Original Article

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ERECTILE DYSFUNCTION AND CAVERNOUS VENO-OCCLUSIVE DISEASE

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Abstract

Goal

To provide a state-of-the-art literature review on veno-occlusive diseases as a pathomechanism of vasculogenic erectile dysfunction (ED).

Methods

A comprehensive systematic literature search was conducted followed by sorting, review, and summarizing.

Results

The systematic review of the literature reveals a significant number of recent studies dealing with new minimally invasive methods to provide a potential solution of caverno-venous leakage. Even the long-term results reported demonstrate considerable improvement of ED caused by this condition. Furthermore, 3-D computed tomography cavernosography (CT-cavernosography) is a new technology, which can provide high-resolution images of venous drainage from any angle and shows to be very helpful for both the diagnosis of corporal veno-occlusive dysfunction and the anatomical study of the human penile venous system. The application of this technology may also lead to better strategies in venous leak treatment. Over 30 published studies were found in the literature with good results after caverno-venous leak treatment. Altogether, 13 comparable studies including 538 patients were found, in which a mean short-term success rate of almost 80% and a mean long-term success rate of up to 74% was achieved. None of the studies described major complications.

Conclusion

ED is an increasingly important issue, especially in young men. Whereas the current treatment strategies are mostly focused on older men, young patients are seeking more a longer lasting or more definitive solutions, rather than a lifelong medical treatment. Various chronic disorders have been reported to be associated with elevated rates of ED including depression, diabetes, and cardiovascular and neurological disease in older men. Properly selected cases of young men may benefit from treatment of caverno-venous leak treatment. The current strategy in the treatment of ED in young men may be reconsidered.

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Erectile dysfunction (ED) is a big issue in various populations with 30% of young men suffering from this condition with an increasing tendency.¹

Various chronic disorders have been reported to be associated with elevated incidence of ED including depression, diabetes, and cardiovascular and neurological diseases. Such disorders are more common in the elderly, which may partially explain the elevated incidence of ED in men over age 60. In younger patients, the cause for ED is more a vascular problem which affects the storage capacity of the penis. Currently, up to 70% of men with ED are not treated. However, so many men experience considerable distress from their condition, that the increasing awareness of ED, as well as the availability of noninvasive treatments, may result in a greater proportion of patients seeking treatment, and eventually regaining satisfaction with their sex life.²

The goal of this review report is to provide a stateof-the-art systematic review of the literature on cavernous veno-occlusive dysfunction as a pathomechanism of vasculogenic ED.

METHODS

A literature search was conducted to systematically review, sort, evaluate and summarize the literature and provide a comprehensive report. A structured review of English-language articles on PubMed published till 2017 coupled with the examination of tables of contents of high-impact journals to identify articles related to venous leak treatment was performed. These articles were appraised for their importance to medicine.

RESULTS

Treatment schemes are currently mainly focused on dealing with the relevant chronic disorders in elderly patients. The current first-choice treatment option is utilizing a PDE5-Inhibitor,³ which is dealing with the symptom only and has a success rate of approximately 70%. But several reports demonstrate remarkably lower success rates. Virag et al.⁴ found, that of 157 patients, who had completed his initial study, the efficacy of and satisfaction with sildenafil was considered good in only 31.84%, fair in 29.29%), and bad in 38.85% of the patients. In the case of significant venous leakage

disease, no patient reported a good treatment result with sildenafil and 83% reported a bad response.⁴

Additionally, one has to be aware that PDE5-inhibitor therapy is not a curative treatment. In the case of early onset of ED, it can mean a lifelong treatment with all the known disadvantages of the therapy. Additionally, for several reasons, treatment rates of ED are clearly lower than the prevalence rates. One major reason is the fact, that most healthcare payors are currently excluding reimbursement of this medically and so-cioeconomic condition.²

Furthermore, if cavernosography is used to define the presence of a cavernous veno-occlusive dysfunction with venous leakage, a condition where the loss of blood from the penis is higher the supply level, in impotent patients 86% fall into the category of venous leakage. Other studies report about a percentage of 89% venous leakage in case of organic ED. These data support recent observations that there is a high incidence of venous leakage as defined by these criteria in the young men population with organic impotence.

Interestingly, veno-occlusive dysfunction as a cause for ED is not just a condition found in humans. Several reports demonstrate ED due to cavernous-veno-occlusive dysfunction in various animal species, including bulls and boars. ^{7–10}

It can be found clinically that bulls can also be unable to achieve an erection when stimulated with an electroejaculator and in natural breeding trials. Vascular shunts can be located as a cause of ED by serial contrast radiography of the corpus cavernosum penis. If surgical correction of the shunts is attempted by wedge resection of the tunica albuginea, this surgical correction is successful in 50% of the treated animals and the bulls can be returned to service.¹⁰

Simple isolated ligation of the deep dorsal vein in humans for the permanent cure of ED due to venous leak is up till now not recommended, due to some reported low long-term success rates.^{3,11,12}

The only in this context cited article in the EAU guidelines 2010³ is from the report of Wespes. ¹² Unfortunately, this article may not be qualified to substantiate such a statement. Of 130 patients with vascular ED who underwent various surgical procedures, only 11 patients were treated with venous resection. For further evaluation, only 7 patients were eligible after

48 months in this group of which only one patient reported about sexual satisfaction. No IIEF-Score or Quality-of-Life evaluation was conducted before and/or after surgery. A reliable guideline statement about the success of this intervention can probably not be made from this number of patients with this evaluation method. Nevertheless, success was stated for penile revascularization in 2 out of 2 patients. The authors assert, that this finding is evidence enough to recommend penile revascularization for young patients with traumatic arterial lesions. This statement was adopted into this guideline version, too.

Another, more serious study was performed earlier in 1999 by Popken et al. In this study, ligature and resection of the superficial and deep veins of the penis (DPVL) was performed in 122 patients. All patients were non-responders to intracavernosal injection of alprostadil (SKAT),11 which is a very difficult initial starting point to prove the effectiveness of such a procedure. Twenty-six percent had ectopic veins, 38% leakage through the crural veins and 24% a glandular or spongiosal shunt. After the 70-month follow-up, 14% of the 122 patients were able to achieve an adequate spontaneous erection and 19% also responded to SKAT. Taking in account that these patients were strong candidates for a penile implant, the success rate of 33% seems to be excellent in this setting.¹¹ In a third of the patients, natural erections could be regained and maintained for a long time. This is an important aspect because in many countries penile implants are not covered by insurance companies and therefore most of these patients cannot afford this expansive therapy option.

In the most recent guidelines of the EAU from 2016¹³ the aforementioned literature citation is replaced by a Meta-Analysis of Sohn et al. ¹⁴ The recommendation of the EAU is still: Vascular surgery for veno-occlusive dysfunction is no longer recommended because of poor long-term results. The cited literature does not at all support this recommendation, because it states that; "While caverno-venous occlusion disease (CVOD) surgery is still considered investigational, it may be offered in special situations." Furthermore, the literature processed in this publication of Sohn et al. is from 1997 to 2005 and does, therefore, not reflect the current state of research.

The members of the 3rd International Consultation on Sexual Medicine in Paris 2009 published their conclusions and recommendations in 2 recent articles in 2010. 15,16

In this context, a compilation of outcome data of simple ligation techniques published until 2005 was discussed. ¹⁴ In this literature citation, a wide variety of success rates was found. For the authors, no single operative technique seemed to be superior to others, and a steep decline of success has to be noted with the length of follow-up in single ligation procedures. But, the authors stated, that young patients with site-specific congenital, posttraumatic or post-inflammatory leaks may be considered for vein ligation with informed consent. The choice of operation offered should be decided on available wisdom and infrastructure, the experience and preference of the operating surgeon, and the basis of the site, nature, and size of the leak. ¹⁴

In contrast to these previous findings, various modified and improved technologies with much better short- and long-term outcomes has been recently described.

The first report of arterialization of the deep dorsal vein was published in 1981 by Virag et al. ¹⁷ with a long-term success rate of 80%. Additionally, a multidisciplinary approach with emphasis on hemodynamic tests was used to diagnose 421 patients with arteriogenic, venogenic, or mixed arteriogenic/venogenic impotence who underwent a vascular surgical procedure. With an average follow-up of nearly 5 years, approximately 50% of patients were cured and an additional 20% were improved. ¹⁸ After an average follow-up of 3 years, patients in the venous ligation group (n= 110) in 68% of the cases had good results. In the deep dorsal vein arterialization group (n= 153) 74% of the patients reported good results.

Current publications explored, that 3-D CT-cavernosography can provide high-resolution images of venous drainage from any angle. Therefore, the authors conclude that the images obtained by 3-D CT-cavernosography are very helpful for both the diagnosis of corporal veno-occlusive dysfunction and the anatomical study of the human penile venous system and may lead to better strategies in venous leak treatment. ^{18–22}

Interrestingly penile venous surgery with ligation of the crura for venous leakage has revealed good long-term results and high patient satisfaction. The unanimously stated conclusion from these studies is, that this technique should be offered in young men with primary cavernosal ED. Young patients with a normal penile arterial system and no risk factors such as diabetes had the best chance to improve erection and have a good postoperative success. ^{23–29}

Several further publications on minimally invasive venous leak procedures for ED have been published. Basche et al. described a technique of retrograde embolization carried out via the femoral vein by coaxial technique using Histoacryl-Lipiodol solution in order to embolize all angiographically identified insufficient veins. At one-year follow-up, all patients treated still achieved spontaneous erections without any additional medical treatment.³⁰

Cayan et al. described a highly selected group of young patients (mean age 34.6 years) with primary venogenic ED, who were submitted to extended venous ligations including crura ligation with umbilical tapes.²³ Mean postoperative follow-up was 42.9 months and IIEF scores were used for success evaluation. IIEF-5 score rose statistically significant from 6.7 to 16.3 and patient satisfaction was complete in 57.7%.

Hsu and coworkers described a venous stripping procedure in selected patients with isolated CVOD excluding untreated systemic disease. Of 341 patients 178 patients were submitted to this procedure and further 163 were left without surgery. IIEF-5 score increased from 9.7 to 21.6 after a mean follow-up of 7.7 years in the operated group, while patients under observation only showed a decrease of IIEF-5 score from 10.4 to 7.9. Operation time ranged from 2.1 to 5 hours and local anesthesia was used with additional acupuncture. All these publications denied serious complications, as well as penile shortening or loss of sensation.

Most recently an article on the outcome of crural ligation for isolated crural venous leakage in 14 young patients was published by a study group from the Memorial Sloan Kettering Cancer Center and Columbia University. The IIEF score was raised from 18 to 24 after 1 year of follow-up. Seventy-one percent experienced unassisted postoperative sexual intercourse. The authors conclude that crural ligation may be a

promising approach in those rare young patients with primary venogenic ED and isolated crural leakage.

Vale et al. reported a high long-term successful outcome in 63.6% after ligation of the deep dorsal vein.³² In a further study from Chen a highly significant change in IIEF score after long-term observation was stated for patients who underwent deep dorsal vein stripping.³³ Very recently Zang reported about very good long-term success rates after deep dorsal vein embedding (100%), respectively.³⁴

A further newly described method is the embolization technique. During this approach, either antegrade or retrograde venous closure can be performed.^{30,35–43} Results from these studies are demonstrated in Table 1.

Unlike in urology, in general surgery, there are clear guidelines for the treatment of varicose veins. 44 One of the important principles is the proximal compression of the vein, which is treated with a sclerosing/embolization agent. The reason is lying in the mode of action in these agents. The longer and concentrated the substance can stay at the venous wall, the more effective is the sclerosing action of the medication. If applied as microfoam, it can be even more effective, due to better visibility under X-ray and more homogeneous contact to the endothelium. 45

Another reason responsible for the good long-term outcome of the procedure might be the application of a Computed tomography cavernosography with 3-D reconstruction.

The superior visualization of the complex venous draining system in a 3-D CT-cavernosography before (see Figure 1) and after sclerotherapy (see Figure 2) was first described by Virag⁷ and could be verified by Uhl²¹ and Xu.⁴⁸ Figure 1 shows the complex situation in venous leakage disease and the need for a more complex renovation of the situation. It might also explain the fact, that neither simple ligation of penile veins nor ligation of crural veins could solve the problem of venous leak disease. Furthermore, these pictures might reveal the up to now unexplained relation between ED and hemorrhoids⁴⁹ and possible ED after hemorrhoid sclerotherapy,⁵⁰ due to the fact that the related veins are connected via the deep pelvic vein system. These results also demonstrate the urgent need to re-explore the venous drainage system with new higher sophisticated techniques.

TABLE 1 Literature of Embolization Technique Used in Treatment of Erectile Dysfunction^{18, 23,30,32,34–38,41,47,52,53}

Author	Year	Method	# of Patients	Short (12 months)	Long (>12 months)
Schild	1993	embolization retrograde	53	n/s	75.5%
Vale	1995	ligation	27	70%	63.6%
Nakata	2000	antegrade embolization - ethanol	23	87%	78%
Peşkircioğlu	2000	embolization- N-butyl cyanoacrylate	32	n/s	68.7%
Miwa	2001	sclerotherapy ethanol	10	70%	50%
Basche	2003	retrograde embolization	4	n/s	100%
Cayan	2008	venous surgery and crural ligation	26	0,731	64,5
Kutlu	2009	embolization	32	yes	yes
Zhang	2009	embedding deep dorsal vein	17	0,8235	n/s
Aschenbach	2013	endovascular embolization	29	0,888	n/s
Rebonato	2014	anterograde embolization	18	0,81	n/s
Herwig	2015	sclerotherapy, airblock, valsalva	96	80.21%	72.73%
Carrino	2016	sclerotherapy, airblock, valsalva	171	n/s	0,906
			n = 538	Mean 79.06%	Mean 73.74%

In a very recent study of Herwig and Sansalone these aspects are applied in a newly described technique, which reaches the deep dorsal vein system, as well as the crural venous system. 17,46,47 When preparing the deep dorsal vein at the proximal penis shaft, the ligation of the vein distally closes the primary leak from the deep dorsal vein. In addition, the afore localized major leakage point revealed by 3-D CT-cavernosography can be closed by several distal and proximal ligations. Afterward a 5F-angiokatheter is placed in the proximal part of the vein. Under Valsalva maneuver, which has to be performed by the patients, the blood flow is reduced in the lower pelvis equal to the compression described in general surgery guidelines. When injecting polidocanol as a sclerosing agent during this time, the agent can stay longer at the venous wall and the effect of the sclerosing therapy is maximized. No residual crural or deep dorsal vein leakage could be detected after integrate combined ligation of the deep dorsal vein and antergrade sclerotherapy procedure (see Figure 2). Therefore, this method is providing therapy for deep dorsal vein and crural venous leakage in a minimally invasive setting at the same time. 17,46,47

With this newly described technique, at 3-month follow-up 77 out of 96 patients (80.21%) reported as having erections sufficient for vaginal insertion without the use of any drug or additional device. Four (4.17%) patients did not report any improvement. Follow-up with colour Doppler ultrasound and CT-cavernosography revealed a new or persistent venous leakage in 8 (8.33%) of the patients. After a follow-up of 12 months (n = 22) 16 (72.73%) patients still reported as having a strong enough erection for sexual intercourse. Four (18.18%) patients used PDE5 inhibitors and 2 (9.09%) patients did not report any change to their preoperative state. As before, the authors denied serious complications.

These data have been supported by a report of Carrino et al. who reported a success rate of over 90% in over 170 patients treated with this sclerotherapy treatment. Furthermore, the cure rate for ED was 77%, which exceeds the effectiveness of PDE5-inhibitor therapy by far⁴⁷ and offers a long-term cure for the problem.

These new and encouraging results in almost 540 patients show a short-term success rate of about 80% and long-term success in 73,7 % in highly selected patients. The recent good results with this technique

FIG. 1 The superior visualization of the complex venous draining system in a 3-D computed tomography cavernosography before sclerotherapy.



FIG. 2 The superior visualization of the complex venous draining system in a 3-D computed tomography cavernosography after sclerotherapy.



lead Rebonato et al.⁵¹ to the statement, that, embolization techniques should be considered in all the cases of confirmed ED due to VOD, especially in young patients. Although the technique is not always successful restoring completely the erectile function, in most cases, the patients have a satisfactory erectile function just resorting to oral pharmacotherapy (PDE5 inhibitors) response, delaying the time to apenile prosthesis.

Although further confirmation with well-designed multi-center, randomized, controlled studies is needed, these results should lead to reconsideration of the treatment of cavernous veno-occlusive dysfunction with leakage, with these minimally invasive methods in the therapy of ED. The described methods are minimally invasive, are carried out with local anesthesia and do not contain major risks or complications. Possibly, a combined therapy model is needed to support the mostly young patients and prevent them at least partially from lifelong continuous medical treatment.

CONCLUSION

Despite the assumption that treatment of cavernoocclusive leak may be considered experimental, this systematic literature review suggests possible acceptable short-term and long-term success rates in properly selected cases, justifying a new look at this the treatment of caverno-venous leak in young men. Modern techniques such as 3-D computerized tomography with cavernosography may provide unprecedented opportunities for imaging and surgical planning. In addition, minimally invasive techniques may replace or add to an open surgical approach.

DISCLOSURE

None.

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