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PRIAPSM

# Clinical Outcomes of Periprocedural Antithrombotic Therapy in Ischemic Priapism Management

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## ABSTRACT

**Background:** Priapism is a urologic emergency consisting of a painful erection lasting greater than 4 hours; antithrombotic therapy (ATT) have recently been recommended as an adjunct in the treatment of ischemic priapism.

**Aim:** To determine the short- and long-term outcomes of periprocedural ATT in the management of acute ischemic priapism.

**Methods:** A retrospective review of patients seen at the University of California, San Francisco, from 2008 to 2019 was carried out to identify those evaluated for acute priapism. Information regarding duration of priapism, etiology, treatment, periprocedural and postprocedural ATT type and dose, and follow-up data was collected.

**Outcomes:** ATT use was the exposure of interest; outcome variables included priapism resolution, repeat episodes, long-term complications, and follow-up.

**Results:** 70 patients with at least 1 detailed record of an acute priapism episode between 2008 and 2019 were identified. Of the 70 patients who underwent management for an acute episode of priapism, 59 (84%) received intracavernous injection of phenylephrine with or without corporal aspiration. Of the 4 patients who received ATT at the same time as intracavernous injection, none had additional priapism episodes. In the 55 patients who did not receive immediate ATT, 22 (40%) required at least 1 shunting procedure. The 9 patients who received ATT concurrently with shunting experienced less recurrence than the 13 patients who did not receive ATT (11% vs 69%, respectively $P = .012$). There were no significant differences in long-term erectile dysfunction ($P = .627$), fibrosis ($P = .118$), genitourinary pain ($P = .474$), and urinary issues ($P = .158$) between those who received ATT and those who did not.

**Clinical Implications:** Our findings suggest that ATT has a role in preventing priapism recurrence; we observed that long-term repeat priapism episodes are less frequent in those who received periprocedural ATT compared with those who did not and that ATT may especially reduce recurrence in cases when shunting was required

**Strengths & Limitations:** This is the first study looking at the clinical outcomes of periprocedural ATT in the management of ischemic priapism. It is limited by the fact that it is a single-center study, types of ATT were heterogenous, and the exact timing of priapism management could not be measured for everyone.

**Conclusion:** In spite of its limitations, these preliminary findings are promising and warrant further exploration of the use of ATT in the management of ischemic priapism. **Ramstein JJ, Lee A, Cohen AJ, et al. Clinical Outcomes of Periprocedural Antithrombotic Therapy in Ischemic Priapism Management. J Sex Med 2020;17:2260−2266.**



**Key Words:** Anticoagulation; Priapism; Sexual Dysfunction; Surgical Management

## INTRODUCTION

Priapism is a urologic emergency whereby normal physiologic mechanisms of penile tumescence and detumescence are compromised resulting in a persistent, painful erection lasting greater than 4 hours.[1−3] Priapism has an incidence of 0.34−1.5 events per 100,000 person-years in the general population.[4,5] Ischemic priapism is the most common type of priapism, constituting more than 95% of cases.[6,7] The pathophysiology of ischemic priapism involves

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venous outflow occlusion and subsequent blunting of arterial inflow,[8] which drives interstitial edema, cavernous muscle necrosis, fibroblast proliferation, and endothelial destruction, resulting in erectile dysfunction (ED).[9] Prompt management of acute episodes of ischemic priapism is important in avoiding long-term deleterious outcomes including refractory ED and penile shortening.[1]

Recently, antithrombotic therapy (ATT) has been recommended as an adjunct in the treatment of ischemic priapism.[10] The study suggests that ATT may play a role in preventing thrombotic occlusion of shunts, the process thought to cause early recurrent priapism. Hemostasis in the intact corpora cavernosa limits clotting because of the confluence of anticoagulating and fibrinolytic factors present within the endothelium.[11] However, a surgical shunt damages the endothelium and exposes the collagen within the tunica albuginea to the hemostatic blood, an underlying mechanism by which these early shunts clot.[10]

Although some literature suggests ATT may trigger priapism,[12–15] several case reports have indicated that ATT may play a role in the management of priapism, particularly in the context of cavernosal shunting procedures.[10] Preoperative aspirin and heparin, followed by a 5-day course of postoperative aspirin and clopidogrel is one suggested algorithm to avoid recurrence of priapism. This regimen has been associated with improved outcomes including preserved erectile function.[16] However, no studies have been carried out with real patient data to explore the outcomes of ATT utilization in the management of acute priapism, including procedure success, priapism recurrence, and follow-up complications. In the present study, we investigated the therapeutic benefit of ATT for the acute management of priapism. We hypothesized that ATT would improve immediate treatment outcomes. We further hypothesized that use of ATT would be associated with (i) lower risk of priapism recurrence and (ii) decreased long-term ED.

## METHODS

### Retrospective Chart Review

Our institutional review board provided study approval (protocols #18-26688 and 19-29062). Charts were identified on the basis of the International Classification of Disease code for priapism (N48.30). We selected charts that had documentation of at least 1 encounter detailing an episode of priapism that included at minimum a date, location of management, and treatment. Patients were classified as "acute" if they had at least 1 record of acute priapism management, including episodes summarized in notes from outside hospitals. Patients were excluded from the analysis if they were being followed up in clinic for recurrent or stuttering priapism that had not required acute emergent management or if they had no note detailing the acute management of a priapism episode.

### Chart Review and Data Compilation

The following data were collected: demographics, identification of the first priapism episode (at an outside facility or at our institution), identification of subsequent priapism episodes, number and frequency of follow-up visits, etiology, periprocedural ATT type and dose when available, and long-term complications related to priapism management. For primary and subsequent priapism episodes, we also collected information on timing of the episode (date, length of episode before acute management, length of stay in the hospital) though these latter data were intermittently missing from the chart review and thus not included in the analysis of this study. The type and timing of ATT was noted with respect to the initial treatment with aspiration with or without phenylephrine, as well as subsequent shunt procedures and repeat episodes. Follow-up visit patterns were determined based on documentation after management of a priapism episode. Long-term follow-up was ascertained by analysis of follow-up encounters in electronic medical records or by contacting the cohort of patients who had an acute episode of priapism recorded at the University of California San Francisco (UCSF). Long-term follow-up data from electronic medical records were available for 40 patients. Those with no electronic long-term follow-up records were contacted by phone. A total of 52 of 70 (74%) follow-up data were obtained using this mixed methodology. Those who were contacted were asked, "Since you were treated for priapism at UCSF, have you experienced another episode of a painful erection lasting more than 4 hours?" "If so, did you seek medical help? When and where?" and "Since you were treated at UCSF, did you experience any urinary or erectile issues that were not present before your priapism episode?" Note that long-term follow-up data were obtained on every patient who required a shunt as part of their treatment.

### Exposure and Outcome Variables

Our primary exposure variable was any recorded use of ATT for a priapism episode. Our primary outcome variables of interest were repeat episodes of ischemic priapism, follow-up visit patterns, and long-term genitourinary (GU) complications. GU complications included pain with erections, lower urinary tract symptoms, ED, or penile curvature. These data were based on chart review and follow-up questions.

### Statistical Analysis

Descriptive statistics were used to characterize the study population. For categorical variables, Chi-square was used when all N were greater than 5, and Fisher's exact tests were used when at least 1 N was less than 5. *t*-test was used for continuous variables. *P*-value of less than or equal to .05 was considered statistically significant. Statistical tests used for each variable are summarized in table legends. STATA 15 (Statacorp, College Station, TX) was used for all analyses.

## RESULTS

### Demographics

From 1 January 2008 to 12 December 2018, 146 patients were identified to have a history of priapism at our institution.

**Table 1.** Demographics by type of priapism management

| Demographic exposure variables | Total (N = 70) | ATT given at least once (N = 25) | No ATT recorded (N = 45) | *P*-value |
|---|---|---|---|---|
| Mean age at first priapism episode (SD) | 43.3 (14.7) | 48.1 (2.9) | 40.6 (2.1) | **.039** |
| Smoking history; N (%) | | | | |
| Never | 40 (57) | 12 (48) | 28 (62) | .249 |
| Former | 17 (24) | 7 (28) | 10 (22) | .589 |
| Current | 13 (19) | 6 (24) | 7 (16) | .384 |
| Hypertension; N (%) | 22 (31) | 10 (40) | 12 (27) | .25 |
| Diabetes; N (%) | 4 (6) | 2 (8) | 2 (4) | .539 |
| Illicit drug history; N (%) | 17 (24) | 9 (36) | 8 (18) | .088 |
| Methamphetamine history; N (%) | 12 (17) | 7 (28) | 5 (11) | .072 |
| Priapism cause; N (%) | | | | |
| Idiopathic | 14 (20) | 6 (24) | 8 (18) | .533 |
| ED drug | 28 (40) | 6 (24) | 22 (49) | **.042** |
| Trazodone | 7 (10) | 6 (24) | 1 (2) | **.004** |
| Other drug | 14 (20) | 6 (24) | 8 (18) | .533 |
| Trauma | 3 (4) | 1 (4) | 2 (4) | .93 |
| SCD | 4 (6) | 0 (0) | 4 (9) | .125 |

ATT = antithrombotic therapy; ED = erectile dysfunction; SCD = sickle cell disease; SD = standard deviation.
"ATT given at least once" includes the patients who received anticoagulation for an acute priapism episode. "No ATT recorded" includes the patients who had no record of receiving anticoagulation immediately before, during or after a priapism episode. T-test used for "mean age at first priapism episode". For other variables, Chi-square used when N > 5, Fisher's exact when N < 5.
Significant *P* values <.05 bolded.

From that group, 101 had documentation of priapism management. Of these, 70 had detailed acute priapism episodes with a cumulative 118 separate episodes of priapism documented across this group. The average age at the first recorded episode was 43 years (range 8–77), 30 of 70 (43%) had a history of smoking, 22 of 70 (31%) had hypertension, 4 of 70 (6%) had diabetes, and 17 of 70 (24%) endorsed recreational drug use (including 12 of 70 [17%]) with a history of methamphetamine use. The cause of priapism was primarily secondary to an ED medication (28 of 70; 40%), followed by other drugs (14 of 70; 20%), idiopathic cause (14 of 70; 20%), and trazodone (7 of 70; 10%). Those who received ATT were older than those who did not ($P = .039$). Those who experienced priapism secondary to an ED drug were less likely to receive ATT ($P = .042$), whereas those who experienced priapism secondary to trazodone were more likely to receive ATT ($P = .004$) than those who did not (Table 1).

## Types of Anticoagulation Used in Acute Priapism Management

Of the 70 patients included in this analysis, a total of 18 patients received some form of ATT during their priapism course, often more than once if they experienced a failed treatment or a subsequent repeat episode of priapism. A total of 118 separate episodes of acute priapism were recorded across the 70 patients. The use of perioperative antithrombotic use was very heterogeneous. In the 118 separate episodes of acute priapism recorded, 31 (26%) included ATT as part of the management. In the periprocedural period, 16 of 31 (52%) received a one-time dose of subcutaneous heparin and 18 of 31 (58%) received a one-time dose of aspirin 325 mg, with 12 of 31 (39%) receiving both. Postoperatively, 17 of 31 (55%) received aspirin 81 mg daily for 5 days and 10 of 31 (32%) received clopidogrel 75 mg daily for 5 days, with 6 of 31 (19%) receiving both. 3 (10%) episodes received the 4-drug regimen suggested by Lue and Garcia[10] (perioperative subcutaneous heparin, perioperative aspirin, postoperative clopidogrel, postoperative aspirin). Aspirin was given in 30 of the 31 (97%) episodes managed with ATT.

## Comparing ATT vs No ATT Administration

### ATT with Initial Corporal Aspiration

As demonstrated in Figure 1, 55 of the 59 (93%) patients who underwent corporal aspiration with or without phenylephrine for acute ischemic priapism were *not* given periprocedural ATT, whereas 4 (7%) received ATT. None of those 4 patients experienced a subsequent short-term (within 48 hours, $P = .158$) or long-term (beyond 48 hours, $P = .046$) episode of priapism compared with those who did not receive ATT alongside aspiration. Of those who *did not* receive ATT around the time of corporal aspiration (n = 55), 23 of 59 (39%) had no further episodes of priapism recorded, 10 of 59 (17%) had a repeat episode at a later time after discharge, and 22 of 59 (37%) required a shunting procedure owing to failed corporal aspiration (Table 2).

### ATT With Shunt

Overall, 22 patients required at least one shunt procedure, and 10 of 22 (45%) experienced priapism recurrence across the ATT

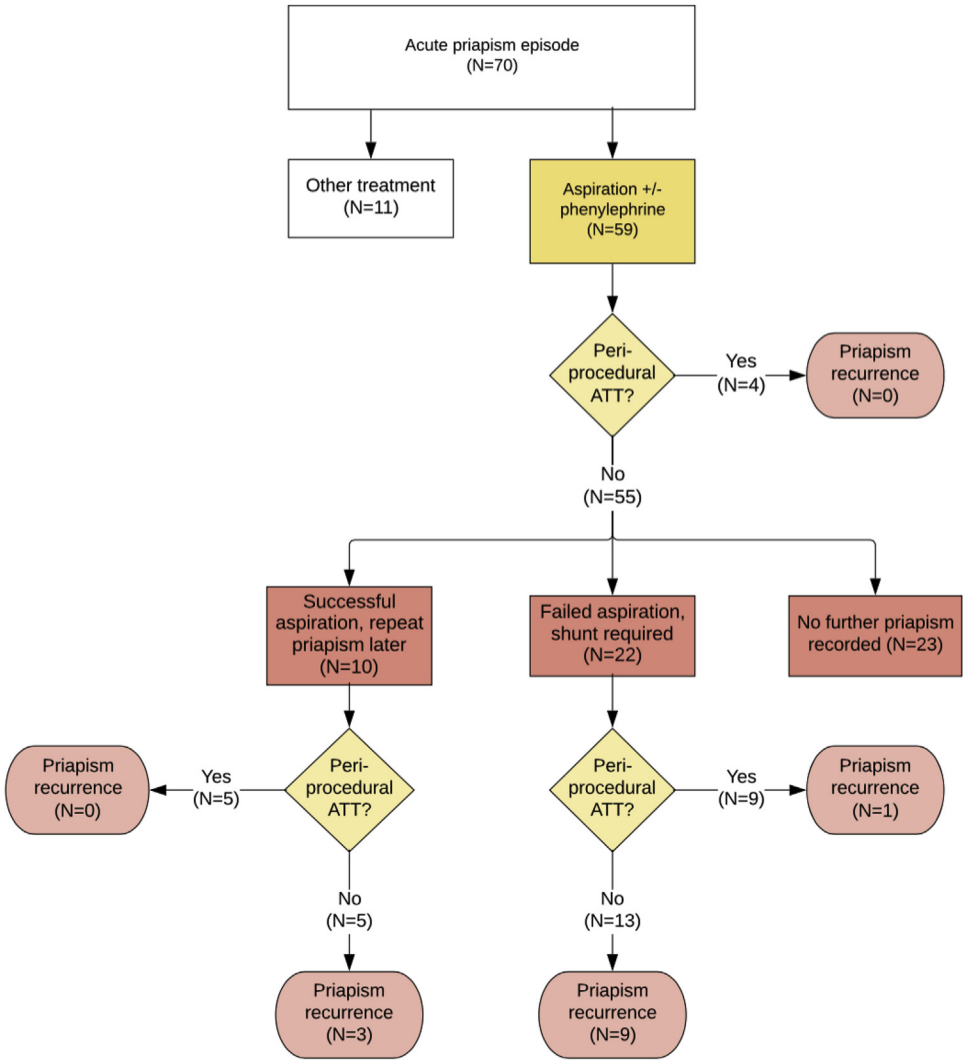


**Figure 1.** Patterns of priapism recurrence based on periprocedural antithrombotic therapy. "Other treatment" includes those who received medical management (ketoconazole, pseudoephedrine), had spontaneous resolution, or who declined treatment. "ATT" indicates that some form of periprocedural anticoagulation was administered. ATT = antithrombotic therapy. Figure 1 is available in color online at www.jsm.jsexmed.org.

and non-ATT groups. In those 22 patients, 9 (41%) received ATT, and 1 episode of priapism recurrence was recorded (11%); on the other hand, 13 of 22 (59%) did not receive periprocedural ATT, and 9 episodes of priapism recurrence were recorded (69%). In other words, there was an 84% decrease in priapism recurrence in the shunt group that received periprocedural ATT compared with the shunt group that did not receive periprocedural ATT after failed aspiration ($P = .012$).

### Follow-Up Complications

There were no significant differences in long-term ED ($P = .627$), fibrosis ($P = .118$), GU pain ($P = .474$), and urinary issues ($P = .158$) between those who received ATT and those who did not (Table 3). Erectile function, urinary issues, and GU pain were self-reported by the patients at follow-up visits. Fibrosis was measured by color duplex ultrasound. There were no reports of bleeding complications in those who received ATT for priapism.

## DISCUSSION

In this study, we demonstrate a decreased risk of priapism recurrence when periprocedural ATT is included in acute management. None of the patients who received ATT as part of the initial corporal aspiration procedure required surgical shunting, and none of them had records of long-term priapism recurrence. The use of ATT during shunting procedures led to significantly lower rates of immediate repeat procedures and future priapism recurrences. There were no significant differences in long-term urological complications between those who received ATT and those who did not. Overall, these findings suggest a potential therapeutic role for periprocedural ATT in both the initial and surgical management of priapism.

Previously, ATT had been regarded as a potential cause of priapism rather than a therapeutic tool. Heparin-induced priapism has been reported and hypothesized to be a direct consequence of heparin-induced thrombocytopenia leading to vaso-occlusion of

**Table 2.** Outcomes of antithrombotic use during management of acute ischemic priapism episode

| Postprocedural outcome events | With ATT | Without ATT | *P*-value |
|---|---|---|---|
| Repeat priapism episode recorded within 48 h of aspiration (N) | | | |
| Yes | 0 | 22 | .158 |
| No | 4 | 35 | |
| Any priapism episode recorded after aspiration, with/without ATT (N) | | | |
| Yes | 0 | 32 | **.046** |
| No | 4 | 25 | |
| Successful first T-shunt after failed aspiration (N) | | | |
| Yes | 8 | 4 | **.012** |
| No | 1 | 9 | |

ATT = antithrombotic therapy.
"Successful" is defined as resolution of symptoms with no further records of repeat priapism. Fisher's exact statistical test used for all variables.
Significant *P* values <.05 bolded.

penile tissue.[15,17] Warfarin-induced priapism has been hypothesized to lead to a paradoxical short-term hypercoagulable state and subsequent vaso-occlusive complications including priapism.[18,19] Several case reports have summarized devastating outcomes of AC-induced priapism, including penile gangrene and loss of appendage.[13,14,20,21] Although these potential side effects are certainly severe, they remain rare. For example, less than 20 cases of heparin-induced priapism were reported between 1970 and 2000.[15] As such, we argue that the therapeutic aspect of ATT in the management of acute priapism outweighs the rare instances of ATT-induced priapism or at the very least, that some ATT are safer to use than others in the acute treatment of priapism.

During typical corporal aspiration with or without phenylephrine, the success rate has been reported between 74% and 91%.[22–24] The success of aspiration/phenylephrine of 47 patients who were first treated at UCSF was 40 (85%), whereas our overall findings was 42 of 70 (63%) owing to the large number of referred cases. In fact, 23 of 70 (33%) of the patients in our cohort were sent from an outside facility after failed initial management, where most were subsequently managed by shunting. In our study, those who received periprocedural ATT during aspiration had no recorded repeat priapism episodes compared with those who did not receive ATT. Although we report that administration of ATT during corporal aspiration at initial presentation may be beneficial, the sample size is too small (N = 4) to make definitive conclusions. No studies have established a role for ATT during corporal aspiration, and the findings we report warrant further exploration.

ATT has been proposed as a key element for priapism patients who require shunt procedures on the theory that this may help prevent premature shunt closure. In 2004, Lue et al[10] suggested a mechanism where the surgical creation of a shunt leads to a wounded tunica albuginea, rich in collagen. Exposure to collagen may precipitate platelet aggregation, fibrin clots, and closure of the shunt from thrombosis, which may lead to priapism recurrence. Prevention of thromboembolic complications in various surgeries is reliant on use of ATT.[25–28] Given that persistent or recurring priapism secondary to premature closure of the shunt is a thromboembolic complication, we apply that rationale to management of the vascular disorder of priapism after corporal shunting.

While these results are promising, this study does have limitations. We report a single-center series. Durations, doses, and

**Table 3.** Follow-up visit patterns based on ATT use in acute priapism at UCSF

| Patients with at least 1 follow-up visit (in-person or phone) | Total (N = 52) | ATT given at least once (N = 20) | No ATT recorded (N = 32) | *P*-value |
|---|---|---|---|---|
| Average number of days between first priapism episode and first follow-up visit (SE) | 170 (77) | 55 (34) | 238 (119) | .257 |
| Average number of urology outpatient visits after d/c (SE) | 1.14 (0.21) | 1.32 (0.35) | 1.04 (0.27) | .541 |
| Patients with long-term GU dysfunction recorded; N (%) | 24 (46) | 8 (40) | 16 (50) | .482 |
| Erectile dysfunction | 23 (44) | 8 (40) | 15 (47) | .627 |
| Fibrosis | 4 (8) | 3 (15) | 1 (3) | .118 |
| GU Pain | 6 (12) | 3 (15) | 3 (9) | .474 |
| Urinary issues | 3 (6) | 0 (0) | 3 (9) | .158 |

ATT = antithrombotic therapy; d/c = discharge; GU = genitourinary; SE = standard error.
T-test was used for "average number of days between first priapism episode and first follow-up visit" and "average number of urology outpatient visits after d/c". Chi-square was used for "patients with long-term GU dysfunction recorded" and "erectile dysfunction." Fisher's exact was used for "fibrosis," "GU pain," and "urinary issues."

types of ATT used in the acute management of priapism were heterogenous. ATT was more likely used in older patients and when the etiology of priapism was trazodone and less likely used when the etiology was ED drugs, for reasons yet to be determined. Exact timing of priapism episodes, which could not be measured precisely for all the charts included in this study, could be a potential confounding factor in our findings. This is also a retrospective study, meaning causation cannot be inferred from our results. Although follow-up data were obtained for the majority of the patients, our follow-up questionnaire was limited, and some patients were not successfully reached. These limitations notwithstanding, to our knowledge, this is the very first study of its kind to look into the clinical outcomes of priapism based on the use of ATT as part of acute management.

## CONCLUSIONS

The use of ATT in the management of ischemic priapism may lower the risk of long-term repeat ischemic priapism episodes. In addition, the use of ATT may play a preventive role in the recurrence of disease, while reducing risks of long-term GU complications such as pain with erections, lower urinary tract symptoms, ED, or penile curvature with no increase in bleeding complications. While our analysis is not without its own set of limitations, these promising preliminary findings warrant further exploration of the use of ATT in the management of ischemic priapism, particularly when surgical management is indicated.

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## STATEMENT OF AUTHORSHIP

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