Surgical and minimally invasive treatment of ischaemic and non-ischaemic priapism: A systematic review by the EAU Sexual and Reproductive Health Guidelines panel

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ABSTRACT

Surgical treatments for ischemic priapism (IP) include shunts or penile implants. Non-ischemic priapism (NIP) is usually the result of penile/perineal trauma causing an arterial fistula and embolisation may be required. We conducted a systematic review on behalf of the EAU Sexual and Reproductive health Guidelines panel to analyse the available evidence on efficacy and safety of surgical modalities for IP and NIP. Outcomes were priapism resolution, sexual function and adverse events following surgery. Overall, 63 studies (n=923) met inclusion criteria up to September 2021. For IP (n=702), surgery comprised distal (n=274), proximal shunts (n=209) and penile prostheses (n=194). Resolution occurred in 18.7-100% for distal, 5.7-100% for proximal shunts and 100% for penile prostheses. Potency rate was 20-100% for distal, 11.1-77.2% for proximal shunts, and 26.3-100% for penile prostheses, respectively. Patient satisfaction was 60-100% following penile prostheses implantation. Complications were 0-42.5% for shunts and 0-13.6% for IPP. For NIP (n=221), embolisation success was 85.7-100% and potency 80-100%. The majority of studies were retrospective cohort studies. Risk of bias was high. Overall, surgical shunts have acceptable success rates in IP. Proximal/venous shunts should be abandoned due to morbidity/ED rates. In IP >48 hours, best outcomes are seen with penile prostheses implantation . Embolisation is the mainstay technique for NIP with high resolution rates and adequate erectile function.

Introduction

Priapism is defined as a prolonged erection lasting over 4 hours in the absence of sexual stimulation, which persists despite orgasm(1). Priapism is generally divided into three main groups namely non-ischaemic (high flow), ischaemic (low flow) and stuttering (recurrent)(2). Based on the arterial inflow parameters two main groups can be identified: ischaemic priapism (IP) (low-flow or veno-occlusive type), which is the main type representing 95% of all priapic episodes and non-ischaemic (NIP) or high-flow priapism (arterial type). These have different pathophysiological mechanisms, presentation, diagnostic work-up, management and prognosis (3).

Ischaemic priapism is characterized by reduced or diminished intracavernosal arterial inflow. A number of causes of ischaemic priapism have been identified, including the use of erectogenic agents and haematological disorders such as sickle cell disease (SCD). Less common causes include paraneoplastic syndromes, spinal cord injuries, recreational drugs (e.g., marijuana, cocaine) and second-generation antipsychotics (4). If IP is left untreated for > 4 hours it can cause a form of compartment syndrome, ultimately leading to permanent erectile dysfunction (ED), due to necrosis and fibrosis of the cavernosal tissues. The longer the duration of IP, the worse the severity ED and deformity, therefore IP should always be treated as a urological emergency (5). Histopathological examination of the corpora cavernosa demonstrates that within 12 hours of IP there are insignificant changes to the tissue ultrastructure. Between 12 and 24 hours, there are some alterations in the trabecular smooth muscle cells (SMC), but endothelial damage and fibrin clots are still minimal. However, after prolonged IP (24-48 hours), there is pronounced endothelial destruction, exposure of the basement membrane and subsequent thrombocyte adherence. After 48 hours there is advanced thrombus formation, denuded endothelium, necrotic SMC with transformation into fibroblast-

like cells and dense infiltration by inflammatory cells (6). Therefore, histopathologically, there appears to be irreversible structural changes to the corpora cavernosa after 48 hours. This was not apparent in high-flow priapism, suggesting more benign and favorable long-term outcomes. Non-ischemic priapism is typically related to either perineal or penile trauma and the interval between trauma and priapic episode can be days or even weeks. A fistula forms between a cavernosal artery and the lacunar spaces and unregulated arterial inflow induces an erection. Due to an intact venous system, there is normal venous outflow and as a result, erections are not rigid (7).

Various diagnostic pathways have been proposed, with penile blood gas analysis representing the fundamental diagnostic modality to differentiate between ischemic and non-ischemic priapism (8). Penile imaging of various types is also recommended, including the use of Doppler Ultrasound and Magnetic Resonance Imaging (MRI). The current EAU Guidelines on Sexual and Reproductive Health suggest performing a penile MRI to assess tissue damage in cases of refractory priapism or delayed presentation to predict smooth muscle viability[7,9,10].

A stepwise approach of various (non-)surgical options is recommended in clinical practice guidelines for the management of ischaemic priapism (9). If conservative options fail to lead to resolution, then an escalation strategy of various surgical options is undertaken. Distal shunts are the primary treatment of choice, followed by penoscrotal decompression or proximal shunts in refractory cases. If de-tumescence does not occur with these measures or in the case of priapic episodes lasting more than 48 hours, insertion of a penile prosthesis (usually malleable) is recommended(9–11). In the context of rapid tissue degradation, there is significant controversy at which time point irreversible SMC necrosis and subsequent ED occurs. Therefore, the aim of this systematic review was to define which treatment is optimal during which time frame of the IP episode.

Management of NIP does not represent a urological emergency, as venous outflow is intact and therefore, there is no risk of compartment syndrome. Conservative management includes watchful waiting, compression[12,13]. If these measures fail to address the priapism, selective arterial embolization can be used to close the fistula (12). In very rare occasions, open surgical ligation of the fistula has to be performed, although is technically challenging and associated with complications (8).

As the proportion of patients requiring surgical management for IP and NIP is small, a variety of options have been described mainly in case series. In this systematic review, we aimed to assess the efficacy and safety of proposed surgical modalities in the treatment of IP and NIP.

Materials and methods

Search strategy, selection of studies and data extraction

This manuscript was commissioned and undertaken by the EAU Sexual and Reproductive Health Guideline Panel. The protocol search strategy were depicted in Figure 1.

In short, EMBASE, MEDLINE, Cochrane and clinicaltrial.gov databases were explored systematically. Two reviewers performed the abstract, full texts and data extraction independently (UM and RV). An independent arbiter resolved any conflicts (KD). The search was restricted to the English language. Study inclusions were all randomized controlled trials (RCTs), quasi-RCTs, non-randomized comparative studies (NRCS), observational studies (including cohort studies, case-control/comparative studies, single-arm studies) and case series. Studies with less than 5 patients for case series or less than 5 patients per group for comparative studies were excluded. Moreover, commentaries, reviews, abstract-only and editorial commentaries were also excluded.

Types of participants

For ischemic priapism

The study population included all males (children/adults) who presented with priapism, excluding patients with SCD. The diagnostic criteria for IP comprised clinical and corporal blood gas analysis: persistent and painful erection with rigidity of the corpora cavernosa lasting for more than 4 hours unrelated to sexual activity or beyond sexual stimulation with evidence of deoxygenated blood ($pO2<30$ mmHg, $pCO2>60$ mmHg, and $pH<7.25$) on corporal aspiration (3).

For non-ischemic priapism

The study population included males (children/adults) presenting with NIP due to perineal or penile blunt trauma. Diagnostic criteria for NIP comprised of clinical and corporal blood gas analysis demonstrating arterial blood. Moreover, a definitive diagnosis was performed using Doppler ultrasound and super-selective radiological arteriography.

Types of interventions

For ischemic priapism

The intervention for priapism events were distal corporglandular shunts (e.g., Winter shunts, Al-Ghorab, Ebbehoj, T-shunts), open proximal shunting (caverno-/corporo-spongiosal, e.g., Quackels, Greyhack, Barry), venous shunting (caverno-/corporo-saphenous), corporal disruption (with or without an implantable penile prosthesis (IPP)) tunneling, Burnett corporal snake (T-shunt with tunneling), corporal excavation ((Hegar) dilators), transglandular T-shunt, IPP (malleable or inflatable).

For non-ischemic priapism

Interventions included radiological transcatheter arterial embolization (TAE) of arterio-venous fistula.

Types of outcome measures

The studies needed to report one or more of the following outcomes: i) resolution of acute priapism; ii) preservation of sexual function; iii) failure to resolve priapism; and, iv) surgical adverse events (e.g., penile prosthesis infection, erosion, injury to adjacent organs, prosthesis malfunction, need for revision surgery, need for removal of prosthesis, penile shortening, patient dissatisfaction, bleeding, fistula, urethral injury, wound infection). For studies where outcomes are not reported at the pre-specified time points, a descriptive text is provided.

Primary outcome measures include type of intervention, duration of IP and resolution of priapic episode.

Secondary outcome measures were adverse surgical events and erectile function.

Results

Quantity of evidence identified

The study selection process is outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) flow diagram (Figure 1). A total of 2626 abstracts were screened, of which 117 full texts were retrieved for further screening, with 63 studies meeting the inclusion criteria. The manuscripts were exclusively single-arm cohort studies and case series. Thus, the quality of evidence was considered low and risk of bias high. Risk of bias graph and summary are shown in figures 2 and 3 respectively.

Efficacy data of single arm studies for surgical shunts in ischemic priapism

In total, 35 single arm cohort studies assessed the efficacy of various surgical shunts in resolving IP (13–47). Baseline characteristics can be found in Table 1.

Accurate comparison of different (sub)types of shunts was often not possible due to separate results not being reported in the studies.

Distal shunts

Various distal shunt techniques (i.e., Winter's, Ebbehoj, T- and Al-Ghorab shunts with or without intracoporeal tunneling) were reported as primary IP treatment in 20 studies with varying results. Shunts were described in 8 studies ((13–19,45)) including a total of 119 patients (108 Winter's shunts, 6 Ebbehoj and 5 Al-Ghorab, respectively). Detumescence rates varied among studies depending on the time interval between IP onset and shunt surgery. In 5 studies ((14,17–19,45)) where median IP duration was ≤36 hours, success rates ranged between 77.7 and 100%. An overall complication rate of 18%. Sexual function was poorly reported with ED ranging between 0 and 100%. Among the 3 other studies ((13,15,16)) median time to IP alleviation ranging from 48 to 105 hours and detumescence rates between 12.5 and 42%. Nixon

et al. and Pal et al. independently reported reintervention with Al-Ghorab and proximal shunts in cases of Winter's shunt failure with success ratios of 66-100%. Due to numerous repeat procedures complications were difficult to attribute to one or other shunt technique. Overall, ED rates were 71-90% among a total of 68 patients.

T-shunts were described in 5 studies ((20,23–26)) including 70 patients of which 27 patients also underwent intracorporal tunneling using Hegar dilators. Median IP time was 48-96 hours and the overall rate of successful detumescence was 70%. In the study by Zacharakis et al. the authors reported a detumescence rate of 100% if the IP episode was <24 hours, while only 55% if 24-48 hours and 0-30% if 48-96 hours, respectively. Moreover, ED severity was associated with the duration of IP. Overall, 20-80% of patients had ED measured by either IIEF-5 or SHIM questionnaires in 3 studies. Other than the aforementioned re-interventions and ED, complications were scant.

Canguven et al. (27) described the transient distal shunt. Here, a sterile closed system blood collection set with two 21G needles were used. After the filling of the shunt-set, the needle on the other end was inserted into the glans to utilize the corpus spongiosum. The study included 15 patients with a median IP duration of 7.8 hours and detumescence in 10 out of 15 patients (66.6%). Sexual function was reported to be unchanged.

Al-Ghorab shunts (with or without Burnett snake maneuver) were performed as the primary procedure in 5 studies ((28–32)) and 64 patients. Success rates were high, ranging between 80 and 100% after a median IP duration of 36-75 hours. Overall occurrence of ED with this procedure was high (47-90%). Other complications occurred <10%.

Muneer et al.(33) investigated the non-surgical treatment options for stuttering priapism. Described were penile prosthesis in 3 patients, orchidectomy in 2 patients (both 100% success), TAE in 5 (20% success), Winter's shunt (n=1), Al-Ebbehoj shunt (n=1), cavernosal ligation

(n=1) and phenylephrine drug delivery system (n=1) (latter four procedures had 0% success rates).

Penoscrotal decompression

A novel technique of penoscrotal decompression (PSD), which involves uni- or bilateral proximal corporal incision, has recently been proposed by Baumgarten et al.(48) . 10 patients underwent unilateral and 15 bilateral PSD. Resolution rates were 8/10 (80%) and 15/15 (100%), respectively. Median priapism duration was 71 hours. Out of 15 patients who had adequate follow-up, 9 (60%) had sufficient erectile function for penetration with or without PDE5-I.

Proximal shunts

Various proximal shunts have been described in the literature with the two most common techniques being corpora-spongiosal (Quackle's) and corpora-saphenous (Grayhack) shunts, although they were not described separately and thus amalgamated here. These were performed in 14 studies ((13,34–44,46,47)) accruing 184 patients. Median duration of IP ranged between 5.6 and 168 hours. Detumescence was achieved in 54-100% of patients. Conversely, the study by Klein et al. described the resolution of IP in only one out of 8 (12.5%) patients with subsequent 87.5% ED rate. Additionally, Pantaleo-Gandais et al. and Lawani et al. described a total of 31 patients receiving crural incisions/cavernotomies. Results of the cavernotomies were not described separately, but 49/53 (92.5%) of patients in the study by Lawani et al. achieved resolution IP after 24 hours. Overall, potency rates were 22.8-54.3% across studies.

Micoogullari et al. described Barry's deep dorsal vein shunt technique and reported 100% resolution rate in 10 patients with no adverse events and 8/10 patients preserved erectile function.

Kilinc et al. described the use of a corpora-cephalic vein shunt in 15 patients. Mean duration of IP was 20.1 hours with a 86,6% achieving detumescence. Three out of 13 (23%) patients at follow-up reported ED at 12 months. No major complications were reported.

Penile prosthesis insertion for ischemic priapism

Penile prosthesis insertions after conservative therapy or distal shunts were described in 7 studies ((9,21,22,49–52)). In early penile prosthesis insertion, median time to surgery was between 35 and 209 hours. In total, 194 patients received penile implants for prolonged IP with 32 patients receiving an inflatable penile prosthesis (IPP) and 162 a malleable penile prosthesis (MPP). All patients achieved detumescence in each study and had a 90-100% overall satisfaction, with 84-100% of patients resuming sexual intercourse. One study by Zacharakis et al. made a distinction between early penile implantation (n=68) (median IP 7 days) and delayed penile implantation (n=27) (median IP 5 months). In the early implantation group, only 8.8% (6/68) of patients required revision, and increased to 26% (7/27) with delayed implantation. Moreover, satisfaction was higher in the early implants (96%) compared to the delayed (60%) group. Lastly, penile shortening occurred in 2.9% (2/68) of the early patients versus 40% (11/27) of the delayed prostheses. In all other studies, complications were limited and can be viewed in detail under Table 1.

Embolisation (TAE) for non-ischemic, high-flow priapism

Overall, 22 studies (12,53–73) accruing a total of 221 patients have been found dealing with TAE for NIP. Median duration of NIP before surgery was ranging between 1 and 117 days. The most frequent complication was the need for re-embolization (re-TAE) and occurred in 80.9% of studies (17/21) and in 6.3-40% of patients either during short- or long-term follow-up. Sexual

function was mostly (78-100%) maintained at the level of premorbid states (12,53–73). Other complications were scarce.

DISCUSSION

In the present study, the available literature was reviewed systemically for the surgical treatment options and outcomes for priapism. Specifically, distal and proximal shunt variations and penile prosthesis implantation for IP and TAE for NIP were analysed. Of the 63 retrieved articles, all were retrospective, single arm cohort studies and case series. Therefore, based on the overall poor quality of available evidence, results should be interpreted with caution.

As IP is a true urological emergency, delaying effective treatment by "self-help" options or oral pharmacotherapy are ill-advised. In this context, the near absent corporal blood flow would impede the efficacy of medications such as oral pseudoephedrine (74). Intracavernosal interventions (aspiration + irrigation with cold saline and/or phenylephrine) should be commenced as soon as possible. Considering the high success rates, surgical shunting should not be attempted until aspiration and saline irrigation and alpha-adrenergic agents have been performed. The decision, however, to end non-surgical treatment and commence surgical interventions is ultimately based on the clinician's choice and it depends mainly on the duration of the priapic episode itself. With increasing priapism duration, the detumescence rates achieved by intracavernosal irrigation becomes exceedingly small. Anoxia and acidosis of >36-48 hours causes significant tissue damage and an impaired contractile response of the smooth muscle cells to alpha adrenergic agonists such as phenylephrine (75).

If this fails, a distal corpora-glandular shunt should be performed. The ideal shunt (Winter's, Al-Ghorab, Al-Ebbehoj, T-shunt with or without intracorporal tunneling) therefore could not be defined from the available data. Most studies included small patient populations and relied

on retrospective data collection; moreover, there have been no studies directly comparing the various distal shunts or the necessity of intracorporal tunneling. Winter shunts appears to be effective in IP lasting less than 36 hours, with detumescence rates between 77.7 and 100%. T-shunts appear to be 70% effective in treating IP episodes of 48-96 hours, but ED was reported to occur in 20-80% of cases. Additionally, Al-Ghorab shunts (with or without tunneling) have very high success rates (80-100%), but with the added drawback of even higher deleterious effects on erectile function (47-90%). Complications with distal shunts included (low) rates of cavernositis, hematoma, urethro-cutaneous fistula, urethral injury and skin necrosis. Moreover, in the study by Baumgarten et al. penoscrotal decompression was highly effective with 80-100% detumescence rates (48).

The use of proximal shunts should be considered optional and a largely historic procedure. Several proximal shunts are described including corpora-spongiosal (Quackels), corpora-saphenous (Grayhack) and corpora-cephalic shunts. Across the 13 studies, outcomes were not reported rigorously and the patient cohorts were highly heterogenous. There was an overall high detumescence rate of 54-100% along with low potency rates of 23-54%. The low number of studies and publication years (nearly all studies published between 1972 and 2000) suggests proximal shunts are a historical procedure, with very few surgeons now utilizing these procedures. Moreover, due to the paucity of data, the extent of long term sequelae (e.g., ED, fistulae, infections) may be severely underestimated.

For shunt-refractory IP or untreated IP >48 hours a penile prosthesis implantation can be considered. This was investigated in 7 studies including 194 patients, with a large proportion (162/194, 83.5%) undergoing a MPP implantation. The available data suggests penile prosthesis implantation to be highly effective in achieving detumescence (100%), resuming ability to have penetrative intercourse (84-100%) and high overall satisfaction (90-100%). If performed early, revision rates were low (ca. 9%) and penile length was preserved in all but 3%

of patients. If the decision is made to perform delayed implantation, the patient should be made aware of increased complication rates (26% revision rates) and penile length loss in 40% of patients. The difference between malleable and inflatable prostheses is difficult to assess, since MPP accounted for 83.5% of all implanted devices in refractory priapic episodes.

Considering non-ischemic priapism, conservative management included perineal compression, which can be performed under US guidance. Regarding surgical approaches, the use of TAE (either unilaterally or bilaterally) is described in 22 studies. A variety of materials has been described in the literature including autologous blood clots, microcoils, gelatin sponges, polyvinyl alcohol (PVA), N-butyl-cyano-acryl (NBCA) and combinations of different materials. NIP should be treated within 3 months of onset, as there is some evidence that corporal fibrosis may occur after this time point. Overall, it was considered a very safe (namely, rarely reported cases of groin hematoma) and effective procedure (78-100%, with full erectile function recovery in 78-100%), although with relatively high (6.3-40%) re-embolization rate.

Limitations

The majority of the included studies were retrospective case series with heterogeneous methodology and it is therefore difficult to make direct comparisons of interventions between studies. Similarly, outcomes of treatment in the short and long-term were often lacking as well as reports of complications from the different interventions. Therefore, the current findings should be interpreted with caution.

Future perspective

A prospective multicentre registry capturing both early (e.g., resolution rates) and late (e.g., erectile function) surgical treatment outcomes would add to the evidence base in this area.

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CONCLUSION

Failure of conservative management of ischemic priapism should prompt rapid surgical treatment using distal shunts. T- or Al-Ghorab shunts with or without intracorporeal tunneling resulted in high detumescence rates, although lead to a significant risk of erectile dysfunction. If available, immediate placement of malleable penile prosthesis can be considered in selected patients with low flow priapism longer than 48 hours.

High-flow priapism can often be successfully managed using transcatheter arterial embolization, although repeat embolization may be necessary to achieve full detumescence.

CONFLICT OF INTEREST

The authors have no relevant conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

AUTHOR CONTRIBUTION STATEMENT

Concept and design: UM, AC, RV, KD, LB, PC, NC, MG, GH, VM, GIR, TT, MIO, CB, JC, YY, GC, HJ, AK, JIMS, PV, ECS, SM, AS; Acquisition of data: UM, AC, RV, KD; Analysis and interpretation of data, UM, AC, RV, KD, SM, AS; Drafting of the manuscript: UM, AC, RV, KD, LB, PC, NC, MG, GH, VM, GIR, TT, MIO, CB, JC, YY, GC, HJ, AK, JIMS, PV, ECS, SM, AS; Critical revision of the manuscript for important intellectual content: UM, AC, RV, KD, LB, PC, NC, MG, GH, VM, GIR, TT, MIO, CB, JC, YY, GC, HJ, AK, JIMS, PV,

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Supplementary methods

Search strategy, selection of studies and data extraction

Assessment of risk of bias

The 'risk of bias' (RoB) of each manuscript was reviewed by two independent authors (UM, AC). Resolution of disagreements was performed by consulting a third author (KD). RoB in RCTs was assessed by using the *Cochrane Handbook for Systematic Reviews of Intervention*. This included 'random sequence generation'; 'allocation concealment'; 'blinding of participants and personnel'; 'blinding of outcome assessment'; 'incomplete outcome data'; 'selective reporting'; and others. RoB in non-randomised articles were determined by all of the above domains, and a surplus item to assess the risk of findings being explained by confounding. Sequence generation and allocation concealment were retained as domains but were assessed by default as 'high risk of bias' given the non-randomised nature of these studies. Four of the most important potential confounders for benefit and harm outcomes were developed *a priori* with clinical content experts (EAU Sexual and Reproductive Health Guidelines Panel). The potential confounding factors were:

- Comorbidity including infections, haematological and neurogenic disorder
- Usage of medication such as ant-depressant and alpha blockers.
- Alcohol and drug use
- Use of erectogenic medications (such as intracavernosal injections)

For each study, a pragmatic assessment of the confounding bias risk was performed. We considered the following queries:

1. Was there a consideration of the prognostic confounder? (yes/no)? If ‘no’, a high RoB was attributed to this confounder. If ‘yes’ go to question 2.
2. Was there a balance in the confounder between the interventional/treatment and control group (yes/no)? If ‘yes’, the study was considered a low RoB. If ‘no’, go to question 3.
3. If the authors controlled for the confounder (e.g. statistical was controlled for in the analysis, for example by statistical analysis - multivariable regression models or propensity score matching). If ‘yes’, the study was considered a low RoB. If ‘no’ risk of bias was high.

RoB in non-comparative studies cannot be assessed with the above method. Therefore, external validity of non-comparative studies was addressed (can the results of this study be applied to different people, places or time?). This was done by assessing: (1) the presence of an a priori protocol? If ‘no’, RoB was high. (2) Was there an inclusion of the total population or were study participants selected consecutively? If ‘no’, the study was considered at high RoB. (3) Was there a complete outcome data collection for all patients and/or missing data sufficiently clarified or unlikely to be relevant to the outcome? If ‘no’, the study was at ‘high’ RoB. (4) Were all pre-specified and expected outcomes of interest reported? If ‘no’, the study was at high RoB. (5) Appropriate measurement of primary benefits and harms? If ‘no’, the study was at high RoB. If ‘yes’ could be answered to all 5 questions, then the study was at low risk of bias. The ROBINS-1 tool was a pragmatic approach informed by the methodological literature(76,77).