysfunction (ED) caused by traumatic localized arterial lesions can be treated successfully by penile revascularization (PR) surgery. We aimed to determine the subjective and objective outcomes of PR surgery in patients with arteriogenic ED.

Materials and Methods: We searched for relevant publications released up to May 2008 in the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and Biological Abstracts. The citation lists of review articles and included trials were also searched. Studies on different operative techniques of PR for men with ED due to traumatic penile arterial lesions were selected. Data on participants' characteristics, study quality, population, intervention, cure, and adverse effects were collected and analyzed.

Results: There were 25 studies on comparison of the PR operative techniques. Concerning subjective cure, men younger than 30 years old had better results than older ones (odds ratio, 3.7; 95% confidence interval, 2.2 to 6.4; \( P = .001 \)). Venous leak (odds ratio, 1.8; 95% confidence interval, 1.2 to 2.6) and history of smoking (odds ratio, 3.4; 95% confidence interval, 2.2 to 5.6) influenced success rate. Inconsistent measurements of outcomes limited the findings, and none of the studies were randomized controlled trials.

Conclusion: Traumatic patients with arteriogenic ED might benefit from PR. Patient selection is vital for a successful outcome. Variations in penile vascular anatomy are also likely to be important when individualizing penile revascularization. In a limited number of highly selected individuals, PR can be successful for the long-term. Randomized controlled trials examining PR techniques are warranted.

Keywords: penis surgery, erectile dysfunction, vasculogenic impotence, penis blood supply, treatment outcome, meta-analysis

INTRODUCTION

Background
The first penile revascularization (PR) surgery was reported in 1972 by Michal and colleagues.(1) One decade later, Crespo and colleagues reported a 76% subjective success rate after arterio-arterial anastomosis in a large series of 257 patients,(2) and Virag reported that 74.9% of their patients were content after deep dorsal vein arterialization.(3) Thereafter, the indication criteria and surgical mode had largely been established by late 1990s. Penile blood flow depends on the internal pudendal arteries, which are branches of the internal iliac arteries. The internal pudendal artery courses within the pudendal canal and is at risk of injury with fracture of the inferior pubic ramus.(4) The internal
Pudendal arteries are often likely to be injured when the patient falls astride an object. Any other arterial diseases reducing blood supply to the penis, both in flow and pressure, can lead to disturbances of erection. This is true for lesions of the hypogastric as well as smaller vessels such as the penile arteries.\(^5\,^6\)

Erection is a complex physiological process in which vascular factors play a pre- eminent role. Therapeutic options for men with arteriogenic erectile dysfunction (ED) are mainly administration of phosphodiesterase type 5 inhibitors, intracavernous injections of vasoactive agents (for example, prostaglandin E\(_\text{1}\), papaverine/ phentolamine, or triple drug), intrarethral administration of prostaglandin E\(_\text{1}\), and administration of centrally acting drugs.\(^7\,^8\)

However, all of these methods circumvent the patient’s problem temporarily, and patients are not cured of impotence, remained dependent on these treatments for the remainder of their sexually active lives. We need an effective treatment that cures the problem permanently.

Penile revascularization is a treatment option for such patients. The preliminary results of PR surgeries seemed promising, and these treatment options have gained popularity. However, the long-term outcome has not been as good as expected. Many techniques of PR have been used for the treatment of arteriogenic ED.\(^9\,^{10}\) Most of these vascular reconstructions use the inferior epigastric artery (IEA). Surgical techniques for PR are divided into 3 groups: venous arterialization, arteriovenous shunting, and arterio-arterial shunting.\(^{11\,-\,16}\)

Information concerning the relative effectiveness, safety, acceptability, and costs of these different PR techniques is vital for decision making by both physicians and patients. However, the majority of studies to date are retrospective case series. These studies are problematic as they may underestimate failure rates for a number of reasons, including lower failure rates observed by experienced surgeons and short-term follow-up periods. We conducted a systematic review of the medical literature to evaluate the efficacy and safety of PR in the treatment of arteriogenic ED, and summed the influencing factors on the outcomes up by meta-analysis.

Objectives

This review aimed to look at the short-term and long-term benefits of PR surgery. We also examined factors responsible for failure, including diabetes mellitus, smoking, alcoholism, general arteriosclerosis, obesity, coronary heart disease, hyperlipidemia, arterial hypertension, patient age at the time of surgery, and the surgical technique. Finally, we attempted to provide the selection criteria for better patient selection. The outcomes identified were primarily related to subjective and objective improvements in ED and the duration of improvement.

The following hypotheses were to be addressed: (1) PR surgery cures arteriogenic ED; (2) different surgical techniques have different long-term results; (3) PR surgery is better than pharmacological interventions; (4) highly selected patients benefit more from PR surgery; and (5) intracavernosal injection of vasoactive drugs combined with PR surgery is better than PR alone.

MATERIALS AND METHODS

Criteria for Selecting Articles

Type of Study. Due to the lack of randomized controlled trials on this topic, nonrandomized comparative studies (where participants were their own controls) were selected for review.

Participants. Men with arteriogenic ED due to trauma were considered.

Intervention. The primary intervention that this review was concerned with was PR surgery.

Outcome Measures. The main outcome measure was satisfactory intercourse without additional therapy. Secondary outcomes included duration of favorable response, overall satisfaction rate, quality-of-life outcome measures, and intervention-related complications. Nonresponders to pharmacotherapy showing response after surgery were classified as having a partial success.

Search Methods

The following MeSH terms and text words
were used: impotence, erectile dysfunction, penile, revascularization, treatment, arteriogenic, and vasculogenic. Our search strategy included an electronic search of the MEDLINE, confined to a period from 1966 to May 2008, to identify all relevant published studies on PR. We also searched the Cochrane Central Register of Controlled Trials (The Cochrane Library 2007, Issue 4), the EMBASE (1980 to May 2008), and the Biological Abstracts (1980 to May 2008). The reference lists of the identified studies was checked for additional citations. In addition, information on the ongoing clinical trials was sought by searching the clinical trials registry web site of the National Institute of Health (http://www.clinicaltrials.gov). No language restriction was considered in our search strategy.

Review Methods
The literature search results were screened, and by consensus among the authors, relevant articles were retrieved. Data was extracted from each identified paper and included information on study design, participants, type of PR, and outcome measures. As there were no randomized trials identified, when the study fulfilled the inclusion criteria, data concerning methods of the trial, participant characteristics, intervention details, and outcome measures were independently extracted using a standard extraction form.

The identified articles were selected for inclusion in the review on the basis of appropriateness as determined by at least 2 of the authors without prior consideration of the results. As no quantitative synthesis could be done, it was not possible to carry out any sensitivity analyses to assess the effects of differences in methodological quality. Some studies had multiple publications; these were treated as a single source of data. The data were analyzed in the Review Manager 4.2.8 software (RevMan 4.2.8, Cochrane Library, Oxford, UK).

Description of Studies
Search Results. The search criteria identified 64 studies. A total of 18 studies did not meet our inclusion criteria and were excluded. All the remaining 46 studies involved patients who had undergone some form of PR. In 4 studies, laparoscopy had been used for PR. None of these studies described the experience level of the surgeons.

Types of Interventions. An extensive workup is done for each patient prior to PR. The extent and types of workup varied in different studies. However, the mainstay of the workup included full examination and a series of laboratory tests. The examination included medical and sexual history and psychiatric examination. Laboratory testing consisted of hormonal evaluation (follicle-stimulating hormone, luteinizing hormone, thyroid hormones, testosterone, prolactin), nocturnal penile tumescence with or without the erectometry test, duplex ultrasonography with periodic measurement of hemodynamic parameters, color Doppler ultrasonography, duplex Doppler ultrasonography, dynamic infusion pharmacologic cavernosometry and cavernosography, and selective internal pudendal arteriography or digital subtraction angiography. Penile revascularization surgery is usually done in patients younger than 50 years. Various techniques are used. The IEA is used to establish new arterial blood flow for most penile revascularization techniques. The following techniques were reported in the selected articles: (1) end-to-end anastomosis of the IEA to the dorsal artery in various modifications; (2) anastomosis of the IEA to the deep dorsal vein at the base of the penis (Virag procedures), with a few modifications without (Virag I-III, Furlow-Fisher, Lewis) or with creation of a surgical direct anastomosis to the cavernous bodies (Virag IV-VI); (3) direct anastomosis of the IEA to the deep dorsal vein at the base of the penis (Virag procedures), with a few modifications without (Virag I-III, Furlow-Fisher, Lewis) or with creation of a surgical direct anastomosis to the cavernous bodies (Virag IV-VI); (4) Hauri triple anastomosis, consisting of a triple anastomosis between the dorsal penile vein and dorsal penile artery (side-to-side) with the IEA (end-to-side); (5) modified version of the original Hauri technique in which the dorsal penile artery is cut completely and 3 separate end-to-side anastomoses are constructed; and (6) Furlow-Fisher modification of the Virag V procedure.

RESULTS
The studies explicitly excluded men with other
types of ED; therefore, the effects of the PR could be applied to men with arteriogenic ED. The definitions of improvement in ED varied across studies from perception of self-reported improvement to objective assessment of penile erection. None of the studies had the same design, making head-to-head comparisons difficult. Although the era of microsurgical techniques has greatly expanded the number of possible solutions for PR, techniques selected (type of anastomosis) for PR and the experience of the surgeon who will do this are essential for successful PR. There was clinical heterogeneity regarding the patients’ demographics at baseline, type of recruitment and surgical technique, definition of success, and ancillary treatments. The wide range of success definitions and high failure rates also mean that the groups of the studied people differed.

The success rate of penile revascularization was associated with various risk factors, including patient’s age, diabetes mellitus, smoking, alcoholism, obesity, hyperlipidemia, hypertension, preoperative arteriographic findings, surgical technique, and surgeon’s experience. The main risk factors of failure in PR were smoking, diabetes mellitus, hypertension, hyperlipidemia, radiation, coronary heart disease, alcoholism, obesity, cavernosal fibrosis, and distal arteriogenic disease. Penile vascular architecture is a predominant factor in decision making. Patients who do not respond to intracavernous injection therapy have irreversible degenerative changes in the cavernous smooth muscle. (29)

The overall success rate of PR was about 50% after a mean follow-up period of 50 months, (29) of whom 30% had experienced spontaneous erections and 20% had pharmacologically induced erections (partial response). Long-term failure had been reported in about 50% of the men. Surgical complication rate was approximately 30%. Thrombosis, hyperemia of the glans, and priapism were the common complications of PR.

There was a strong correlation between success and the elapsed time from the operation (odds ratio [OR], 3.6; 95% confidence interval [CI], 2.8 to 5.6). The success rate in all series tended to diminish as follow-up period increased. The success rate in the nonsmokers was twice as high as that in the smokers (OR, 3.4; 95% CI, 2.2 to 5.6). The presence of venous leak (OR, 1.8; 95% CI, 1.2 to 2.6) and type of procedure (OR, 2.8; 95% CI, 1.6 to 4.6) had a significant impact on success rate ($P = .03$ and $P = .01$, respectively). The impact of age was greatest; patients younger than 30 years old showed better success rates than the older ones (OR, 3.7; 95% CI, 2.2 to 6.4; $P = .001$).

Anticoagulants, usually aspirin, are recommended for 6 months after the operation. A patent microvascular anastomosis can be documented postoperatively by selective internal iliac arteriography. The surgical procedure for PR should be determined according to the anatomical variation of the penile artery and the pattern of arterial obstruction.

**DISCUSSION**

To the best of our knowledge, this systematic review with the data that were used summarizes all the studies that exist on this topic. There were several strengths and limitations in this review. The search was thorough and systematic without language restrictions. Two reviewers independently performed the study selection and data extraction to minimize errors. No trials were identified examining various surgical techniques in various patients groups. No controlled clinical trials examining various surgical techniques have been conducted to date. Variations in populations, interventions, and outcome measures, rather than study quality, resulted in heterogeneity between studies. Selection criteria varied for the same interventions. Pooling analysis was questionable because of clinical and methodological differences across the studies included in the present report. Future research is required to determine predictors of the long-term curative effects of PR in men from different age and etiologic groups.

Despite extensive efforts to standardize outcome assessment for ED, the included studies measured a variety of outcomes, including self-reported symptoms and improvement and severity of ED. The measurement of outcomes was inconsistent within and across the studies.

Since the first report of PR by Michal and coworkers in 1973, (29) several modifications have been made and the outcome of this surgery
has been improved significantly and reached a level sufficient for general consideration.\(^{23}\)

Currently, the only feasible cure of arteriogenic ED is PR.\(^{15,23-25}\) Success rates are difficult to compare because of varying definitions of success, different patients’ demographics, and different risk factors. Some physicians perform PR only in patients who respond to intracavernous injection of vasoactive drugs, and others do so only in nonresponders.\(^{15,23}\) There are multiple reasons for failure of PR. The most common causes of failed PR are inappropriate patient selection and misdiagnosis. Selective angiography of the hypogastric arteries and their branches is essential to evaluate potential candidates for PR. Patient history, physical examination, and even selective angiography of the hypogastric arteries are not always accurate indicators of a vasculogenic etiology.\(^{15}\) After pelvic fracture, it is impossible to be certain whether a patient with vasculogenic impotence does not have a concomitant cavernosal nerve injury. Color and power Doppler ultrasound technology have greatly enhanced the capacity to study hemodynamics and penile vascular anatomy.\(^{13,30-36}\) The patency of the whole length of cavernous artery and individual anatomical variations should also be examined. The traditional assessment without a detailed study of cavernous arterial anatomy can result in unsuccessful PR.

Variations in penile vascular anatomy should also be considered when individualizing PR procedures. The anatomical variations of the penile artery are common.\(^{37}\) Deep dorsal vein arterialization surgery for arteriogenic ED was introduced by Virag and colleagues,\(^{38}\) and then, it was modified by Furlow and associates.\(^{28}\) In the technique of end-to-end anastomosis of the IEA to the dorsal artery, the major obstacle is discrepancy of the lumina between the IEA and the dorsal artery. This can result in low flow rates, which is susceptible to stasis and thrombosis. Later in 1986, creation of an anastomosis between the IEA and the deep dorsal vein and the dorsal artery of the penis was introduced by Hauri.\(^{39}\)

Patient selection is vital for a successful outcome in PR. Patients with the following criteria have had better outcomes: an age less than 30 years; fewer than 2 risk factors; and no history of smoking, diabetes mellitus, hypertension, or hyperlipidaemia. In highly selected patients, PR can be successful for more than 10 years.\(^{40}\) In a population-based study, after adjusting for the strong effect of age on the incident of ED, men with diabetes mellitus, hypertension, peripheral vascular disorders, hypercholesterolemia, and coronary artery disease had a significant increase in the risk of ED.\(^{41}\) Ideal candidates for PR are young patients (younger than 30 years) with discrete arterial insufficiency (pudendal, common penile, or cavernous arteries) resulting from trauma-induced arterial occlusive disease and without significant concomitants risk factors. Patients with significant risk factors are poor candidates for PR and they should be encouraged to consider other options for treatment of impotence.\(^{42}\) In diabetic men, the response rate to sildenafil is lower.\(^{43}\) In the workup of patients with vasculogenic ED, both functional and anatomic evaluation of penile arterial blood flow is essential. Duplex ultrasonography is an excellent screening modality to evaluate intrapenile anatomy and the functional parameters of the cavernous and dorsal arteries. The operative risk of patients being evaluated for PR procedures should be carefully assessed and the concomitant risk factors should be minimized. When there are communicating branches between the dorsal and cavernosal arteries, Hauri procedure is a better option. The technique should be individualized depending on the pathological findings in each case. Where possible, physiological revascularization procedures are preferred.

To prevent priapism, the inflow should be connected to the dorsal vein rather than implanted into the corpus cavernosum.\(^{23,44}\) Hyperemia of the glans is due to dorsal vein arterialization that can cause pain, skin ulceration, and urethral compression.\(^{23,45}\) To harvest the IEA, a long pararectal incision is necessary. This can cause some problems, such as cosmetic issues, postoperative pain, long hospitalization, and hernia formation.\(^{38,46}\) To resolve these problems, laparoscopic-assisted mobilization of the IEA and microsurgical PR can be used.\(^{19,20}\) Laparoscopy
provides many benefits, including decreased postoperative pain, reduced hospitalization and recovery time, and better cosmetic outcomes. Meticulous microsurgical techniques are essential for completing patent microanastomoses. With the exception of direct anastomosis of the IEA to the corpus cavernosum, other surgical techniques are currently used for surgical treatment of vasculogenic ED. Extensive vascular evaluation is necessary to define fully the exact nature of the injury. As standardized criteria for patient selection, follow-up protocol and success definition have yet to be identified.

CONCLUSION

Implications for Practice
Penile revascularization can successfully treat ED in selected patients with vasculogenic ED. High-quality trials regarding PR are unavailable. Practitioners should bear in mind that greater experience in a revascularization technique is associated with higher rates of PR success.

Implications for Research
Since these results are based on small studies, the evidence would be stronger if confirmed by large trials. Effectiveness data were limited; however, the effectiveness of PR is largely determined by the patient selection criteria rather than the surgical technique. In addition, work is needed in the standardization of follow-up protocols, evaluation of PR success and failure, patient selection, and statistical analysis. Randomized trials comparing various surgical techniques are warranted. These studies should evaluate efficacy, complications, quality of life, cost implications, and long-term outcomes of PR surgeries.

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CONFLICT OF INTEREST
None declared.

REFERENCES


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