

# Comparison of outcomes in malignant vs. non-malignant ischemic priapism: 12-year experience from a tertiary center

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## ABSTRACT

**Objective:** Data on outcome of patients with ischemic priapism (IP) due to malignant causes are scant. In this study, we compared outcome of patients with malignant vs. non-malignant IP in adult North Indian men.

**Material and methods:** We analyzed medical records of patients with IP who presented to a large tertiary care referral center from August 2005 to July 2017.

**Results:** Data of 71 patients were analyzed. The median age was 30 years (range 17-65). The average duration of symptoms was 4.39 days (range 1-10). Most common etiology was idiopathic in 29 (40.84%), chronic myeloid leukemia (CML) in 24 (33.80%), and drug-induced in 15 patients. Thirty-eight patients underwent distal shunts, while nine patients underwent proximal shunt procedure. Men with malignant priapism (CML) had significantly lower success rates with interventions, prolonged hospital stay, and higher complications ( $p<0.05$ ). Most complications after shunt surgery were minor (Clavein grade 1 and 2). After shunt surgery, bleeding at shunt site was observed in 14 cases, and wound infection developed in five patients. Prevalence of erectile dysfunction in patients at follow-up was high.

**Conclusion:** Men with malignant priapism (CML) had significantly lower success rates with interventions, prolonged hospital stay, and higher complications than men with non-malignant priapism.

**Keywords:** CML; ischemia; low flow; malignancy; priapism; shunts.

## Introduction

Priapism is the full or partial erection of penis unrelated to sexual activity or beyond sexual stimulation that persists for four or more hours.

<sup>[1]</sup> Priapism incidence has been reported to be 0.3-1.0/100,000 males/year.<sup>[2]</sup> As compared to high-flow and stuttering priapism, low flow (ischemic priapism, IP) is the more common type of priapism.<sup>[1]</sup> In IP, there is a persistent and painful erection due to decreased or absent arterial inflow resulting in marked rigidity of the corpora cavernosa, which resembles penile compartment syndrome.<sup>[1,3]</sup> IP is a urological emergency that requires prompt treatment. The successful management of IP involves achieving timely detumescence and preserving the erectile function. Based on the geographic location, various etiologies of priapism have been reported in the literature.<sup>[4-6]</sup> Only a few studies have reported etiology and outcome of

patients with IP from the Indian subcontinent.

<sup>[7]</sup> To the best of our knowledge, literature on outcome of patients with IP due to malignant causes is scant. So in this study, we compared the outcomes of IP based on etiology (malignant vs. non-malignant) in adult North Indian men.

## Material and methods

We analyzed data of all patients with IP who presented to a large tertiary care referral center between August 2005 and July 2017. Informed consent was obtained from all the participants for treatment, and ethical approval for this study was taken from the institutional ethics committee (3018/Ethics/R-cell-18). The diagnostic criteria for IP comprised clinical and corporal blood gas analysis criteria: persistent and painful erection with rigidity of the corpora cavernosa lasting for more than four hours un-

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related to sexual activity or beyond sexual stimulation with evidence of dark deoxygenated blood ( $pO_2 < 30$  mmHg,  $pCO_2 > 60$  mmHg, and  $pH \leq 7.25$ ) on corporal aspiration.<sup>[1,5]</sup> Penile color Doppler ultrasonography (CDU) was performed only in doubtful cases. Medical records were analyzed for age, chief presenting complaints, past episodes, duration of symptoms, drug history, history of perineal trauma, blood dyscrasias, management performed (conservative/surgical), complications, and hospital stay. Based on the presentation and etiology, the management of patients was individualized. Therapeutic aspiration with or without intracavernous irrigation with sympathomimetics (phenylephrine aliquots of 200  $\mu$ g injected every 5–10 min) was initially attempted until detumescence was achieved. In case of failure to achieve detumescence, a percutaneous/surgical shunt procedure was performed after repeated aspirations.<sup>[5]</sup> Use of phenylephrine was omitted in patients with hypertension. In case of failure to achieve detumescence after repeated aspirations, a distal shunt procedure (Winter/Ebbehøj/Al-Ghorab) followed by a proximal shunt procedure (Quackle's) was performed. When sufficient detumescence was achieved, patients were discharged. The complications were graded as per modified Clavien-Dindo classification system.<sup>[8]</sup> The erectile function during follow-up was assessed using a validated abridged five-item version of International Index of Erectile Function (IIEF-5) questionnaire at the sixth-month follow-up.<sup>[9]</sup> It comprises five questions with each item being scored on a five-point ordinal scale.<sup>[9]</sup> Based on the IIEF-5 score, erectile dysfunction (ED) is divided into five categories: severe (5–7), moderate (8–11), mild to moderate (12–16), mild (17–21), and no ED (22–25).<sup>[9]</sup> For all patients, proper laboratory evaluation (including peripheral smear, hemoglobin electrophoresis, and/or bone marrow examination) and hematology consultation were performed.

### Statistical analysis

All the statistical analyses were performed using IBM Statistical Package for the Social Sciences (IBM SPSS Statistics Corp.; Armonk, NY, USA) version 22. Continuous data were expressed as mean  $\pm$  standard deviation. Quantitative data were analyzed using the unpaired student t-test, while qualitative data was analyzed using the chi-square test. A p value of  $<0.05$  was considered significant.

## Results

The baseline demographic parameters are described in Table 1. Of 88 men who presented with IP, 71 patients who had complete medical records were reviewed. The median age of presentation was 30 years (range 18–65). Five patients had diabetes mellitus and hypertension as added co-morbidities. In ten patients (14.08%), the episode was precipitated by sexual intercourse. The average duration

**Table 1. Demographic and baseline characteristics of patients**

Parameter	Value
No. of patients studied	71
Median age, year (range)	30 (18–65)
<b>Complaints</b>	<b>Number of patients</b>
Penile pain	55
Sustained erection	65
Penile turgidity	71
Average duration of symptoms, day (range)	4.39 (1–10)
<b>Cause</b>	<b>Number of patients</b>
• Idiopathic	29
• Chronic myeloid leukemia	24
• Sickle cell disease	2
• Essential thrombocythemia	1
• Drug-induced/psychoactive substance abuse	15
<b>Treatment received</b>	<b>Number of patients</b>
Penile aspiration $\pm$ phenylephrine irrigation	71
<b>Distal shunt</b>	38
• Winter's shunt	30
• Ebbehøj	6
• Al-Ghorab	2
<b>Proximal shunt</b>	
• Quackle's	6
• Grayhack	3
Average hospital stay, day (range)	7.4 (3–15)

**Table 2. Outcome of patients with ischemic priapism**

Treatment received	Average duration of presentation (days)	Number of patients with successful detumescence	Success rate (%)
Penile aspiration $\pm$ alpha adrenergic agonist (phenylephrine) irrigation	4.34 $\pm$ 1.86	15	21.12
Distal shunt	4.42 $\pm$ 1.98	1	42.01
Proximal shunt	5.00 $\pm$ 1.50	5	55.55

**Table 3. Comparison of outcomes based on cause of ischemic priapism**

Parameter	CML (n=24)	Other causes (n=47)	p
Age of presentation (year)	27.50±6.45	32.19±9.64	0.34
Mean duration of presentation (days)	4.25±1.42	4.47±2.06	0.15
<b>Treatment received</b>			
Aspiration	6	18	0.72
Distal shunt	12	26	
Proximal shunt	6	3	
Number of patients with successful detumescence	8	28	0.04
Hospital stay (days)	10.12±3.12	6.02±2.69	0.01
Number of patients developing Complications	11	9	
• Wound infection	2	3	0.02
• Bleeding	9	5	
• Skin necrosis	0	1	

CML: chronic myeloid leukemia

of presentation after the onset of symptoms was 4.39 days (range 1-10). The most common complaints were penile pain (n=55; 77.46%) and sustained erection (n=65; 91.5%). Tender and rigid phallus was observed in almost all patients. Two patients (2.8%) presented with a prior history of stuttering priapism. Most common etiology was idiopathic in 29 (40.84%) and chronic myeloid leukemia (CML) in 24 (33.80%) patients. In 15 patients, priapism was either drug-induced or secondary to psychoactive substance ingestion. Three patients took sildenafil; two each took papaverine, risperidone, and clozapine; and six patients gave history of ingesting some local herb to enhance sexual performance. The average hospital stay was 7.4 days (range 3-15). The outcomes are stratified in Tables 2 and 3 based on time of presentation, intervention performed, and cause of priapism. Men with malignant priapism (CML) had significantly lower success rates with interventions, prolonged hospital stay, and higher complications (p<0.05). Most complications after shunt surgery were minor (Clavein grade 1 and 2). Wound infection developed in five patients, while bleeding at shunt site was observed in 14 cases. One patient developed superficial skin necrosis. Only 21 patients (29.57%) returned for follow-up in the next six months. Of these, only 15 patients resumed sexual activity, and reported moderate to severe ED at sixth-month follow-up.

## Discussion

Ischemic priapism is an acute urological emergency. Any treatment delay leads to irreversible damage to corporal tissue ul-

timately resulting in ED.<sup>[10]</sup> There is progressive hypoxia, hypercarbia, and acidosis.<sup>[1]</sup> The corporal tissue has evidence of interstitial edema by 12 hours followed by endothelial destruction of sinusoids and thrombocyte adherence at end of 24 hours.<sup>[3]</sup> If timely intervention is not performed, then necrosis of cavernosal tissue and eventual fibrosis can occur after 48 hours of onset.<sup>[1,3]</sup>

The median age of our cohort was 30 years, which is almost similar to that reported by Ekeke et al.<sup>[11]</sup> Previous studies have indicated that priapism mostly presents during first (5-10 years) and fourth decade (30-40 years) of life.<sup>[11-13]</sup>

More than 70% patients (50/71) presented after >72 hours of onset with longest duration noted to be 10 days. Most patients were married and sexually active. Delayed presentation of priapism is a more common occurrence in developing countries than that in the Western world.<sup>[11,12]</sup>

Most priapism episodes in this study did not have any precipitating cause such as sexual intercourse or drug intake. Various possible etiologies for IP have been described in literature including hemoglobinopathies (SCD), iatrogenic causes like intracavernosal injections (papaverine hydrochloride/prostaglandin E2), phosphodiesterase 5 (PDE5) inhibitors, psychiatric medications (risperidone, clozapine etc.), and alpha-1 blockers.<sup>[14,15]</sup>

In a study conducted by Ekeke et al.<sup>[11]</sup> in Nigeria, Africa, sickle cell disease (SCD) contributed to 55.56% cases of priapism. Drug-induced priapism is mainly seen in the Western world.<sup>[5]</sup> Psychoactive substance abuse like cocaine may directly contribute to IP or be a precipitating factor.<sup>[16]</sup> A detailed patient history as well as blood and urine toxicology analysis may be helpful to prevent recurrences.<sup>[16]</sup>

Hematological malignancies like CML may present with priapism as an initial manifestation of the disease. In this study, around one-third (24/71; 33.80%) cases were affected with CML. In patients with CML, the sinusoids of corpora cavernosa may get clogged due to aggregation of leucocytes leading to blockage of emissary and dorsal veins, hence resulting in venous return blockade.<sup>[17]</sup> Additionally, splenomegaly in these cases may compress intra-abdominal veins resulting in venous congestion in the sinusoids.<sup>[17]</sup>

For patients with CML with priapism, adjuvant treatment such as systemic chemotherapy and leukapheresis have been proposed besides traditional management.<sup>[18]</sup> All patients with CML received systemic chemotherapy with hydroxycarbamide/tyrosine kinase inhibitors in consultation with hematology. Corporal blood gas analysis and CDU are an integral part of the diagnosis of priapism.<sup>[1]</sup>

Color Doppler ultrasonography can be used to differentiate low-flow and high-flow priapism as an alternative/adjunct to corporal blood gas analysis.<sup>[5]</sup> CDU can also be used to document the patency of shunt procedures in the post-operative period.<sup>[1,19]</sup> In our study, most patients were diagnosed with help of initial aspirate on corporal blood analysis, and CDU was performed for diagnosis in cases with equivocal findings (21 cases).

Priapism lasting more than four hours should be promptly managed with immediate penile aspiration, which is both diagnostic as well as therapeutic in some cases. Although there is little improvement in potency reported for cases presented after >72 hours, first-line treatments (ice packs, penile aspiration etc.) decrease local pain and improve intracorporal circulation.<sup>[5]</sup> The reported success rates of penile aspiration combined with sympathomimetic irrigation in the literature vary from 43% to 81%.<sup>[20]</sup> Penile aspiration with/without irrigation with sympathomimetics was successful in achieving complete detumescence in around 21.12% of cases in our study. The lower success rates may be attributable to delayed presentation (average duration 4.39 days). The success rates with first-line treatments (penile aspiration combined with sympathomimetics) further decrease with prolonged time of presentation.<sup>[5,21]</sup> In patients with delayed presentation (>72 hours), tissue anoxia, glucopenia, and acidosis impair smooth muscle contractility despite use of alpha agonists.<sup>[21]</sup> Pal et al.<sup>[7]</sup> reported success rates of 15.7% with first-line managements. The mean duration of priapism in their study was 96.7 hours.<sup>[7]</sup> The patients with CML may have different patterns of platelet dysfunction that might account for the lower success rates and increased complications making shunt surgery risky in these patients.<sup>[22]</sup>

In this study, 47 patients underwent some shunt surgery as these cases failed treatment with penile aspiration plus sympathomimetic irrigation. The use of distal shunts-Winter's shunt, T/Ebbehøj shunt, T-shunt + tunneling (modification of Al-Ghorab procedure)-is the standard second-line approach to manage IP when conservative measures fail.<sup>[5]</sup> A total of 38 patients underwent distal shunt procedure (30 patients Winter's procedure, six patients Ebbehøj, and two patients Al-Ghorab procedure), while nine patients underwent proximal shunt (Grayhack's/Quackle's) procedure. The patient's on-table improvement of detumescence was variable, and only 50.70% patients reported successful detumescence. The lower success rates of shunt surgeries in this study could be explained by the fact that ours is a tertiary referral center; and we usually cater to a population that has delayed presentation, and usually presents after consulting elsewhere.

More than 90% of patients admitted that initially they took conservative treatment from unqualified persons, and later on presented to us when the symptoms failed to subside. Most of the complications including wound infection and local bleeding were managed conservatively.

Erectile dysfunction is a commonly reported problem in the follow-up period of men with IP who have delayed presentation.<sup>[4]</sup> In a study conducted by Gottsch et al.<sup>[23]</sup>, the authors reported that only six out of 35 patients reported satisfactory erection following management of priapism. Normal erectile function after management of priapism with Winter's, Al-Ghorab, and Grayhack shunt was reported in 50%, 33.3%, and 25% of patients, respectively, by Tabibi et al.<sup>[24]</sup> In IP, delayed presentation (>48 hours), marked penile fibrosis, and failure to achieve complete detumescence may contribute to ED development.<sup>[25]</sup> In this study, we encountered moderate to severe ED at sixth-month follow-up in previously sexually active persons despite performing timely shunt surgery. The key reasons for this include that more than half of patients presented after 72 hours of onset of symptoms. These patients were managed with oral phosphodiesterase-5 inhibitors (sildenafil/tadalafil) initially; however, long-term data are lacking.

Insertion of the early penile prosthesis is advocated by some authors for priapism that lasts more than 48-72 hours as invariably there are increased chances of future ED.<sup>[26]</sup> Immediate insertion of the penile prosthesis has been considered technically easier, and has been shown to preserve penile length.<sup>[27,28]</sup> On the other hand, others hold the opinion that early insertion of the penile prosthesis has high complication and revision rates.<sup>[28]</sup> However, immediate penile prosthesis insertion could not be performed at our center due to financial constraints. MRI may be used to evaluate penile fibrosis in cases presenting after 48 hours.<sup>[29]</sup> However, routine use of MRI is not practical, and it is mainly used in diagnosis of unusual cases.<sup>[29]</sup> Given its acute nature and the impossibility of performing prospective and randomized trials, priapism is a difficult topic to research.

Limitation of this study were that it did not include any pediatric patients; the diagnosis of priapism was based mainly on clinical criteria and corporal blood gas analysis; immediate penile prosthesis insertion could not be performed in patients with >72 hours of onset; and long-term follow-up data on sexual function outcome are lacking. In developing countries such as India, the disease dynamics is complicated (due to social stigma, poor socio-economic condition, ignorance of the disease, lack of specialists etc.); hence, most patients have delayed presentation, they hide the disease very often, and consult unqualified persons/practitioners of indigenous medicine before presenting to specialists.

In conclusion, most patients with IP had a delayed presentation. Men with malignant priapism (CML) had significantly lower success rates with interventions, prolonged hospital stay, and higher complications than men with non-malignant priapism. The prevalence of ED was high during follow-up.

**Ethics Committee Approval:** Ethics committee approval was received for this study from King George's Medical University Institutional Ethical Committee (3018/Ethics/R-cell-18).

**Informed Consent:** Written informed consent was obtained from patient who participated in this study.

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