Outcomes of low-flow priapism and role of integrated penile prosthesis management

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Abstract

Background: The natural history of priapism and predictors of erectile dysfunction (ED) remain vague due to defective reporting, different management techniques and variable follow-up durations. Acquiring more information concerning the prognosis of erectile function after priapism can help to assess the burden of post-priapism ED. Also, it may guide the decision-making process regarding penile prosthesis insertion in refractory and late post-priapism ED. In this study, we tried to evaluate the state of erectile function after recovery and how far penile implant surgery could be integrated in the early and late management of priapism-related ED.

Methods: We included 72 patients with low-flow priapism who were managed via a stepwise approach starting from aspiration through percutaneous distal shunt up to distal shunt. Immediate placement of a penile prosthesis was completed in eight refractory patients, including three that were inserted even before an open distal corporoglanular shunt.

Results: Nearly two-thirds (70.3%) of recovered priapism patients developed ED, but penile prostheses were inserted only in 35.5% of ED cases. There were no differences in the short- and long-term complications of immediate versus delayed prosthesis placement except for difficulty with the insertion of the penile prosthesis in delayed procedures.

Conclusions: Immediate placement of a penile prosthesis is a good treatment option in the setting of refractory priapism with comparable outcomes to those of patients with post-priapism ED who received prostheses. Immediate penile prosthesis insertion was further justified by the high incidence of post-priapism erectile dysfunction.

1 Background

Long-lasting penile erections are closely associated with the Greek god Priapus, who is the son of Dionysus, god of the vine, and Aphrodite, goddess of beauty. When Aphrodite was pregnant, the story was that her mother, Hera, was jealous and placed her hands on the belly of her daughter, uttering a curse. As a result, Aphrodite gave birth to Priapus, a misshapen dwarf with a large, erect penis. This myth expresses the mysterious nature of priapism till now [1].

Priapism is a relatively uncommon medical emergency [2]. Low-flow priapism, also known as ischaemic priapism, is a persistent unwanted painful erection that lasts more than 4 h characterised by little or no cavernosal blood flow and abnormal cavernous blood gases [3].

Low-flow priapism has been reported due to a variety of causes. Haematological diseases, metabolic or neurological disorders and some erectile dysfunction (ED) medications have been implicated [4–7]. Priapism is very rare in men who use phosphodiesterase-5 inhibitors; meanwhile, an incidence of 0% to 35% has been reported in men taking intracavernosal injection, depending on the drug used and how the study defined priapism [8–12].

The goal of treatment of men with ischaemic priapism is to regain a detumescence state, relieve compartment syndrome and regain proper erectile function [13]. The available techniques to obtain complete detumescence range widely and can be applied in a stepwise pattern, starting with cavernosal aspiration and irrigation with...
or without intracavernosal injection of vasoactive agents like phenylephrine [13].

Delays in treatment and refractory cases lead to cellular, molecular and morphological changes in the corpus cavernosum and, finally, permanent ED results from tissue injury [14]. ED is the outcome in 50% of cases. However, recovery of erectile function may be seen in up to 44% of patients who experience ischaemic or low-flow priapism for 24–36 h [15].

Recently, some studies have recommended the immediate insertion of a penile prosthesis in refractory cases because of the high incidence of fibrosis within the cavernosal spaces in the long term, which may make delayed prosthesis insertion a difficult task [16].

In this series, we attempted to discern the long-term outcomes of patients with low-flow priapism after introducing different treatment modalities and to assess the degree of ED after recovery in correlation with the timing of penile implantation (either immediately intraoperatively or during long-term follow-up after recovery of ischaemic priapism) in men with refractory ED.

2 Methods

We selected a retrospective cohort of 114 patients who had been diagnosed and treated for low-flow priapism between April 2012 and May 2018. Contact with the patients was established in 103 cases at different post-priapism intervals ranging from 38 to 64 months, with a median follow-up duration of 43 months.

We retrieved the files of the 103 patients’ who were we were able to contact. We could make use of the uniform protocol of our institute to study the results of selected cancer. The management of patients included a thorough clinical examination of patients presenting to the emergency department with priapism with a special emphasis on assessing the duration, rigidity, history of erectogenic drugs, intracavernous injection ICI, psychiatric disease and blood disease. All patients had documented penile duplex ultrasound scans confirming low-flow priapism in their files.

Eight of 103 patients were ultimately excluded before the study commenced as three were diagnosed with sickle cell disease and managed conservatively by repeated aspiration with oxygenation, alkalisation and adequate hydration, and five were found to have refractory priapism and either underwent immediate prosthesis placement or were barred from the procedure due to availability/administrative issues. Finally, an additional 23 patients were excluded during and after the study period due to different medical causes as illustrated in the flowchart in Fig. 1, and a total of 72 patients were included.

Informed consent was obtained in all cases after patient counselling about the available management modalities, treatment failure, alternatives and possibility of ED. Immediate placement of a malleable penile prosthesis was adequately explained as an alternative choice together with its consequences. Local penile block was performed prior to aspiration with or without irrigation with 30 mg/1 mL of ephedrine diluted in 10 mL of distilled water. In all cases, 1 mL of diluted ephedrine was injected intracorporally every 5 min up to 10 injections total until detumescence was observed with monitoring of both pulse and blood pressure. Intraoperatively, 2 mL of aspirated blood was routinely sent for blood-gas analysis. Immediate recovery was confirmed by relief from painful penile rigidity and peak systolic velocity PSV of cavernous blood flow of more than 28 cm/s on penile duplex ultrasound. Refractory cases were subjected to percutaneous glanulocavernous shunt insertion; if this failed, patients were shifted to an open distal shunt.

Eight patients with refractory priapism received penile prosthesis immediately under spinal anaesthesia. Following adequate sterilisation and surgical draping, closure of button corporotomy of the distal shunt was performed in five cases with absorbable Vicryl 2 sutures (Ethicon, Somerville, NJ, USA) immediately after dilation. The insertion of a semi-rigid malleable penile prosthesis (Genesis, Coloplast) was done through subcoronal incision. The anchoring suture was taken through the body of the cylinders of the prosthetic implant to the edge of the corporotomy to prevent extrusion in patients with failed open distal shunt. All patients received amikacin 250 mg and vancomycin 1 gm by slow intravenous infusion with the decision to proceed with the prosthetic insertion and for up to 48 h postoperatively with monitoring of renal function.

Patients who received penile prosthesis implants underwent the same procedure described above except for closure of the corporotomy. Corporeal dilation was performed with carefully controlling the axial torque.

Patients were continued on an oral antibiotic course for 2 weeks. The patient was seen in the postoperative period at least twice weekly. Approximately, 4–6 weeks after implantation, patients were taught how to use the prosthesis. Patients were instructed not to have intercourse before the passage of 6–8 weeks. All patients with prostheses were discharged on the third day and showed no mechanical dysfunction at the last follow-up visit.

Included patients were prospectively evaluated at the outpatient’s clinic, where an explanation of the nature and aim of the study and a written informed consent form were provided. After granting approval, patients underwent a throughout clinical examination with complete medical and sexual history, focusing on the onset and duration of priapism, history of previous intermittent attacks, presence or absence of haematological disorders,
Fig. 1 Flow chart of study cases and outcome of erectile function

114 patients with low flow "priapism"
- 11 lost contact
- 3 patients with sickle cell "disease"
- 3 patients with cardiac dysfunction (class II or more according to American Heart "Association"
- 5 patients refractory priapism refused "immediate prosthesis"
- 9 patients due to presence of uncontrolled/complicated "DM"
- 8 patients with late onset hypogonadism (serum testosterone level < 250 ng/dl corrected after SHBG serum "level"
- 3 patients were excluded due to sexual inactivity

72 patient included in the "study"

Evaluation of ED (SHIM "score, Penile duplex...etc.

8 patients had immediate penile prosthesis excluded from ED evaluation

45/64 had ED (70.3%)

24 patients needed penile "prosthesis"

16/45 patients needed late penile prosthesis (35.5%)
comorbidities and any previous management attempts and their results. The evaluation of erectile function in all patients except those who received prostheses immediately was performed. Evaluations were performed using the Sexual Health Inventory for Men questionnaire and penile duplex ultrasound. Patients also underwent laboratory investigations including total and free serum testosterone levels, sex hormone-binding globulin, prolactin, estradiol, thyroid-stimulating hormone, triiodothyronine, thyroxine and haemoglobin A1c for diabetic patients. Cardiac consultations were conducted in all cases with ED for the assessment of cardiac function and diagnosis of ischaemic heart disease.

All data were analysed using the Statistical Package for the Social Sciences software version 18.0 (IBM Corporation, Armonk, NY, USA). Data were statistically described as mean ± standard deviation (SD), median and range or frequency (number of cases) and percentage when appropriate. A comparison of numerical variables between the study groups was performed using the Mann–Whitney U test for independent samples. When comparing categorical data, the Chi-squared test was used, while Fisher’s exact test was used instead when the expected frequency was less than five counts.

Our study was performed according to the ethical considerations of the Declaration of Helsinki and with local ethical committee approval.

3 Results
The mean ± SD age was 41.2 ± 17.4 years, ranging from 8 to 71 years among all study patients, with 52.8% of patients being 19–45 years old (Table 1). In 47% of cases, the cause of priapism was not identified and the case was classified as idiopathic, followed by ICI during penile duplex ultrasound in 33.3% and 19.4% appearing after ICI home therapy (Table 1).

One-quarter of patients sought medical advice within the first 6 h after the onset of priapism, with a mean ± SD duration of priapism of 31.7 ± 26.4 h, ranging from four to 90 h (Table 1). Aspiration with or without injection of vasoactive agent was the most commonly used modality, with recovery in 45 cases (62.5%), followed by percutaneous distal shunt in 17 cases, including three that were unresponsive and who progressed to immediate penile prosthesis placement. The remaining 10 of 72 cases received open distal shunts from the start; five achieved detumescence and the other five received immediate penile prostheses (Table 1).

Detumescence was achieved in 88.9% of cases after active management (Table 2). Patients who presented at 48–72 h or later showed a significant difference in the proportion of recovered/unrecovered cases when compared to those coming earlier than 48 h. (Table 2).

When comparing between recovered and unrecovered cases, we found that there was no statistically significant difference regarding the mean age at onset, but there were statistically significant differences regarding early recovery and the mean duration of priapism (Table 2). Also, there were no statistically significant differences concerning the distribution of different age groups between recovered/unrecovered cases (Table 2). No significant difference in the rate of successful recovery between the different causes of priapism was apparent (Table 2).

After the exclusion of cases with immediate penile prostheses, ED affected 67.2% of the study population at 5 years of follow-up. Patients with mild ED according to the Sexual Health Inventory for Men totalled 57.8% of all ED cases (Table 3). Penile prostheses were required in 25% of recovered cases, in addition to eight cases who received immediate intraoperative penile prostheses; thus, penile prostheses were necessary in 33.3% of total cases of priapism included in this study (Table 3). Smaller prosthesis girths (median: 9.5 mm) and shorter hospital stay lengths (all patients were discharged on the first postoperative day) were recorded in 16 of 43 ED patients who received delayed penile prostheses after recovery from priapism as compared with those given immediate prostheses. (Median girth was 11 mm and

### Table 1 Descriptive of study patients

| Parameter                          | Subcategories                  | No (n = 72) | %   |
|------------------------------------|--------------------------------|-------------|-----|
| Age groups                         | <19 years                      | 7           | 9.7 |
|                                    | 19–45 years                    | 38          | 52.8|
|                                    | 45–65 years                    | 15          | 20.8|
|                                    | >65 years                      | 12          | 16.7|
| Causes of Priapism                 | Idiopathic                     | 34          | 47.2|
|                                    | Post-ICI for Duplex            | 24          | 33.3|
|                                    | Post-home ICI therapy          | 14          | 19.4|
| Duration of priapism (h)           | Less than 6 h                  | 18          | 25.0|
|                                    | 6–12 h                         | 8           | 11.1|
|                                    | 12–24 h                        | 11          | 15.3|
|                                    | 24–48 h                        | 12          | 16.7|
|                                    | 48–72 h                        | 15          | 20.8|
|                                    | More than 72                   | 8           | 11.1|
| Different management level of study cases | Aspiration and irrigation   | 23          | 31.9|
|                                    | Aspiration, irrigation with vasoactive agent | 22 | 30.6|
|                                    | Percutaneous shunt             | 17          | 23.6|
|                                    | Open distal glanular shunt     | 10          | 13.9|
| Success                            | Recovery                       | 64          | 88.9|
|                                    | Refractory                     | 8           | 11.1|


hospital stay median length was 3 days.) However, there were no statistically significant differences regarding the frequencies of different short- and long-term complications in patients with immediate versus delayed prostheses. Even at different intervals of penile prosthesis placement, there was no statistically significant difference (Table 4).

Considering erectile function in the long-term after priapism, the study results documented that there was no statistically significant difference between the mean age at onset of priapism, frequency distribution of age groups, mean duration of priapism until active treatment, modality of treatment and development of ED (Tables 5).

We also found that the aetiology of priapism had no significant impact on the rate of occurrence of ED after priapism at 5 years of follow-up (Table 5).

4 Discussion

The uncommon presentation of priapism and emergency nature made it difficult to recruit large number of cases. Also, proposal of prospective studies addressing different aspects of priapism diagnosis and management is...
challenging and requires very long duration. In our study, we tried to bypass such difficulties by gathering any priapism cases during or before the study retrospectively by reviewing patient files and contacting them for prospective evaluation at any time at different post-priapism interval. Furthermore, uniform management always was the role of our institute which enabled us to address late outcome of priapism in relatively short study duration.

It was reported that among patients with ischaemic priapism, resolution occurred in 81% of patients treated with epinephrine, in 70% treated with metaraminol, in 43% treated with norepinephrine and in 65% treated with phenylephrine [14].

In our study, we excluded those with haemoglobinopathies due to unusual presentation [15], different prognosis and outcome as potency may be reserved in many cases in a different age groups [16].

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Table 5 Factors affecting occurrence of late onset ED post-recovery of low-flow priapism

| Parameter                  | Subcategories               | No   | ED (n = 64) | p value |
|----------------------------|------------------------------|------|------------|---------|
| Time to initial management | Less than 6 h.              | 16 (34%) | 2 (11.8%) | 0.5     |
|                            | 6–12 h                       | 4 (8.5%) | 4 (23.5%) |         |
|                            | 12–24 h                      | 6 (12.8%) | 5 (29.4%) |         |
|                            | 24–48 h                      | 10 (21.3%) | 4 (23.5%) |         |
|                            | 48–72 h                      | 8 (17%) | 2 (11.8%) |         |
|                            | More than 72                 | 3 (6.4%) | 0 (0%)     |         |
| Age groups                 | < 19 years                   | 7 (14.9%) | 0 (0%)     | 0.4     |
|                            | 19–45 years                  | 23 (48.9%) | 10 (58.8%) |         |
|                            | 45–65 years                  | 9 (19.1%) | 3 (17.6%) |         |
|                            | > 65 years                   | 8 (17%) | 4 (23.5%) |         |
| Cause of priapism          | Idiopathic                   | 19 (40.4%) | 8 (47.1%) | 0.2     |
|                            | Post-ICI for Duplex          | 14 (29.8%) | 6 (35.3%) |         |
|                            | Post-home ICI therapy        | 7 (14.9%) | 3 (17.6%) |         |
| Level of management        | Aspiration and irrigation    | 18 (38.3%) | 5 (29.4%) | 0.1     |
|                            | Aspiration with injection of vasoactive agent | 18 (38.3%) | 4 (23.5%) |         |
|                            | Percutaneous shunt           | 8 (17%) | 6 (35.3%) |         |
|                            | Open distal glanular shunt   | 3 (6.4%) | 2 (11.8%) |         |

There were no statistically significant factor that affected occurrence of ED on 5-year follow-up of recovered low-flow priapism.

Similarly, our results showed that 100% of refractory priapism cases were those who sought care at least 2 days after the onset of priapism (Table 2).

Aspiration with or without injection of a vasoactive agent was successful in nearly two-thirds of cases initially. However, once the patient failed percutaneous shunting and was considered for an open distal corporoglanular shunt, there was a 50% risk of failure to reach detumescence in our series (Table 1).

The decision to place a distal corpora glanular and/or proximal corporospongiosal shunt depended upon the surgeon’s experience and preference. However, as a principal consideration, it is better to introduce a distal shunt—either percutaneous or open corporoglanular—before moving to try the proximal one [19]. In our series, we had no cases with proximal shunts because we prefer to avoid this method and have no experience with this kind of surgery.

An intractable case of low-flow priapism with a duration of more than 48 h was almost ended by severe ED in addition to the great possibility of intracorporal damage. In this situation, an argument can be made for going directly to intraoperative insertion of a semi-rigid penile prosthesis to avoid corporal damage if the surgery is delayed with subsequent severe ED [17]. Thus, we have previously adopted immediate intraoperative penile implants in men with intractable ischaemic priapism. In this series, we performed immediate intraoperative penile prosthesis placement in eight patients,
three of whom previously failed distal percutaneous shunting and five of whom failed with open distal shunting to relieve priapism. Justification for this policy is that the insertion of a semi-rigid penile prosthesis after the occurrence of intracorporeal damage and severe cavernous fibrosis following prolonged intracorporeal priapism or recurrent priapism is considered a formidable surgical challenge with a high incidence of complications [12, 20–22].

The most important intraoperative and postoperative complications in cases marked by immediate insertion of a penile prosthesis include urethral injury, erosion of the tunica albuginea, distal migration of the prosthesis through the distal corporoglanular shunt site, wound and/or penile skin infection and decreased penile length [23]. Also, it was reported that previous percutaneous shunt and/or open distal shunt procedures in addition to the presence of advanced tissue oedema are risk factors for wound and implant infections, respectively [24]. We tried to prevent such complications by closure of the corporotomy and using an anchoring suture to prevent migration of the cylinders. Also, we only used semi-rigid penile implants, which are also cost-effective and less liable to erosion and extrusion.

Regarding more late priapism-related events, unrecov- ered priapism has irreversible consequences for affected patients, occurring secondary to a disturbance in the cavernosal anatomy, in addition to functional changes in the two corpora cavernosa, which result in refractory ED with intracavernosal fibrosis [4, 5, 7, 22, 24, 25]. Those anatomical and functional changes are the result of limited or no cavernosal arterial flow, with subsequent ischaemic changes and acidosis that is relieved only by release from compartment syndrome. Hypoxic and inflammatory changes are evident 12 h after the onset of priapismic attacks, with destruction of the sinusoidal endothelium [26]. It has been reported that extensive necrosis of cavernous smooth muscle in men presented at a mean time point of 48 h; however, there is no specific cut-off point after which irreversible damage becomes evident. Therefore, timely treatment of this urological emergency is highly important [27].

In our series, nearly two-thirds of patients presented with ED in our study by 5 years. There was a higher incidence of ED in our study than that reported by previous research because we extended the duration of priapism to at least 36 h [27]. Also, ED developed in 90% of patients with ischaemic priapism of more than 24 h in duration, which was reported by a previous study [27].

Our results in this series indicate that there was no statistically significant difference between the age group distribution and the occurrence of ED. Also, no significant relationship between different durations of priapism, cause of priapism, management modality and occurrence of ED was apparent.

A high incidence of penile prosthesis implantation in post-priapism ED cases was noted in our study in that one-third of patients with late ED received a penile prosthesis. Also, we experienced difficulty in dilating patients with recovered priapism, which may be a consequence of corporeal fibrosis or the healing process at the site of the distal shunt, which, in most cases, limited the dilation to a smaller girth of the prosthetic cylinder than that believed to be needed.

Despite the intraoperative difficulty in dilation prior to the insertion of a penile prosthesis in delayed ED cases, no perforation or urethral injuries were recorded due to carefully controlled dilation from the subcoronal incision. All cases resolved well despite three with postoperative skin infections and one with superficial infection originating at the shunt site, which were treated promptly (Fig. 2). Our results showed no clinically or statistically significant difference in the rate of early or late complications after penile prosthesis placement.

5 Conclusion

Initial management in the early hours with aspiration and irrigation with or without intracavernosal injection of sympathomimetic drugs can relieve most cases of ischaemic priapism. However, once refractory priapism is encountered, an immediate penile prosthesis may be needed despite distal shunting in the initial treatment.

![Fig. 2 A case of immediate penile prosthesis after failed percutaneous distal shunt, mild superficial infection occurred at site of shunt but was treated promptly](image-url)
Late post-priapism ED occurred in nearly two-third of recovered priapism patients, with nearly one-third requiring penile prostheses. There was no difference in the early and late complication rate between immediate and delayed prostheses apart from a surgical challenge inherent with the insertion of penile prostheses in delayed cases. Thus, immediate penile prosthesis placement is preferred in unrecovered cases of priapism as an alternative to more complex shunt procedures.

Abbreviations
ED: erectile dysfunction; SD: standard deviation.

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Authors’ contributions
All authors have read and approved the submitted manuscript, and they are personally accountable for the author's own contributions. AMF designed research idea, practical part including advanced patients’ evaluation and percutaneous distal shunting procedure and assisted in penile prosthesis insertion, collected data, carried out statistical analysis and wrote manuscript.

Ethics approval and consent to participate
Our study was done on human participant after well-informed written consent at every step of management and at study inclusion which is a basic requirement of the institutional review board; patients who refused the study were announced for alternative choices and excluded from the study. Study was done according to ethical consideration of Helsinki Declaration and with commitment to ethical committee, namely Research Ethics Committee of Ministry of Health (IRB No. 0000687).

Availability of data and materials
Data are available and ready to be shared.

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Consent for publication
All patients who received any medical service at our institute signed in informed consent for publication of their data conditioned with the privacy and coding of their data.

Competing interests
The authors declare that they have no competing interests.

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