American Urological Association

# The Diagnosis and Management of Priapism: an AUA/SMSNA Guideline (2022)

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## EXECUTIVE SUMMARY

### Purpose

Priapism is a persistent penile erection that continues hours beyond, or is unrelated to, sexual stimulation and results in a prolonged and uncontrolled erection. Given its time-dependent and progressive nature, priapism is a situation that both urologists and emergency medicine practitioners must be familiar with and comfortable managing. Although non-ischemic priapism (NIP) is not an urgent urologic issue, prolonged (>4 hours) acute ischemic priapism, characterized by little or no cavernous blood flow and abnormal cavernous blood gases (i.e., hypoxic, hypercarbic, acidotic) represents a medical emergency and may lead to cavernosal fibrosis and subsequent erectile dysfunction. All patients with priapism should be evaluated emergently to identify the sub-type of priapism (acute ischemic versus non-ischemic) and those with an acute ischemic event provided early intervention. This Guideline provides a clinical framework for the diagnosis, evaluation, and treatment (non-surgical and surgical) of acute ischemic priapism, NIP, recurrent ischemic priapism, and priapism in patients with sickle cell disease. The treatment of patients with a prolonged erection following intracavernosal vasoactive medication is also included.

### Methodology

A comprehensive search of the literature included on acute ischemic priapism and NIP was performed by Emergency Care Research Institute for articles published between January 1, 1960 and May 1, 2020. A search of the literature on NIP, recurrent priapism, prolonged erection following intracavernosal vasoactive medication, and priapism in patients with sickle cell disease was conducted by Pacific Northwest Evidence-based Practice Center for articles published between 1946 and February 19, 2021. Study designs included narrative reviews, systematic reviews, randomized controlled trials, controlled clinical trials, diagnostic accuracy studies, and observational studies. Searches identified 4117 potentially relevant articles, and 3437 of these were excluded at the title or abstract level for not meeting inclusion criteria for any key question. Full texts for the remaining 680 articles were ordered, and ultimately 203 unique articles were included in the report. When sufficient evidence existed, the body of evidence for a particular treatment was assigned a strength rating of A (high), B (moderate), or C (low), and evidence-based statements of Strong, Moderate, or Conditional Recommendation were developed. Additional information is provided as Clinical Principles and Expert Opinions when insufficient evidence existed.

# GUIDELINE STATEMENTS

## Diagnosis of Priapism

1. In patients presenting with priapism, clinicians should complete a medical, sexual, and surgical history, and perform a physical examination, which includes the genitalia and perineum. (*Clinical Principle)*

2. Clinicians should obtain a corporal blood gas at the initial presentation of priapism. (*Clinical Principle)*

3. Clinicians may utilize penile duplex Doppler ultrasound when the diagnosis of acute ischemic versus non-ischemic priapism is indeterminate. (*Expert Opinion)*

4. The clinician should order additional diagnostic testing to determine the etiology of diagnosed acute ischemic priapism; however, these tests should not delay, and should be performed simultaneously with, definitive treatment. (*Expert Opinion)*

## Initial Management of Acute Ischemic Priapism

5. In a patient with diagnosed acute ischemic priapism, conservative therapies (i.e., observation, oral medications, cold compresses, exercise) are unlikely to be successful and should not delay definitive therapies. (*Expert Opinion)*

6. Clinicians should counsel all patients with persistent acute ischemic priapism that there is the chance of erectile dysfunction. *(Moderate Recommendation; Evidence Level: Grade B)*

7. Clinicians should counsel patients with an acute ischemic priapism event >36 hours that the likelihood of erectile function recovery is low. (*Moderate Recommendation; Evidence Level: Grade B)*

## Pre-Surgical Management of Acute Ischemic Priapism

8. Clinicians should manage acute ischemic priapism with intracavernosal phenylephrine and corporal aspiration, with or without irrigation, as first line therapy and prior to operative interventions. (*Moderate Recommendation, Evidence Level: Grade C)*

9. In patients receiving intracavernosal injections with phenylephrine to treat acute ischemic priapism, clinicians should monitor blood pressure and heart rate. (*Clinical Principle)*

## Surgical Management of Acute Ischemic Priapism

10. Clinicians should perform a distal corporoglanular shunt, with or without tunneling, in patients with persistent acute ischemic priapism after intracavernosal phenylephrine and corporal aspiration, with or without irrigation. (*Moderate Recommendation, Evidence Level: Grade C)*

11. In patients with persistent acute ischemic priapism after a distal corporoglanular shunt, the clinician should consider corporal tunneling. *(Moderate Recommendation, Evidence Level: Grade C)*

12. Clinicians should counsel patients that there is inadequate evidence to quantify the benefit of performing a proximal shunt (of any kind) in a patient with persistent acute ischemic priapism after distal shunting. (*Moderate Recommendation, Evidence Level: Grade C)*

## Post Shunting Management of Acute Ischemic Priapism

13. In an acute ischemic priapism patient with a persistent erection following shunting, the clinician should perform corporal blood gas or color duplex Doppler ultrasound prior to repeat surgical intervention to determine cavernous oxygenation or arterial inflow. (*Moderate Recommendation, Evidence Level: Grade C)*

## Penile Prosthesis

14. Clinicians may consider placement of a penile prosthesis in a patient with untreated acute ischemic priapism greater than 36 hours or in those who are refractory to shunting, with or without tunneling. (*Expert Opinion)*

15. Clinicians should discuss the risks and benefits of early versus delayed placement with acute ischemic priapism patients who are considering a penile prosthesis. (*Moderate Recommendation, Evidence Level: Grade C)*

## Recurrent Ischemic Priapism

16. Clinicians should inform patients with recurrent ischemic priapism that optimal strategies to prevent subsequent episodes are unknown. *(Conditional Recommendation; Evidence Level: Grade C)*

17. Clinicians should inform patients with recurrent ischemic priapism that hormonal regulators may impair fertility and sexual function. *(Strong Recommendation; Evidence Level: Grade B)*

## Sickle Cell Disease and other Hematologic Disorders

18. In patients with hematologic and oncologic disorders such as sickle cell disease or chronic myelogenous leukemia, clinicians should not delay the standard management of acute ischemic priapism for disease specific systemic interventions. *(Expert Opinion)*

19. Clinicians should not use exchange transfusion as the primary treatment in patients with acute ischemic priapism associated with sickle cell disease. *(Expert Opinion)*

## Prolonged Erection Following Intracavernosal Vasoactive Medication

20. In patients presenting with a prolonged erection of four hours or less following intracavernosal injection pharmacotherapy for erectile dysfunction, clinicians should administer intracavernosal phenylephrine as the initial treatment option. (*Expert Opinion)*

21. Clinicians should utilize intracavernosal phenylephrine if conservative management is ineffective in the treatment of a prolonged erection. *(Moderate Recommendation; Evidence Level: Grade C)*

22. Clinicians should instruct patients who receive intracavernosal teaching or an in-office pharmacologically-induced erection to return to the office or Emergency Department if they have an erection lasting >4 hours. (*Expert Opinion)*

## Non-Ischemic Priapism

23. Clinicians should counsel patients that non-ischemic priapism is not an emergency condition and should offer patients an initial period of observation. (*Expert Opinion)*

24. In a patient with diagnosed non-ischemic priapism, the clinician should consider penile duplex ultrasound for assessment of fistula location and size. (*Expert Opinion)*

25. In patients with persistent non-ischemic priapism after a trial of observation, and who wish to be treated, the clinician should offer embolization as first-line therapy. (*Moderate Recommendation, Evidence Level: Grade C)*

26. Non-ischemic priapism patients should be informed that embolization carries a risk of erectile dysfunction, recurrence, and failure to correct non-ischemic priapism. *(Moderate Recommendation; Evidence Level: Grade C)*

27. In non-ischemic priapism patients with a persistent erection after embolization of the fistula, the clinician should offer repeat embolization over surgical ligation. *(Moderate Recommendation, Evidence Level: Grade C)*

# INTRODUCTION

Priapism is a condition resulting in a prolonged and uncontrolled erection. Although the incidence rate is relatively low, because of its time-dependent and progressive nature, priapism is a situation that both urologists and emergency medicine practitioners must be familiar with and comfortable managing. Although non-ischemic priapism (NIP) does not require urgent urologic intervention, prolonged (>4 hrs) acute ischemic priapism represents a medical emergency and may lead to cavernosal fibrosis and subsequent erectile dysfunction (ED).[1, 2] All patients with priapism should be evaluated emergently to identify the sub-type of priapism (acute ischemic versus non-ischemic) and those with an acute ischemic event provided early intervention.

Given the significant heterogeneity of men presenting with acute ischemic priapism, the current Guideline emphasizes that specific interventions should be individualized based on clinical history and findings. While less-invasive, stepwise methods may be appropriate for most situations, others may be best managed using expedited surgical interventions. Decisions must also be based on patient objectives, available resources, and clinician experience. As such, a single pathway for managing the condition is oversimplified and no longer appropriate. Using this new, diversified approach, some men may be treated with intracavernosal injection (ICI) of phenylephrine alone, ICI of phenylephrine and aspiration, with or without irrigation, distal shunting, or non-emergent placement of a penile prosthesis.

Since the last American Urological Association (AUA) priapism guideline,[3] several other additions have been made to address various diagnostic modalities. Specifically, the role of imaging (e.g., ultrasound, CT, MRI) is clarified during the initial diagnosis as well as post-treatment, such as with men exhibiting persistent pain or perceived rigidity post distal shunting.

New additions to the guideline also include greater detail on the role of:

- adjunctive laboratory testing in the diagnosis and determination of the etiology of priapism.
- early involvement of urologists when patients present to the emergency department.
- enhanced data for patient counseling on risks of ED and surgical complications.
- ICI phenylephrine, with or without irrigation, to manage acute ischemic priapism
- novel surgical techniques (e.g., distal shunting with tunneling) in acute ischemic priapism patients.
- early penile prosthesis placement in management of acute ischemic priapism.
- pharmacologic agents to prevent recurrent ischemic priapism.
- conservative management of NIP.
- management of priapism associated with hematologic and oncologic diseases.

Because priapism is rare and unpredictable, there is a dearth of high-level evidence-based data available from which strong evidence-based recommendations may be derived. Rather, most series represent small, single-site, retrospective, outcomes-based reports, with limited

follow-up available and inconsistencies in reporting of outcomes. Similarly, as acute ischemic priapism is associated with ED (whether treated or untreated) and is progressive in nature, outcome reporting of various treatment strategies is inherently biased. These limitations preclude the ability to compare different treatment approaches or provide definitive recommendations in many cases. However, as with other AUA Guidelines, a thorough review of the available literature was performed, with all relevant articles reviewed and considered during the creation of recommendation statements. In cases where the Panel did not feel there was enough information to warrant a particular statement, additional discussion was presented within the supporting text.

The objective of the current Guideline is to provide a practical guide that is directive in cases where evidence is more abundant while remaining flexible to allow for clinician judgment. As such, the Guideline does not establish a fixed set of rules for the treatment of priapism. Above all, it does not pre-empt physician judgment in individual cases. Variations in patient subpopulations, physician experience, and available resources will necessarily influence choice of clinical strategy. Adherence to the recommendations presented in this document cannot assure a successful treatment outcome.

## Definitions

Priapism is a persistent penile erection that continues hours beyond, or is unrelated to, sexual stimulation. Typically, only the corpora cavernosa are affected. For the purposes of this Guideline, the definition of priapism is restricted to erections of >4 hours duration. In contrast, a 'prolonged erection' may be defined as an erection which persists longer than desired but <4 hours. There are two general classifications of priapism:

***Acute Ischemic (veno-occlusive, low flow):*** a nonsexual, persistent erection characterized by little or no cavernous blood flow and abnormal cavernous blood gases (i.e., hypoxic, hypercarbic, acidotic). The corpora cavernosa are fully rigid and tender to palpation. Patients typically report pain. A variety of etiologic factors may contribute to the failure of the detumescence mechanism in this condition. Acute ischemic priapism is an emergency. As the natural history of untreated acute ischemic priapism includes days to weeks of painful erections followed by permanent loss of erectile function, the condition requires prompt evaluation and may require emergency management.

Resolution of acute ischemic priapism is characterized by the penis returning to a flaccid, nonpainful state, with restoration of penile blood flow. However, oftentimes, persistent penile edema, ecchymosis, and partial erections occur and mimic unresolved priapism. This often relates to the duration of priapism and may also signify segmental regions of cavernosal ischemia/necrosis.

***Non-ischemic (arterial, high flow):*** a persistent erection that may last hours to weeks and is frequently recurrent. Although the underlying physiology is incompletely understood, it likely results from unregulated control of arterial inflow and cavernous smooth muscle tone. Erections are nearly always non-painful, and cavernosal blood gas measurements are consistent with arterial blood. In contrast to acute ischemic priapism, the non-ischemic variant is not considered a medical emergency.

Both acute ischemic priapism and NIP may recur over time. The term ***recurrent ischemic priapism***, commonly known as "stuttering" priapism and signifies a recurrent subtype of acute ischemic priapism, in which unwanted painful erections occur repeatedly with intervening periods of detumescence. For the purposes of this guideline, recurrent ischemic priapism is narrowly defined as being a condition in which a patient experiences recurrent ischemic episodes with or without meeting the previously cited 4-hour time criteria for priapism. Management of this condition requires not only treatment of acute episodes, but also focuses on future prevention and mitigation of an acute ischemic event necessitating surgical management.

## Panel Formation

The Panel was created in 2018 by the American Urological Association Education and Research, Inc. This guideline was developed in collaboration with the Sexual Medicine Society of North America (SMSNA). The Practice Guidelines Committee (PGC) of the AUA selected the Panel Chairs who in turn appointed the additional panel members with specific expertise in this area, in conjunction with SMSNA. Additionally, the Panel included a representative of the American College of

Emergency Physicians. Funding of the Panel was provided by the AUA; panel members received no remuneration for their work.

# Methods and Methodology

## Acute ischemic priapism and non-ischemic priapism

### Literature Search

A comprehensive search of the literature was performed by staff in the Clinical Excellence and Safety Group at the Emergency Care Research Institute (ECRI). ECRI searched Medline and EMBASE for articles published between January 1, 1960 and May 1, 2020. Study designs included narrative reviews, systematic reviews, randomized controlled trials (RCTs), controlled clinical trials, diagnostic accuracy studies, and observational studies (i.e., cohort studies, with and without comparison groups; case-control designs; case series).

### Study Screening and Selection

Relevant references retrieved by the literature searches were loaded into Distiller SR, systematic review software (Evidence Partners, Ottawa, Ontario, Canada). All screening through the abstract level was performed in Distiller SR. One analyst (Dr. Jeff Oristaglio) performed initial title screening and his list of excluded studies was reviewed by Dr. Stacey Uhl to confirm that no potentially relevant studies had been excluded. One analyst (Dr. Oristaglio) performed screening at the abstract level. References deemed with potential to satisfy the inclusion criteria (outlined below) and provide evidence for addressing one or more of the key questions specified by the panel were retrieved in full text for review by the team. Five analysts participated in full-text screening and approximately 10% of the studies at this level were reviewed by at least two analysts (double-screening). Conflicting decisions between analysts were tracked, reviewed, discussed, and resolved by consensus before individual analysts were allowed to screen full-text studies independently. This assured that a suitable sample of studies covering most of the key questions were assessed by all analysts and that decisions on inclusion or exclusion were understood. For all excluded studies, the reason for exclusion, and the level at which it was excluded (based on abstract or full text review) was recorded.

### Inclusion Criteria

*General Criteria*

To focus the analysis on the most relevant evidence, only peer-reviewed journal articles published in English from January 1, 1960 to May 1, 2020, reporting data on human subjects with relevance to one or more of the key questions were considered. With regard to enrollment size, only individual case studies (n=1 subject) were systematically excluded, though some studies of this type were allowed when the quantity of evidence for a particular question was very low.

In summary, general inclusion criteria were as follows:

- published, peer-reviewed full-length individual studies or systematic reviews,
- individual studies limited to those not included in relevant systematic reviews (to avoid double-counting of evidence),
- published guidelines with systematic reviews and acceptable methodological details (including study quality assessment) and abstractable data,
- studies that enrolled or analyzed human male participants,
- studies that were published in the English language, and
- studies that had a patient enrollment of ≥2 per group at follow-up (except in instances of very limited evidence).

*Exclusion criteria were as follows:*

- studies not published in English,
- case reports (n=1 studies), except in instances of very limited evidence,
- narrative reviews,
- guidelines or reviews with no systematic literature search or methodological details (e.g., risk of bias assessment),
- opinions/editorials/commentaries,
- conference abstracts, and
- in vitro studies or animal studies.

**Assessment of Study Quality**

Ideally, different key questions required different types of evidence in terms of trial design and study type. However, realizing that the evidence base for this topic would be limited, very liberal inclusion criteria was adopted. The vast majority of studies were observational in design and most of these were retrospective. The criteria set for assessing the quality of different study designs, prior to formal assessments, are listed below. Note that there were not any RCTs with comparisons that addressed any of the specified key questions. Because of this, while RCTs with relevant data were accepted, they were typically graded as observational studies.

For assessing RCTs, an adaptation of the Cochrane risk-of-bias instrument was used, which assessed five of its seven domains:

- random sequence generation,
- allocation concealment,
- incomplete outcome data,
- selective outcome reporting, and
- other potential sources of bias (e.g., lack of balance in group baseline characteristics).

The Cochrane domains concerning blinding, which is not practically or ethically feasible for surgical interventions, were not considered.

- For non-randomized comparative trials, the following domains were assessed:
- prospective versus retrospective design,
- consecutive enrollment,
- baseline comparability of groups,
- use of statistical controls for confounding,
- incomplete outcome data,
- selective outcome reporting, and
- other potential threats to validity.

For diagnostic accuracy studies, appropriate items from the QUADAS (Quality Assessment of Diagnostic Accuracy Studies) instrument were used:

- Was a consecutive or random sample of patients enrolled?
- Was a case-control design avoided (when the true status of patients was known prior to inclusion in the study)?
- Did the study avoid inappropriate exclusions (i.e., spectrum bias)?
- Were the index test results interpreted without knowledge of the results of the reference standard?
- Was the reference standard likely to classify the target condition correctly?

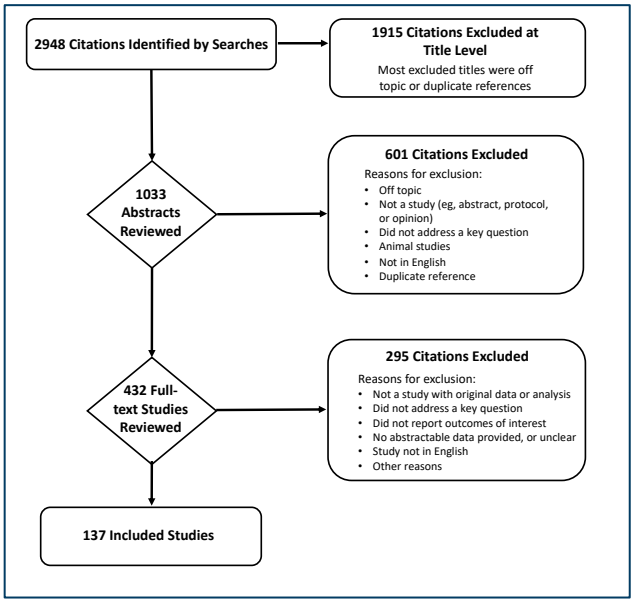
Finally, and most importantly, for this evidence base, observational and single-arm studies were assessed with the following domains:

- prospective versus retrospective design,
- consecutive enrollment,
- methodological detail (e.g., specification of follow-up time),
- incomplete outcome data,
- selective outcome reporting, and other potential threats to validity (e.g., lackingmeasures of dispersion; failure to use appropriate statistical techniques).

**Results**

Searches identified 2948 potentially relevant articles, and 2516 of these were excluded at the title or abstract level for not meeting inclusion criteria for any key question. Full text publications for the remaining 432 articles were ordered, and ultimately 137 unique articles were included for this report.

**Figure 1. Literature Flow Diagram**



## Non-ischemic priapism, recurrent priapism, prolonged erection following intracavernosal vasoactive medication, and priapism in patients with sickle cell disease

### Literature Search

A comprehensive search of the literature was performed by Pacific Northwest Evidence-based Practice Center. A research librarian conducted searches in Ovid MEDLINE (1946 to February 19, 2021), the Cochrane Central Register of Controlled Trials (through January 2021), and the Cochrane Database of Systematic Reviews (through February 19, 2021). Searches of electronic databases were supplemented by reviewing reference lists of relevant articles.

### Study Screening and Selection

Criteria for inclusion and exclusion of studies was based on the Key Questions and the populations, interventions, comparators, outcomes, timing, and study designs (PICOTS) of interest. Populations were male patients of any age with priapism secondary to sickle cell disease, with NIP, or with stuttering priapism; or adult males with a priapism episode following ICI. Stuttering priapism was defined as recurrent episodes <4 hours in duration; priapism following ICI was focused on episodes <4 hours in duration. Interventions included those specific to SCD (e.g., exchange transfusion or hydroxyurea), oral pharmacologic therapies, nonpharmacologic interventions such as ice packs or exercise, and invasive procedures such as aspiration, ICI, and embolization. Comparisons were against no therapy, placebo, or another active intervention. Outcomes included resolution of a priapism event, prevention of recurrent events, preservation of sexual function, and adverse events.

Eligible study designs were RCTs, cohort studies, and case series with at least two patients. We excluded single patient case reports, systematic reviews, narrative reviews, and non-English language articles, as well as in vitro and animal studies. Articles had to be published in peer-reviewed journals in or after 1960.

Two investigators independently reviewed titles and abstracts of all citations using the pre- specified inclusion criteria and screened full-text articles identified during title and abstract review.

### Data Abstraction

For primary studies that met inclusion criteria, information on study author, publication year, study design, country, enrollment dates, sample size, eligibility criteria, population characteristics (age, race, priapism type and etiology, duration of episode), interventions, results, and funding source was abstracted Data abstractions were reviewed by a second investigator for accuracy.

### Risk of Bias Assessment

Two investigators independently assessed risk of bias using predefined criteria. Disagreements were resolved by consensus. For RCTs and cohort studies, criteria for assessing risk of bias was adapted from the U.S. Preventive Services Task Force. Criteria for RCTs included: use of appropriate randomization and allocation concealment methods, baseline comparability of groups, blinding, attrition, and use of intention-to-treat analysis. For cohort studies, criteria included methods for assembling cohorts, attrition, blinding for assessment of outcomes, and adjustment for potential confounding. Risk of bias for case series was not assessed, given the inherent limitations of this study design, with no comparison groups and inability to control for confounders.

RCTs and cohort studies were rated “low,” “medium,” or “high” risk of bias based on the presence and seriousness of methodological shortcomings. Studies rated “low risk of bias” are generally considered valid. Low risk of bias RCTs report clear descriptions of the population, setting, interventions, and comparison groups; utilize valid methods to allocate patients to treatment; clearly report attrition and report low attrition; blind patients, care providers, and outcome assessors; and utilize appropriate analysis of outcomes. Low risk of bias cohort studies utilize appropriate methods to select patients; utilize accurate methods to determine exposures and outcomes; clearly report attrition and report low attrition; and perform appropriate analysis, including control of confounders. Because even well-designed cohort studies are more susceptible to bias and residual confounding than well-conducted RCTs, a low risk of bias cohort study is generally considered less valid than a low risk of bias RCT.

Studies rated “medium risk of bias” are susceptible to some bias, though not necessarily enough to invalidate

the results. These studies do not meet all the criteria for a rating of low risk of bias but have no flaw likely to cause major bias. Studies may be missing information, making it difficult to assess limitations and potential methodologic problems. The "medium risk of bias" category is broad, and studies with this rating vary in their strengths and weaknesses. Therefore, the results of some medium risk of bias studies are likely to be valid, while others are less likely to be valid.

Studies rated "high risk of bias" have significant flaws that may invalidate the results. They have a serious or "fatal" flaw in design, analysis, or reporting; large amounts of missing information; discrepancies in reporting; or serious problems in the delivery of the intervention. The results of high risk of bias studies could be as likely to reflect flaws in study design and conduct as true difference between compared interventions. We did not exclude studies rated high risk of bias a priori but considered such studies to have low reliability.

**Data Synthesis and Rating the Body of Evidence**

Strength of evidence for selected interventions and outcomes was graded using the approach described in the AHRQ EPC Methods Guide for Comparative Effectiveness and Effectiveness Reviews. Interventions and outcomes for strength of evidence assessment were selected based on the evidence available (e.g., RCTs or multiple case series). Strength of evidence assessments were based on the following domains:

- Study limitations, based on the overall risk of bias across studies (low, medium, or high),
- Consistency of results across studies (consistent, inconsistent, or unable to determine when only one study was available),
- Directness of the evidence linking the intervention and health outcomes (direct or indirect), and
- Precision of the estimate of effect, based on the number and size of studies and confidence intervals for the estimates (precise or imprecise).

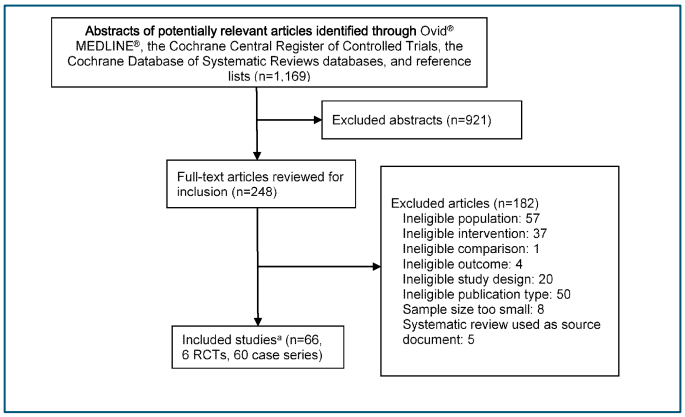
Based on the assessments of the domains described above, the strength of evidence for each intervention was graded as high, moderate, low, or very low. RCTs of interventions start as "high" strength of evidence and are graded down based on the presence and severity of shortcomings in each domain. A "high" grade indicates high confidence that the evidence reflects the true effect and that further research is very unlikely to change our confidence in the estimate of effect. A "moderate" grade indicates moderate confidence that the evidence reflects the true effect and that further research may change the estimate. A "low" grade indicates low confidence that the evidence reflects the true effect and that further research is likely to change the confidence in the estimate of effect and could increase the confidence in the estimate. A "very low" grade indicates evidence either is unavailable or is too limited to permit any conclusion, due to substantial study limitations, inconsistency, or imprecision. In general, evidence based solely on case series was graded "very low" due to the limitations of this study design, in particular the lack of a control group and inability to control for confounders or determine causality.

**Results**

The search and selection of articles are summarized in the literature flow diagram (Figure 2).

Database searches resulted in 1,169 potentially relevant articles. After dual review of abstracts and titles, 248 individual studies were selected for full-text dual review, and 66 studies met inclusion criteria and were included in this review. These included 6 trials and 60 case series, but no cohort studies.

**Figure 2. Literature Flow Diagram**




## Determination of Evidence Strength

The AUA employs a three-tiered strength of evidence system to underpin evidence-based Guideline statements. In short, high certainty by GRADE (Grading of Recommendations Assessment, Development and Evaluation) translates to AUA A-category strength of

evidence, moderate to B, and both low and very low to C (Table 1).

The AUA categorizes body of evidence strength as Grade A (well-conducted and highly-generalizable RCTs or exceptionally strong observational studies with consistent findings), Grade B (RCTs with some weaknesses of procedure or generalizability or moderately strong observational studies with consistent findings), or Grade C (RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes or observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data). By definition, Grade A evidence is evidence about which the Panel has a high level of certainty, Grade B evidence is evidence about which the Panel has a moderate level of certainty, and Grade C evidence is evidence about which the Panel has a low level of certainty.

Level B evidence may include observational studies rated as low quality if findings are consistent and of a strong treatment effect. Panelists can therefore make a stronger statement based on this evidence. In instances where evidence for a given question is rated as level C, this does not mean that the panel cannot make a statement based on the evidence, particularly if findings from included studies are not substantially different. Furthermore, in cases where studies show conflicting evidence or evidence is sparse, panelists may still use clinical judgment to inform a guideline statement. Note that the worst possible rating for RCTs is Level B. Therefore, evidence comprised of RCTs and systematic reviews that included only RCTs would be judged as either Level A or Level B.

## AUA Nomenclature: Linking Statement Type to Evidence Strength

The AUA nomenclature system explicitly links statement type to body of evidence strength, level of certainty, magnitude of benefit or risk/burdens, and the Panel's judgment regarding the balance between benefits and risks/burdens (Table 2). *Strong Recommendations* are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is substantial. *Moderate Recommendations* are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is moderate. *Conditional Recommendations* are non-directive statements used when the evidence indicates that there is no apparent net benefit or harm, when benefits and harms are finely balanced, or when the balance between benefits and risks/burden is unclear.

All three statement types may be supported by any body of evidence strength grade. Body of evidence strength Grade A in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances and that future research is unlikely to change confidence. Body of evidence strength Grade B in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances, but that better evidence could change confidence. Body of evidence strength Grade C in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances, but that better evidence is likely to change confidence. Conditional Recommendations also can be supported by any evidence strength. When body of evidence strength is Grade A, the statement indicates that benefits and risks/burdens appear balanced, the best action depends on patient circumstances, and future research is unlikely to change confidence. When body of evidence strength Grade B is used, benefits and risks/burdens appear balanced, the best action also depends on individual patient circumstances and better evidence could change confidence. When body of evidence strength Grade C is used, there is uncertainty regarding the balance between benefits and risks/burdens; therefore, alternative strategies may be equally reasonable, and better evidence is likely to change confidence.

Where gaps in the evidence existed, the Panel provides guidance in the form of Clinical Principles or Expert Opinions with consensus achieved using a modified Delphi technique if differences of opinion emerged. A Clinical Principle is a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature. Expert Opinion refers to a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence.

| Table 1: Strength of Evidence Definitions | | |
|---|---|---|
| **AUA Strength of Evidence Category** | **GRADE Certainty Rating** | **Definition** |
| **A** | High | We are very confident that the true effect lies close to that of the estimate of the effect |
| **B** | Moderate | We are moderately confident in the effect estimate<br>The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different |
| **C** | Low<br><br><br><br>Very Low | Our confidence in the effect estimate is limited<br>The true effect may be substantially different from the estimate of the effect<br><br>We have very little confidence in the effect estimate<br>The true effect is likely to be substantially different from the estimate of effect |

| Table 2: AUA Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/Burden, and Body of Evidence Strength | | | |
|---|---|---|---|
| Evidence Grade | Evidence Strength A<br>(High Certainty) | Evidence Strength B<br>(Moderate Certainty) | Evidence Strength C<br>(Low Certainty) |
| Strong Recommendation<br>(Net benefit or harm substantial) | -Benefits >Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) is substantial<br>-Applies to most patients in most circumstances and future research is unlikely to change confidence | -Benefits>Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) is substantial<br>-Applies to most patients in most circumstances but better evidence could change confidence | -Benefits>Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) appears substantial<br>-Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation) |
| Moderate Recommendation<br>(Net benefit or harm moderate) | -Benefits>Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) is moderate<br>-Applies to most patients in most circumstances and future research is unlikely to change confidence | -Benefits>Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) is moderate<br>-Applies to most patients in most circumstances but better evidence could change confidence | -Benefits>Risks/Burdens (or vice versa)<br>-Net benefit (or net harm) appears moderate<br>-Applies to most patients in most circumstances but better evidence is likely to change confidence |
| Conditional Recommendation<br>(Net benefit or harm comparable to other options) | Benefits=Risks/Burdens<br>-Best action depends on individual patient circumstances<br>-Future Research is unlikely to change confidence | -Benefits= Risks/Burdens<br>-Best action appears to depend on individual patient circumstances<br>-Better evidence could change confidence | -Balance between Benefits & Risks/Burdens unclear<br>-Net benefit (or net harm) comparable to other options<br>-Alternative strategies may be equally reasonable<br>-Better evidence likely to change confidence |

## Peer Review and Document Approval

An integral part of the guideline development process at the AUA is external peer review. The AUA conducted a thorough peer review process to ensure that the document was reviewed by experts in the diagnosis and management of priapism. In addition to reviewers from the AUA PGC, Science and Quality Council, and Board of Directors, the document was reviewed by representatives from SMSNA, American College of Emergency Physicians, and external content experts. A call for reviewers was placed on the AUA website from April 14 - May 3, 2021 and January 6 - 24, 2022 to allow any additional interested parties to request a copy of the document for review. The guideline was also sent to the Urology Care Foundation to open the document further to the patient perspective. The draft guideline document was distributed to 55 peer reviewers, including 9 external reviewers. All peer review comments were blinded and sent to the Panel for review. In total, 41 reviewers provided comments. At the end of the peer review process, a total of 819 comments were received. Following comment discussion, the Panel revised the draft as needed. Once finalized, the guideline was submitted for approval to the AUA PGC, Science and Quality Council, Board of Directors, and the governing bodies of SMSNA.

# Guideline Statements

## Diagnosis of Priapism

1. **In patients presenting with priapism, clinicians should complete a medical, sexual, and surgical history, and perform a physical examination, which includes the genitalia and perineum. (*Clinical Principle)***

2. **Clinicians should obtain a corporal blood gas at the initial presentation of priapism. (*Clinical Principle)***

3. **Clinicians may utilize penile duplex Doppler ultrasound when the diagnosis of acute ischemic versus non-ischemic priapism is indeterminate. (*Expert Opinion)***

4. **The clinician should order additional diagnostic testing to determine the etiology of diagnosed acute ischemic priapism; however, these tests should not delay, and should be performed simultaneously with, definitive treatment. (*Expert Opinion)***

The optimal method for diagnosing priapism and differentiating acute ischemic priapism versus NIP subtypes has not been defined. Specifically, no studies have directly compared various diagnostic algorithms or provided positive and negative predictive values for one form of testing over another. In the majority of cases, the differentiation of acute ischemic priapism versus NIP may be made using only the history and physical exam. However, in cases where the subtype is indeterminate, additional testing may be warranted.

The initial presentation of priapism often happens acutely and in the setting of an emergency department. Early identification of this diagnosis, as well as the sub-type of priapism, allows for rapid initiation of indicated treatments. Thus, collaboration between emergency medicine physicians and urologic specialists is imperative to the provision of appropriate, timely care.

### History

Understanding the history of the episode of priapism is important as history and etiology may determine the most effective treatment. Historical features that should be identified include the following:

- baseline erectile function
- duration of erection
- degree of pain
- previous history of priapism and its treatment
- use of drugs that might have precipitated the episode (Table 3)
- history of pelvic, genital, or perineal trauma, especially a perineal straddle injury
- personal or family history of sickle cell disease (SCD) or other hematologic abnormality
- personal history of malignancies, particularly genitourinary malignanc

| Table 3: Drugs/Medications Associated with Priapism | |
|---|---|
| **Drug class** | **Documented examples** |
| Attention deficit hyperactivity disorder medications | Atomoxetine |
| Alpha-Adrenergic Blockers | Doxazosin, prazosin, tamsulosin, terazosin |
| Anticoagulants | Heparin, warfarin |
| Antidepressants/Antipsychotics | Bupropion, chlorpromazine, clozapine, fluoxetine, lithium, olanzapine, phenothiazines, risperidone, sertraline, thioridazine, trazadone |
| Antihypertensives | Guanethidine, hydralazine, propranolol |
| Hormone therapy | Gonadotropin-releasing hormone, testosterone |
| Recreational drugs | Alcohol, cocaine, marijuana |
| Vasoactive erectile agents | Alprostadil, papaverine, phentolamine, prostaglandin E1, combination agents |

| Table 4: Key Findings in the Evaluation of Priapism | | |
|---|---|---|
| **Finding** | **Ischemic Priapism** | **Non-ischemic Priapism** |
| Corpora cavernosa fully rigid | U | O |
| Penile pain | U | O |
| Abnormal cavernous blood gases | U | O |
| Hemoglobinopathy or hematologic malignancies | S | O |
| Recent intracavernosalvasoactive drug injections | S | O |
| Chronic, well-tolerated tumescence without full rigidity | O | U |
| Perineal trauma | O | S |
| O: Seldom present; S: Sometimes present; U: Usually present | | |

### Examination

The genitalia, perineum, and abdomen should be carefully examined. In patients with priapism, the corpora cavernosa are typically affected while the corpus spongiosum and the glans penis are not. Further, the corpora cavernosa in acute ischemic priapism patients are often fully rigid and tender, while men with NIP exhibit partial corporal tumescence (Table 4). Abdominal, pelvic, and perineal examination may reveal evidence of trauma or malignancy.

### Corporal Blood Gas

Blood gas testing is the most common diagnostic methods of distinguishing acute ischemic priapism from NIP when the diagnosis cannot be made by history alone. Blood aspirated from the corpus cavernosum in patients with acute ischemic priapism is hypoxic (dark red), while corporal blood in NIP patients is normally oxygenated (bright red). Corporal blood gases in men with acute ischemic priapism typically have a $PO_2$ of < 30 mm Hg, a $PCO_2$ of > 60 mm Hg, and a pH < 7.25. Cavernous blood gases in men with NIP are similar to the blood gases of arterial blood, while normal flaccid penis cavernous blood gas levels are approximately equal to those of mixed venous blood. Typical blood gas values are shown in Table 5.

In the majority of cases presently acutely to the emergency department, a corporal blood gas should be obtained during the initial evaluation to diagnose the priapism subtype. However, there are certain clinical situations where a blood gas may be omitted at the clinician's discretion. Examples include priapism induced by in-office or at home ICI therapies, cases of recurrent ischemic priapism (i.e., SCD), or when the diagnosis is abundantly clear by history and examination alone.

| Table 5: Typical Blood Gas Values | | | |
|---|---|---|---|
| **Source** | **$PO_2$ (mm Hg)** | **$PCO_2$ (mm Hg)** | **pH** |
| Acute ischemic priapism (cavernous blood)[3] | <30 | >60 | <7.25 |
| Normal arterial blood (room air) | >90 | <40 | 7.40 |
| Normal mixed venous blood (room air) | 40 | 50 | 7.35 |

**Radiologic Evaluation**

Penile duplex Doppler ultrasonography (PDUS) is not the primary way to diagnose priapism. While radiologic imaging studies have demonstrated utility in the evaluation and management of priapism, this is largely outside of the acute phase of presentation. As such, imaging studies should not be incorporated into the acute evaluation and management of priapism in the emergency department by non-urologist specialists.

However, imaging may be utilized in less clearly delineated cases to differentiate between acute ischemic priapism and NIP. PDUS findings that are consistent with acute ischemic priapism include bilateral absence of flow through the cavernosal arteries, peak systolic flows <50 cm/sec, mean velocity <6.5 cm/sec, and diastolic reversal (i.e., negative end diastolic velocities).[4] In contrast, NIP is associated with peak systolic velocities of >50 cm/sec.[4] In the non-acute setting, PDUS it may also identify anatomical abnormalities, such as a cavernous artery fistula or pseudoaneurysm in patients who already have been diagnosed with NIP. These abnormalities may occur following a straddle injury or direct scrotal trauma and are, therefore, most often found in the perineal portions of the corpora cavernosa.

Pelvic MRIs have also been described as another potential imaging modality to assist in acute ischemic priapism management. In one notable study, T2-weighted gadolinium-enhanced MRI demonstrated 100% sensitivity in identifying non-viable corporal smooth muscle and which predicted future erectile dysfunction.[5] However, given the time sensitivity of ischemic priapism diagnosis and management, MRI likely does not have a role in the initial diagnostic and treatment phase of priapism.

**Laboratory Evaluation**

The optimal blood tests to identify the etiology of acute ischemic priapism have not been defined and should be selectively ordered based on specific patient risk factors and clinical suspicion. A complete blood count (CBC) is a routine test that may identify elevated white blood cell counts, potentially identifying cases where priapism is due to underlying malignancy (e.g., leukemia). Among men with sickle cell disease, acute ischemic priapism is associated with lower hemoglobin and elevated lactate dehydrogenase, bilirubin, aspartate aminotransferase, reticulocyte count, white blood cells, and platelet counts.[6] Platelet and eosinophil counts may also be elevated in men with acute ischemic priapism. While these laboratory values may contribute to the identification of underlying cause, they often will not be used to guide treatment of the acute presentation.[7, 8]

Hemoglobin electrophoresis, or similar hemoglobinopathy testing, may be appropriate in select clinical scenarios and based on underlying clinical suspicion (e.g., patient race). In most cases, most men with SCD have been diagnosed previously. The yield of identifying men with previously undiagnosed SCD among a cohort of men presenting with priapism is not well established. As such, electrophoresis and other sickle cell testing should be reserved for select clinical scenarios. A reticulocyte count will assist in determining the status of a patient with SCD and other hematologic conditions, may help to identify previously undiagnosed conditions predisposing to priapism and may thus be incorporated into the workup of these patients, along with a CBC.

Screening for psychoactive drugs and urine toxicology may also be performed. Priapism has been associated with certain medications and substances, including drugs of abuse, psychoactive medications, and other classes of medication, both in therapeutic and overdose levels. Despite the role these substances play in the development of priapism, it is notable that testing for potential substances may have a high rate of false negativity, particularly with synthetic and otherwise altered versions of common illicit substances. Additionally, patient history alone may provide much of this information without needing to perform additional testing. Given these associated risks, a thorough medication and social history may provide enough information for the examining practitioner to determine the underlying cause of the priapism presentation without collection of these studies.

## Initial Management of Acute Ischemic Priapism

5. **In a patient with diagnosed acute ischemic priapism, conservative therapies (i.e., observation, oral medications, cold compresses, exercise) are unlikely to be successful and should not delay definitive therapies. (*Expert Opinion)***

As acute ischemic priapism represents a time-sensitive emergency, ineffective therapies that delay resolution are ill-advised. This remains true for acute ischemic priapism events secondary to sickle-cell disease, pharmacotherapy, or other etiologies. No evidence-based recommendations can be made on self-help strategies involving exercise, cool or warm compresses, oral hydration, or masturbation.[9] However, cold compresses should never be used in persons with SCD to avoid provoking vasoconstriction and intravascular sickling. Likewise, oral pharmacotherapy is not recommended for management of acute ischemic priapism. Minimal corporal blood flow characteristic of this condition would preclude efficacy of oral agents, and these drugs may place patients at risk, as seen with the numerous reports of toxicity stemming from oral pseudoephedrine use to treat priapism.[10, 11]

Prior work has shown that oral pseudoephedrine was not better than placebo for achieving resolution of erections induced by intracavernosal alprostadil.[12] Although terbutaline appeared more effective than placebo, it was not significantly better than pseudoephedrine. Subsequent work disputed any value of various doses of terbutaline relative to placebo and noted that this drug has been shown to induce erections.[13, 14] The lack of efficacy for achieving a prompt response is based on bioavailability studies: at 30 minutes following a 10 mg dose of oral terbutaline, serum concentration is zero.[15] It reaches 1 ng/mL at one hour, and peak concentration at six hours. Additionally, peak levels will be much lower in non-fasting subjects.[16]

6. **Clinicians should counsel all patients with persistent acute ischemic priapism that there is the chance of erectile dysfunction. (Moderate Recommendation; Evidence Level: Grade B)**

7. **Clinicians should counsel patients with an acute ischemic priapism event >36 hours that the likelihood of erectile function recovery is low. (Moderate Recommendation; Evidence Level: Grade B)**

The patient with diagnosed acute ischemic priapism should be informed that the natural history of untreated acute ischemic priapism is possible permanent loss of erectile function and corporal fibrosis leading to penile shortening. ED is the most significant complication in patients with prolonged acute ischemic priapism.[17-19] As the duration of acute ischemic priapism increases, so too does necrosis of the smooth muscle tissue, resulting in fibrosis and ED. While the exact time point of irreversible smooth muscle loss is undetermined, it is recognized that smooth muscle edema and atrophy can occur as early as six hours.[17, 18] Bennett and Mulhall demonstrated that sickle cell patients with priapism of >36 hours may have permanent ED with no men studied recovering erectile function.[20] In Zacharakis et al., patients who presented with unresolved acute ischemic priapism >48 hours had extensive necrosis of the cavernous smooth muscle, which resulted in severe ED; >50% of patients with priapism lasting between 24-48 hours had permanent ED.[17]

Managing patients who present with acute ischemic priapism is considered a urologic emergency and the clinician should not treat the patient conservatively. As the duration of the priapism increases, patients may be refractory to first-line treatments, such as ICI of phenylephrine and aspiration, with or without irrigation. In a patient with acute ischemic priapism >36 hours, surgical interventions, such as distal shunting, with or without tunneling, may be required to achieve detumescence; as it is unlikely the acute ischemic event will resolve with ICI therapy of phenylephrine and aspiration. [17 18] While these measures may resolve the symptoms of priapism, patients may develop post-operative ED.[19] Clinical judgement and patient-specific factors will dictate the interventions necessary to resolve the priapic event.

A retrospective chart review of 19 acute ischemic priapism patients by Ortac et al.[18] evaluated detumescence and ED outcomes in patients who failed conservative measures (i.e., aspiration and injection of an intracaversnosal alpha-adrenergic agent) and subsequently underwent shunting, with or without tunneling. Patients were divided into four groups by duration of priapism (<36 hours, 36-48 hours, 48-72 hours, >72 hours). While all patients experienced detumescence, statistical analysis showed that duration of priapism (median: 58 hours) was negatively correlated with post-operative IIEF-5 scores (p=0.046). Sixteen (84.21%) patients experienced post-operative ED; 46.35% (n=9) were unable to achieve any spontaneous erections. The mean post-operative IIEF-5 score across all time durations was 12.68 (range 5-23); patients with priapism <48 hours had higher IIEF-5 (16.4) scores than patients with priapism >48 hours (10; p<0.05). However,

all patients had some degree of ED post distal shunting, with or without tunneling.

In another retrospective chart review of patients with prolonged acute ischemic priapism (n=45; median duration: 96 hours), Zacharakis et al.[17] likewise found a negative correlation between the duration of priapism and developing post-operative ED. Patients were divided into four groups by duration of priapism: <12 hours, 12-24 hours, 24-36 hours, 36-48 hours, >48 hours. All patients, regardless of duration, were refractory to aspiration and ICI and subsequently underwent distal shunting with tunneling. In those with acute ischemic priapism lasting 36 hours, 50% had severe ED and 25% had mild to moderate ED; in patients with priapism events lasting 48 hours, 60% had severe ED and 20% had mild to moderate ED; severe ED developed in 100% of patients who had priapism >48 hrs. Across all patient groups, post-operative IIEF-5 scores were reduced to a mean of 7.7 (from a pre-operative mean of 24), which was related to the duration of the priapism event ($p<0.0005$). Histopathological results corroborate these findings. Each patient had a distal and proximal smooth muscle biopsy taken from the corpora cavernosa; histology results showed that the percentage of viable tissue decreased, and the percentage of fibrosis and necrosis increased, with the duration of the priapism, such that at 36 hours no patients had viable tissue left and necrosis and fibrosis started as early as 12-24 hours.

Similar results were found in other retrospective case series.[19, 21, 22] Pal et al.[19] prospectively observed 19 patients who presented with acute ischemic priapism (mean duration: 96.7 hours), all of whom failed aspiration and ICI and subsequently underwent distal shunting. Only five patients (26.3%) preserved normal erectile function at follow-up. Of the eight patients in the Segal et al. study[21] who were successfully treated with distal shunting (mean duration: 75 hours), none reported return of intact spontaneous erectile function and only two reported partial recovery of erectile function. All patients (n=12; mean duration: 2.8 days) in the study by Lian et al.[22] developed ED following distal shunts plus tunneling; the mean pre-surgical IIEF score was 23.7; the follow-up score was 11.7, indicating a significant decrease in post-surgical erectile function ($p<0.01$).

It is difficult to ascertain if the duration of acute ischemic priapism itself or the surgical procedures to relieve it are primarily responsible for the development of post-operative ED. Age and pre-operative ED may also be contributing factors. Nonetheless, an acute priapism event >4 hours in duration is considered an emergency and requires immediate intervention for detumescence and pain relief. For priapism events >36 hours, immediate intervention with ICI should still be performed, although it is unlikely that this patient population will have any meaningful spontaneous erections.[20] The clinician should counsel the patient that additional surgical interventions, while effective at achieving detumescence, are likely to result in post-operative ED especially in men with acute ischemic priapism of >36 hours.

## Pre-Surgical Management of Acute Ischemic Priapism

8. **Clinicians should manage acute ischemic priapism with intracavernosal phenylephrine and corporal aspiration, with or without irrigation, as first line therapy and prior to operative interventions. (*Moderate Recommendation, Evidence Level: Grade C)***

Given the emergent nature of acute ischemic priapism, ICI with phenylephrine should begin as rapidly as possible following diagnosis. Specifically, intracavernosal treatments should not be delayed due to other systemic therapies (e.g., hydration, exchange transfusion), but may be administered concomitantly in most cases. When a decision must be made between systemic and intracavernosal treatments, intracavernosal therapy should take precedence in the majority of cases.

While efficacy has been reported for epinephrine and ethylephrine, the most frequently used agent is phenylephrine. As no other injectable agent has a comparable sample size within the literature, phenylephrine was compared to all other agents combined and found to have a 28% higher rate of detumescence, while other agents appeared comparable to aspiration alone.[23-28] Although use in this context is off-label, phenylephrine is recognized as the preferred agent of choice. It offers rapid onset, and short duration of action. Alpha-1 selectivity is attractive for reducing the potential for adverse cardiovascular events. See

Appendix A for guidance on dosing and administration of phenylephrine.

Corporal aspiration refers to the intracavernosal placement of a needle followed by withdrawal of corporal blood. Irrigation indicates subsequent instillation of fluid (typically saline) into the corpora. These two procedures are often combined to remove clotted, deoxygenated blood and restore arterial flow and smooth muscle and endothelial function. They may be performed alone or combined with instillations of phenylephrine. See Appendix B for guidance on aspiration and irrigation.

Although a modest amount of data exists regarding various ICI therapies, the Panel was unable to identify any studies that specifically compared aspiration and irrigation with saline to alpha adrenergic injections alone. Rather, several studies reported outcomes on the combination of aspiration, irrigation, and alpha adrenergics.[20, 27, 29-32] Overall results demonstrate successful detumescence in 71-93% of cases, with durations of priapism ranging from 5 to 104 hours (mean durations 10-22 hours). Two studies reported post-treatment erectile function and noted overall preservation in 70-92% of patients, with longer durations of priapism associated with worsened long-term function.[20, 29]

In comparing outcomes data between combination therapy of aspiration, irrigation, and intracavernosal alpha adrenergics to alpha adrenergics alone, results appear to suggest greater resolution rates with combination therapy. Specifically, the need for subsequent shunt surgery was required in 15-28% of patients who received combination therapy compared to 43-63% of patients who received intracavernosal phenylephrine without aspiration and saline irrigation.[20, 27, 30-32]

In evaluating aspiration and saline irrigation as solitary therapy, an RCT was performed to compare varying temperatures (10-37ºC) of irrigation in men with iatrogenic priapism.[33] Patients were treated with 25 mL instillations every 20 minutes until resolution or a maximum of 125 mL was administered. Men who received the coldest saline (10º C) experienced the highest rates of resolution (96% versus 60% in men with saline at 37º C). Those failing to detumesce were subsequently treated with ephedrine and achieved a complete response. Although the study population likely represents an easier to treat group (i.e., shorter duration, iatrogenic) compared to the typical emergency department patient, results suggest the potential benefits of using colder irrigation solutions and further support the additive benefits of combination therapy over aspiration and saline irrigation alone. It is noteworthy, however, that cold saline should never be used in men with SCD so as to avoid precipitating intravascular sickling and potential generalized painful crises.

Based on the above data, clinicians treating acute ischemic priapism may elect to proceed with alpha adrenergics, or aspiration and saline irrigation, or a combination of both therapies based on their clinical judgment. Given the relatively high-resolution rates, surgical shunting should not be performed until both alpha adrenergics and aspiration and saline irrigation have been attempted. Even in cases where preserved erectile function is unlikely, clinicians may elect to perform combined treatments to improve penile pain, if present. Intracavernosal therapies may be deferred when ED is anticipated, and expedited placement of a penile prosthesis is planned.

9. **In patients receiving intracavernosal injections with phenylephrine to treat acute ischemic priapism, clinicians should monitor blood pressure and heart rate. (*Clinical Principle)***

Given the alpha-adrenergic effect of phenylephrine, systemic absorption following intracavernosal administration raises concerns for adverse cardiovascular effects, possibly through coronary vasospasm. Additionally, dosages are often calculated based on bedside preparations that may lack precision. Monitoring patients during and following treatment allows for detection of elevation in blood pressure, tachycardia, or reflex bradycardia.

Blood pressure and heart rate monitoring seems especially prudent in patients with a history of cardiovascular disease, hypertension, prior stroke, and those using medications such as monoamine oxidase inhibitors (MAOIs). Phenylephrine is a direct-acting sympathomimetic (alpha-1 selective) with end organ selectivity, and there are no reports of toxicity when used for priapism in men using MAOI. Potentiation of phenylephrine effects by prior administration of MAOI is most significant with use of oral phenylephrine, which is dissimilar from intracavernosal administration. When parenteral use of phenylephrine has been deemed necessary in patients on MAOI, recommendations have

included use of low starting doses; as such,gradual dose escalation may be reasonable when treating priapism in men using these medications. Should blood pressure spike, this would be detected by monitoring and appropriate medical intervention could be performed.

The number of studies specifically reporting use of continuous monitoring are few, with even fewer commenting on numerical values.[31, 34-37] In most cases, there was no change in heart rate or blood pressure, but even when mild changes were detected, they were not found to be clinically relevant.[31, 34-36]

Although few in number, case reports have described adverse events such as myocardial infarction and intracranial bleeding following intracavernosal phenylephrine. However, some instances were questionable for causation based on the low dose of administered medication (i.e., 100 mcg) or excessive use of pseudoephedrine prior to presentation.[11, 38-40]

It is possible that phenylephrine doses higher than those suggested in prior guidelines may better facilitate prompt detumescence, especially in an acidic corporal environment. A need for less injections seems advantageous for patients and earlier resolution may also mean less physician fatigue factoring into a decision to proceed to shunting. One series featuring a median dose of 1000 mcg (500-2000 mcg) noted absence of adverse effects in all patients; however, none suffered from baseline coronary artery disease or peripheral artery disease, and no patient had a history of using MAOI.[41] Another study featuring a median dose of 1500 mcg noted a decline in diastolic blood pressure and heart rate between admission and discharge, but this was clinically insignificant and possibly confounded by change in pain level and overall clinical condition.[31] Additionally, cumulative doses of 40-50 mg over 1-2 days have been reported without adverse outcomes.[35]

## Surgical Management of Acute Ischemic Priapism

10. **Clinicians should perform a distal corporoglanular shunt, with or without tunneling, in patients with persistent acute ischemic priapism after intracavernosal phenylephrine and aspiration, with or without irrigation. (*Moderate Recommendation, Evidence Level: Grade C)***

A surgical shunt should not be considered as first-line therapy. The decision to initiate surgery requires the failure of nonsurgical interventions. However, deciding when to end nonsurgical procedures and proceed with surgery will depend on the duration of the priapism. For acute ischemic priapism of extended duration, response to ICI of sympathomimetics becomes increasingly unlikely. Phenylephrine is less effective in priapism of more than 48 hours because ischemia and acidosis impair the intracavernous smooth muscle response to sympathomimetics.[42] Under such anoxic conditions, phenylephrine produces poorly sustained phasic contractile responses. In particular, injection of sympathomimetics after 72 hours offers a lower chance of successful resolution and a surgical shunting procedure often is required to re-establish circulation of the corpora cavernosa.[43]

Accordingly, when non-surgical interventions fail, a distal corporoglanular shunt should be considered. The optimal type of distal corporoglanular shunt (e.g., Winter's, Al Gorab, Ebbehoj, T-Shunt) for the treatment of acute ischemic priapism has not been defined. Specifically, no studies have directly compared the various surgical approaches. The overwhelming majority of studies include small patient cohorts and are retrospective in nature, except for one prospective study that included 19 patients.[18]

Similarly, there are no studies comparing shunting alone versus shunting with tunneling. Four studies reporting on various distal shunts with corporal tunneling, including the Burnett snake maneuver, demonstrate generally high rates of immediate success at relieving priapism.[17, 21, 22, 44] In five studies with pre- and post-treatment erectile function information, distal shunts, both with and without tunneling, demonstrate deleterious effects on erectile function. Use of tunneling, however, is associated with greater degradation of post-procedure erectile function compared to distal shunting alone.[17, 18, 21, 22, 44]

Potential non-erectile complications of distal shunting and tunneling procedures include urethral injury, cavernositis, persistence of fistula, infection, and penile skin necrosis.

**11. Clinicians should consider corporal tunneling in patients with persistent acute ischemic priapism after a distal corporoglanular shunt. Moderate Recommendation, Evidence Level: Grade C**

Distal corporoglanular shunts aim to relieve a compartment syndrome through evacuation of blood trapped within the corpora. As an adjunct to needle or scalpel-based opening of the distal end(s) of the corpora, instrument passage (typically a dilator) into the corporal tissue has been used to further facilitate drainage and detumescence. This is referred to as 'tunneling' or 'snaking'. This concept using surgical dilators to evacuate ischemic clotted blood from the proximal crura of the penis through a distal shunt aims to re-establish blood flow. The data to evaluate the utility of tunneling is very limited and of low quality. There are no RCTs or comparative studies, and observational studies preclude unbiased comparisons between distal shunts with and without tunneling.

Pooled data suggest that the addition of tunneling may afford slightly higher rates of successful detumescence. However, the success rates of studies without tunneling are driven lower by the poor results seen with Winter's shunts. Analysis of the literature has shown that scalpel-based shunts (e.g., Ebbehoj, Al Ghorab, Lue T Shunt) provide higher success than needle-based (i.e., Winter's) shunts.[19, 28, 32, 45-59] Another potential factor relevant to comparative success rates is duration of priapism prior to the intervention of interest. In one study of patients managed with tunneling, detumescence was achieved in 100%, 34%, and 0% of cases treated before 24 hours, at or beyond 48 hours, and at or beyond 96 hours, respectively.[17]

While all distal shunts may be detrimental to future erectile function, the limited data suggests the insult of the dilator to the corporal tissue may be greater with tunneling.[17-19, 21, 22] Studies included in the evidence base for this Guideline (one observational[19] and four retrospective chart reviews[17, 18, 21, 22]) reported on erectile function following distal shunt procedures with or without tunneling. In most cases, distal shunts with tunneling had a deleterious effect on erectile function recovery. However, factors such as baseline erectile function and duration of ischemia are confounders. Thus, it is unclear whether tunneling produces an insult detrimental to future ED that exceeds the risk of ischemic priapism itself. Complications including wound infections, fistula, skin necrosis, and gangrene have been reported for distal shunts, with and without tunneling, so it is unclear if the additional corporal disruption imparts greater risk.[49, 60, 61]

**12. Clinicians should counsel patients that there is inadequate evidence to quantify the benefit of performing a proximal shunt (of any kind) in a patient with persistent acute ischemic priapism after distal shunting. (*Moderate Recommendation, Evidence Level: Grade C)***

Proximal shunts are optional for the surgeon, based on clinical judgment and comfort level. In general, it is the Panel's opinion that proximal shunting represents a historical procedure and has largely been replaced by distal shunts with tunneling procedures.

Several proximal shunting procedures have been described to address persistent priapism after failure or suspected failure of distal shunts, including Quackels (corpus cavernosum to spongiosum), Grayhack (corpus cavernosum to saphenous vein), and Barry (corpus cavernosum to deep dorsal vein) procedures. To evaluate the role and efficacy of these procedures, a systematic review was performed of all published literature from 1960 to 2020 where proximal shunts were performed after suspected failed distal shunts. A total of 17 observational studies were included (n=62 patients in total), of which two were moderate and 15 were low quality.[19, 21, 30, 46, 49, 54, 55, 62-71] Specific protocols for managing priapism varied among the studies, including different utilizations of aspiration, irrigation, and ICI therapy; specific distal shunt performed; and number of prior attempted shunts. Similarly, the study cohorts were very heterogeneous and included priapism durations ranging from 6-180 hours and sickle cell and non-sickle cell populations. With few exceptions, outcomes were not measured in a rigorous manner, with detumescence defined clinically and few studies utilizing the standardized IIEF to characterize erectile function post-operatively.

Results demonstrated an overall rate of successful priapism resolution in 76.6% of cases with similar rates among the various procedures. The majority of studies included outcomes of Grayhack and Quackel procedures (n=13 studies), one study utilized the Barry technique, and the remainder failed to report details of the specific procedure. With limited data, the duration of priapism did

not appear to meaningfully impact the ability to achieve detumescence, with successful resolution achieved in 50%, 55.6%, and 60% of men who had priapism for 5-30 hours, 36-72 hours, and >72 hours, respectively. Older men were more likely to experience successful detumescence after the proximal shunt (63.6%, 60%, and 90% for 13 to 29 years, 30 to 44 years, and over 45 years of age, respectively).

Arguably, the two key objectives in achieving detumescence in men with priapism are to preserve erectile function and to reduce post-procedure pain. Using combined data from 12 studies (n=30 patients), and assuming best case scenarios in cases where the data were ambiguous (i.e., considering an ambiguous outcome as successful), only 27.5% of patients experienced preserved erectile function after proximal shunting.[19, 49, 54, 55, 62-69] As with distal shunting, the duration since onset of priapism was a strong predictor of preserved erectile function. Limited data from 5 studies (n=12 patients), demonstrated a strong correlation between the time since onset of priapism and ultimate erectile function outcome ($r=0.78$, $p<0.01$, with one outlier excluded).[19, 49, 54, 68, 69] Using a 72-hour cut-point, all men with successful detumescence prior to this time experienced some degree of preserved erectile function compared to 40% with minimally preserved function beyond that time. These data would argue for more aggressive measures during the first 2-3 days of priapism, with declining benefits when performed beyond that time period.

Beyond the data presented, there are several important clinical considerations in deciding on whether a proximal shunt is appropriate and should be performed. One key issue is the ability to determine if detumescence has been adequately achieved following distal shunting. Particularly in men with more prolonged cases of priapism (>24 hours), edema, ecchymoses, and induration are often indistinguishable from persistent priapism. In this setting, and recognizing an absence of data, is the Panel recommends that a vascular study (such as a PDUS) or cavernosal blood gas should be performed prior to performing additional interventions (repeat distal or proceeding to proximal shunting).

The Panel also recognizes the significant lack of data on proximal shunts. As noted previously, the entirety of published literature available over the past 60 years includes only 62 patients. This paucity of data suggest that proximal shunting procedures are likely rarely performed in contemporary and historical clinical practice. As such, there are likely no surgeons who have extensive experience in this area, and broader training and education on methods of optimizing outcomes are therefore not possible. Additionally, the extent and rate of complications from proximal shunting is understudied and could potentially lead to significant comorbidities such as urethrocutaneous fistulae, urethral strictures, or other similar issues. From a practical standpoint, such limited data would typically relegate a procedure to experimental status. Additionally, some of the described procedures require distinct skillsets outside of a general urologist's training, including performing vascular anastomoses to the saphenous or dorsal penile vein.

With the above recognitions, the Panel suggests that the decision to proceed with a proximal shunt should be based on several factors, including the surgeon's comfort level with the procedure, patient age and pre-operative erectile function, and duration since onset of priapism. Additionally, a proximal shunt should only be considered after failure of more established, conservative procedures, including distal shunting with tunneling. Using these criteria, in situations when surgeons are uncomfortable performing proximal shunts, in the case of older patients, those with poor erectile function at baseline, and men with priapism duration >72 hours, observation or placement of a penile prosthesis may be preferred in lieu of a proximal shunt. Additionally, because of the above-mentioned limitations, the Panel consensus is that proximal shunting should not be considered a mandatory procedure for men who have been confirmed to have failed distal shunting but rather one of several treatment options which may be considered.

## Post-Shunting Management of Acute Ischemic Priapism

13. **In an acute ischemic priapism patient with a persistent erection following shunting, the clinician should perform corporal blood gas or color duplex Doppler ultrasound prior to repeat surgical intervention to determine cavernous oxygenation or arterial inflow. (*Moderate Recommendation, Evidence Level: Grade C)***

In cases where a patient is refractory to shunting, subsequent intervention may be necessary.[72] In this scenario, the clinician must perform a confirmatory test to assess penile hemodynamic characteristics and extent of necrosis/fibrosis to inform secondary treatment decisions[4, 72] and should not base further surgical decisions based on exam alone. The Panel acknowledges this is a complex scenario; therefore, corporal blood gas or imaging should be utilized following shunt procedure to differentiate persistent acute ischemic priapism from reactive hyperemia or conversion to NIP. Evaluating the status of a patient with refractory priapism is particularly important in the event that a patient is referred from another institution and/or the clinician is seeing a patient who had been previously treated elsewhere and a complete patient history may not be available.

Penile corporal blood gas is easily performed and should be utilized in patients when the clinician must establish cavernosal oxygenation status post-shunting. This can help with decision making about proceeding to additional surgical procedures including placement of an immediate penile prosthesis.

The role of imaging is a diagnostic intervention in the management of acute ischemic priapism, particularly in patients who require assessment of arterial inflow during an acute ischemic event. In a diagnosed acute ischemic priapism patient who has undergone a distal shunt, with or without tunneling, post-procedural imaging can determine shunt patency by showing restoration of cavernosal arterial inflow.

Much of the data that examines the use and accuracy of different imaging techniques on priapism patients is indirect (i.e., assessing pre-procedure integrity and viability of penile tissue,[17, 22, 72, 73] ascertaining post-procedure shunt patency[63, 72, 74]) and is not powered to study the accuracy of imaging techniques in patients who have failed shunting surgery and are therefore candidates for further intervention. However, one study by Chiou et al.[72] retrospectively reviewed charts of 24 patients who presented with priapism, 11 of whom were referred from other institutions and were refractory to previous aspiration and ICI therapy (n=2), distal (n=8), or proximal (n=1) shunts. PDUS at presentation showed no detectable cavernosal arterial flow in any of the patients, verifying earlier interventions had failed. Distal shunts were placed in all 11 patients; 12 post-operative PDUS studies in 8 patients were performed, revealing patency in all patients was achieved.

In a retrospective chart review of 52 priapism patients, von Stemple et al.[4] used PDUS of acute ischemic priapism (n=42) and NIP (n=10) patients and compared the results against each other and against tissue biopsy to assess the accuracy of imaging. The acute ischemic priapism patients had either failed aspiration and irrigation but had not yet undergone shunt surgery (n=14), had failed a previous shunt (n=22), or had not yet undergone intervention (n=6). Most of the acute ischemic patients (n=37) had biopsy samples taken at the time of surgical intervention and were analyzed for fibrosis or necrosis and provided a measure of PDUS diagnostic accuracy. PDUS results in the NIP and acute ischemic priapism patients who either failed conservative therapies, or had not had any interventions, appeared to be predictive and accurate; however, the results were mixed in acute ischemic priapism patients who failed shunt placement. Of this latter group, PDUS results were accurate and showed classic ischemic patterns in nine patients; however, in 13 patients, results overlapped between ischemic and non-ischemic parameters and could not reliably predict clinical outcome. Histologically, only three patients showed normal tissue with the remaining showing varying degrees of fibrosis. When compared against PDUS results, there was poor correlation between blood flow and histological outcomes, leading the authors to conclude that MRI might be a better alternative than PDUS to assess for smooth muscle viability/necrosis prior to repeat surgical interventions.

PDUS has traditionally been used to assess blood flow; however, the accuracy is limited, particularly in patients who have undergone previous procedures.[4, 5] It can be difficult to interpret and may be inaccurate for acute ischemic priapism patients, especially in the acute setting when qualified personnel with appropriate expertise are lacking. However, PDUS been shown to be effective in assessing blood flow in many clinical conditions and is an option in a diagnostic setting to differentiate between acute ischemic and NIP.[17, 72] Unfortunately, its use is limited by the number of specialists who can currently perform the procedure. Furthermore, in the emergency department setting or in smaller or rural hospitals, the equipment might not be readily available.

## Penile Prosthesis

**14. Clinicians may consider placement of a penile prosthesis in a patient with untreated acute ischemic priapism greater than 36 hours or in those who are refractory to shunting, with or without tunneling. (*Expert Opinion)***

Although most reported cases of acute ischemic priapism resolve with bedside management, some will require surgical intervention. Shunting, with or without tunneling, may provide detumescence for many patients, but some will be refractory despite repeated efforts. The resultant effect of unrelieved and prolonged priapism (as well as surgical interventions) is ultimately cavernosal smooth muscle necrosis and fibrosis, resulting in permanent ED.[75]

Limited data suggest that men who experience ischemic priapism >36 hours have a very low likelihood of return of spontaneous erections, even in the setting of successful detumescence.[20, 76] One center has shown complete concordance between radiologist-based determination of non-viable corporal tissue on pre-operative penile MRI and the presence of smooth muscle necrosis on intraoperative biopsy.[5] The same group has also reported that ischemic priapism in excess of 36 hours is invariably associated with corporal fibrosis and ED.[17] Given these findings, it is the consensus opinion of the Panel that men who present with priapic episodes lasting >36 hours or those who fail attempts at distal shunting may be considered for early (i.e., within 2 weeks) placement of a penile prosthesis. Alternatively, these men may be managed with conservative therapies such as pain control and outpatient follow-up and bypass more invasive procedures (e.g., surgical shunting).

The ultimate decision should be left to the patient and clinician using an informed, shared decision-making approach. The results of imaging in those with prolonged priapism may assist patient counseling. Likewise, if the prospects of functional recovery are dramatically low, clinicians may wish to weigh and consider the potential detriment of distal shunting for patients who may elect subsequent implant placement.

It is important to note that before considering conservative management or penile prosthesis placement in men with a priapism >36 hours, the timeline should be sufficiently confirmed. Patient histories relating to an exact timeline may often be unreliable, particularly in cases of concomitant substance use, episodes of intermittent detumescence, recurrent priapism (e.g., SCD), or partial (not fully rigid) erections. In these settings, clinical judgment is required to identify the true timeline for onset of ischemia (i.e., onset of severe, persistent penile pain). If the timeline is in question, clinicians should preferentially attempt to decompress the priapism, particularly in younger men or those with high baseline erectile function. Similarly, and as noted elsewhere in this guideline, in men with what appears to be a recurrent priapism post distal shunting should undergo confirmatory testing with a corporal blood gas or PDUS to rule out a return of blood flow before considering further surgical interventions (including prosthesis placement).

Decisions regarding placement of a penile prosthesis in a patient with acute ischemic priapism must be made after weighing multiple factors. These include, but are not limited to, the quality of the history provided relative to duration of persistent priapism, overall condition of the patient, health literacy and comprehension, and physician experience. Perhaps due to the complex nature of such decision-making, there are no RCTs relevant to this pathway. The available data suggests that prostheses placed in the setting of acute ischemic priapism are highly effective in providing detumescence,[32, 75, 77] relief of pain,[78] preservation of penile length,[17, 32, 73, 79] return to sexual activity,[32, 73, 75, 77, 79] and overall satisfaction.[17, 73, 75, 77, 79] Infection rates were below 10% for all studies reviewed.

In theory, avoiding disruption of the distal tunica when the chance of priapism resolution is extremely low may prove advantageous for subsequent penile prosthesis placement. In the work by Zacharakis et al., less than half of the men who received a penile implant within 17 days of priapism onset had undergone prior distal shunting.[80] However, infection (7%) and erosion (3%) were unique to this cohort. The authors noted that distal perforation can occur in up to 6% of patients who have undergone previous shunt surgery. This latter observation would suggest a role for preventative measures to reduce distal perforation, although available data are lacking to suggest an optimal technique at the present time. Of the men who received inflatable devices in delayed fashion (median: 5 months), 80% required narrow base cylinders. In a separate multicenter study with less patients, 40% of men

with prior distal shunts undergoing penile implant placement required narrow base cylinders, and 20% needed subsequent explantation for distal erosion.[81]

15. **Clinicians should discuss the risks and benefits of early versus delayed placement with acute ischemic priapism patients who are considering a penile prosthesis.** ***(Moderate Recommendation, Evidence Level: Grade C)***

Once it has been established that a patient suffering from acute ischemic priapism is a candidate for a penile prosthesis, either because other interventions have failed or the timeline suggests function is not otherwise salvageable, they should be counseled about factors relevant to the timing of device placement.

The Panel identified eight primary non-comparative studies addressing immediate insertion[21, 32, 73, 75, 79, 82-84] and eight which addressed delayed insertion.[5, 17, 21, 68, 78, 85-87] Most involved small patient populations. Definitions of 'early' and 'late' varied by reporting institutions, but those undergoing placement after failed shunting were generally deemed 'late'. For immediate or early placement, duration of priapism ranged from 2 to 720 hours, whereas mean duration in delayed studies ranged from 33 hours to 10.5 months. Early placements more often involved malleable devices, whereas malleable and inflatable versions were more evenly distributed in delayed placement studies. Etiologies varied and were similarly distributed across the grouped studies.

Only one study provided comparative data of early versus delayed penile prosthesis placement.[88] Results demonstrated that patients undergoing delayed placement (n=27) were significantly more likely to report penile shortening and to undergo revision surgery than those who underwent early placement (n=27). Similarly, the delayed group had a higher rate of infection (19% versus 7% for early placement). All cases of erosion and device malfunction were unique to the delayed group and satisfaction was higher for the early placement group (96% versus 60% for delayed placement).

When all data were considered, the reoperation rate was similar for early and delayed placement, and rates of erosion, malfunction or failure, and penile curvature were low for all patients. However, infection rates and penile shortening were higher for delayed placement, and length was related to patient satisfaction.

Clinicians should consider all items of relevance before proceeding with a penile prosthesis in a patient with priapism. Repetitive bedside irrigation procedures may, in theory, increase the chances for bacterial entry into the corpora that could threaten an implant with infection. Distal shunts may have compromised the integrity of the tunica albuginea that would surround an implant, possibly predisposing to erosion. Patients may not be in optimal condition for an implant due to status of comorbid conditions (e.g., diabetes) or use of problematic medications (e.g., anticoagulants, immunosuppressants). The urologist involved for management of priapism may lack the experience, comfort level, or materials to render device placement practical and/or possible.

Conversely, allowing fibrosis to mature within the corporal bodies may render them difficult or impossible to dilate, possibly necessitating use of shorter and/or narrower devices than what may have been feasible earlier in the disease process. The need for aggressive maneuvers may also increase the likelihood for inadvertent corporal and/or urethral perforation.

## Recurrent Ischemic Priapism

Recurrent ischemic priapism has been variably defined within the literature and in clinical practice. It is also commonly confused with non-ischemic entities and likely includes several different underlying clinicopathologic etiologies. For the purposes of the current guideline, recurrent ischemic priapism is narrowly defined as being a condition in which a patient experiences recurrent ischemic episodes, with any frequency or over any period of time, with or without meeting the previously cited 4-hour time criteria for 'acute priapism.'

The key differentiating factor between the current definition of recurrent ischemic priapism and other recurrent priapism-like conditions is the requirement of confirmed penile ischemia. Using this definition, a patient with SCD and prior episodes of ischemic priapism who experiences recurrent painful episodes of prolonged erections would be considered as having recurrent ischemic priapism, whereas a patient with persistent nocturnal, painful erections which have not be shown to be ischemic or have led to true ischemic priapism would be diagnosed with a separate condition.

It is important to recognize that in the case of recurrent ischemic priapism, clinician judgment will override the more rigid definitions used previously to define ischemic priapism. For example, a patient presenting with recurrent ischemic priapism may appropriately be counseled to abort a persistent erection which has not met the 4-hour criteria using at-home phenylephrine injections, whereas these same recommendations may not be appropriate in other clinical settings.

The panel also recognizes that several other subtypes of 'priapism-like' conditions have been defined but are not discussed in the current guideline. Specifically, sleep-related painful erections, undesired prolonged erections, and recurrent NIP all likely represent distinct conditions and pathologies. However, each of these conditions is likely distinct from recurrent ischemic priapism given the lack of underlying ischemia and without the need for emergent intervention. Similarly, very limited data exist on management strategies of these conditions, and their existence and optimal treatments remain investigational at the present time. Further research, including multicenter registries are merited given the relative low prevalence of these conditions and significant heterogeneity in diagnosis and treatment.

16. **Clinicians should inform patients with recurrent ischemic priapism that optimal strategies to prevent subsequent episodes are unknown. (*Conditional Recommendation; Evidence Level: Grade C)***

Evidence is sparse regarding therapeutic prevention of recurrent ischemic priapism. A total of 6 case series studies met criteria for inclusion with a combined total patient n = 148 with 76 of whom had SCD.[89-94]

Preventative strategies in men with idiopathic recurrent ischemic priapism include oral baclofen, dutasteride, phosphodiesterase type 5 inhibitors (PDE5is [tadalafil or sildenafil]), ketoconazole with prednisone, pseudoephedrine, cyproterone acetate, and aspirin. Preventative strategies for men suffering from recurrent ischemic priapism with SCD include the same treatment medications as above but also etilefrine, hydroxyurea and automated exchange transfusion. In general, ketoconazole with prednisone showed the highest success rate but should be used with caution considering its potential liver toxicity, thus warranting frequent assessment of liver function tests. Cyproterone acetate, an anti-androgen not available in the United States, had similarly high levels of complete response but also had high withdrawal rates due to side effects.

While conflicting treatment efficacy was observed for PDE5is; recent reports have suggested that regimented PDE5i therapy may reduce frequency and duration of priapic episodes with no negative side effects.[95] Home self-injection of phenylephrine on an as needed basis was also utilized in some patients and is reasonable as described in the previous AUA priapism guideline[3] but is not a preventative strategy. Selection of a preventative medication for recurrent ischemic priapism should utilize a shared decision-making approach with careful balance of historically reported results versus side effect profile.

17. **Clinicians should inform patients with recurrent ischemic priapism that hormonal regulators may impair fertility and sexual function. (*Strong Recommendation, Evidence Level: Grade B)***

Although some investigators have reported success in lowering the incidence of recurrent ischemic priapism with hormonal manipulation (e.g., ketoconazole, cyproterone acetate) this is not without associated toxicity. Manipulation of the hypothalamic-pituitary-gonadal axis in these patients has the potential to cause fatigue, hot flashes, breast tenderness, changes in mood, and ED.[91] While none of these issues seem particularly urgent (unlike cardiovascular complaints occasionally seen with drugs like pseudoephedrine), they are poorly tolerated among patients, especially in younger men and may have long-term consequences. Therapies capable of downregulating testicular stimulation from the pituitary may negatively impact sperm parameters, and this issue should be discussed in advance with those men interested in preservation of reproductive potential.

## Sickle Cell Disease and other Hematologic Disorders

18. **In patients with hematologic and oncologic disorders such as sickle cell disease or chronic myelogenous leukemia, clinicians should not delay the standard management of acute ischemic priapism for disease specific systemic interventions. *(Expert Opinion)***

Ischemic priapism, both acute (>4 hours) and shorter "stuttering priapism," occurs in association with a number of hematologic and oncologic disorders including:[96-98]

- SCD
- Thalassemia
- Hemolytic anemias (Congential Dyserythropoietic Anemia Type II, unstable hemoglobinopathies)
- Polycythemia
- Thrombotic thrombocytopenic purpura (TTP)
- Thrombophilic states (deficiencies of protein C, S or FxV Leiden)
- Multiple myeloma
- Chronic myelogenous or lymphocytic leukemias
- Solid tumor-genitourinary malignancies

While there have been no robust studies of the management of acute ischemic priapism in men with these disorders, the best intervention is to relieve episodes with prompt intracavernosal phenylephrine and corporal aspiration, with or without irrigation, as in other acute ischemic priapism patients, before proceeding to systemic therapies specific to the underlying disorder. This is also true in pre-pubertal patients.

Published data concerning management of acute ischemic or recurrent ischemic priapism in the setting of hematologic disorders consists of small non-comparative case series with inconsistent indications for treatment, dosing, follow-up periods, and definitions of outcomes. In homozygous sickle cell anemia, the most common form of SCD, priapism occurs in 23-89% of males by age 18.[99] The event is likely so common because SCD is a disorder of intravascular aggregation and lysis of sickled red blood cells, and associated low bioavailability of nitric oxide (a regulator of erections). Most patients with SCD experience recurrent short ischemic priapism events, (lasting <4 hours and commonly referred to as stuttering priapism) but acute episodes and particularly recurrent acute episodes occur commonly enough (both before and after shorter, stuttering events) that education about when to seek urologic attention is a critical part of the patient education in SCD disorders. Patients with SCD, particularly those who have had at least one acute ischemic (>4 hours) or a shorter stuttering episode, should be advised to present for urologic evaluation for priapism episodes of 4 hours or more, so that detumescence can be induced before permanent corporal damage leading to impotence occurs.[100]

Patients presenting with SCD and acute priapism, including pre-pubescent males, should initially be managed with a focus on urologic relief of the erection as outlined in this guideline. Standard sickle cell assessment and interventions should be considered concurrent with initiation of urologic intervention. Specifically, disease specific systemic care should address:[100]

- hydration with IV fluid only if made NPO (maintenance rate) or dehydrated (replace deficit plus maintenance rate); hyperhydration is not indicated and may predispose to acute chest syndrome.[100]
- supplemental oxygenation only if hypoxic.
- pain management with oral or parenteral opioids as per usual painful events (remembering that some patients with SCD may be tolerant to analgesia because of those prior experiences).
- hematologic status comparison of CBC and reticulocyte count to baseline values; this is best done in consultation with the patient's hematologist. Transfusion is not indicated if hemoglobin is near usual value, and over-transfusion may be associated with neurologic events.[101] Acute exchange transfusion is not indicated.
- the presence of other acute sickle cell events: neurologic disorders including acute stroke, acute chest syndrome, biliary colic, renal insufficiency which while not associated with a higher frequency of priapism may present at the same time.
- the use of ice packs and other cold compresses. These should never be used in SCD patients as they may worsen painful events by precipitating intravascular sickling.

The published literature contains a mixture of acute (> 4 hours) and shorter (stuttering) ischemic events, with few RCTs and predominantly small case series of patients followed for two to six months, thus providing low strength evidence, which is often contradictory. Acute exchange transfusion is the most commonly discussed intervention in persons with SCD and priapism, but the reported outcome was days to penile 'softening' with the results of exchange transfusion overlapping the time to resolution reported without transfusion.[102] However, if operative shunting procedures are required, consideration should be given to a simple transfusion of packed red blood cells to raise the hemoglobin to 9-10 g/dl prior to general anesthesia.[100]

Ongoing chronic (monthly) exchange transfusions do appear to be associated with a reduction in acute and stuttering priapism episodes.[103] Similarly, the role of

hydroxyurea is in the possible reduction of recurrent episodes, although this is not well proven, rather than treatment of acute priapism events. Good general care of the underlying SCD (e.g., treatment of sleep disordered breathing/sleep apnea since many episodes of priapism in SCD are reported during sleep, anticipatory management of constipation which is a side effect of frequent non-steroidal and opiate analgesia for painful events) and general health care including psychologic support will also improve the quality of patient's lives for those with recurrent priapism.[100]

In many of the hematologic disorders that predispose to priapism, the patient will already be aware of the condition and consultation with the patient's primary hematologist will allow the urologist to focus on the priapism. Priapism is a complication many of these conditions due to hyperviscosity from either too many circulating cells or formation of intravenous thrombi. A screening CBC and reticulocyte count, and in comparison to the patient's baseline, will establish the patient's current status. Rarely are blood products required before an aspiration and irrigation procedure, the one exception may be with a very low platelet count (<20,000/uL). After relief of acute priapism management of the underlying condition should prevent recurrence in all but SCD. The mechanism of disease and management is different in solid genitourinary tumors.

A significant number of agents have been tried to prevent subsequent priapism episodes: etilefrine, ephedrine, pseudoephedrine, terbutaline, PDE5is (e.g., sildenafil, tadalafil), 5 alpha reductase inhibitors (dutasteride or finaseride), anti-androgens (cyproterone, bicalutamide, leuprolide, stilboesterol) and ketoconazole/prednisone.[24, 92, 104] However, all studies were small, rarely randomized, had high drop-out/non-compliance rates and with poorly defined indications or outcomes. The largest case series (n=49) of etilefrine in adult men with SCD and stuttering priapism reported a complete remission rate of 6.1%, an undefined partial response of 69.4%, and 12.2% withdrawal rate due to adverse effects.[91] No consistent improvement in either the frequency or severity of priapism episodes has been reported with any of the other agents.

**19. Clinicians should not use exchange transfusion as the primary treatment in patients with acute ischemic priapism associated with sickle cell disease. (*Expert Opinion)***

Acute exchange transfusion is the most commonly discussed intervention in persons with SCD and priapism, but the reported outcomes were days to penile softening with the results of exchange overlapping the time to resolution reported without transfusion.[102] Acute exchange transfusion and over transfusion are also associated with the development of hyperviscosity and acute neurologic events (Aspen Syndrome).[101] Delay in the known effective intervention of intracavernosal phenylephrine and corporal aspiration, with or without irrigation, to relieve acute priapism in order to plan and perform acute exchange transfusion is not warranted in men or pre-puberal males with SCD.

While emergency exchange transfusion during acute priapism events can be performed safely in experienced centers, there is no data that it terminates the episodes sooner than established procedures or even the natural history of acute events.[103] For prolonged acute priapism events that cannot be relieved with intracavernosal phenylephrine and corporal aspiration, exchange transfusion can be considered. However, the time to prepare for and perform the procedure with extended red cell antigen matched red cell products, usually 6 hours or more, places the patient at increased risk of impotence from the prolonged ischemic priapism event. However, if operative shunting procedures are required, consideration should be given to a simple transfusion of packed red blood cells to raise the hemoglobin to between 9- 10 g/dl prior to general anesthesia.[100]

After relief of acute priapism with the standard recommended urologic intervention of intracavernosal phenylephrine and corporal aspiration, with escalation to shunt procedures if the prior proves ineffective, as recommended elsewhere in this guideline, chronic treatment with hydroxyurea or a scheduled monthly transfusion program may decrease the likelihood of recurrent priapism events.[103] Ongoing chronic (monthly) transfusions, either automated exchange or simple manual, do appear to be associated with a notable reduction in subsequent acute ischemic and stuttering priapism episodes. Decision to pursue chronic transfusion should be discussion between the patient and their primary hematologist.

Similarly acute use of hydroxyurea is not indicated. Hydroxyurea is an oral ribonucleotide reductase inhibitor that requires weeks to months of continuous use to achieve its effectiveness in increasing fetal hemoglobin and red cell adherence and thus decreasing sickle cell events possibly including priapism.[100] However, given the erratic natural history of recurrent priapism in SCD, the value of hydroxyurea in prevention of subsequent episodes has not been conclusively demonstrated.

## Prolonged Erection Following Intracavernosal Vasoactive Medication

A persistent erection following iatrogenic- or patient self-administration of erectogenic medications into the corpus cavernosum (ICI) represents a distinct pathology when compared to acute ischemic priapism or NIP. As such, the natural history and treatment protocols for a prolonged, iatrogenic erection must be differentiated from guidelines and protocols for true priapism. Given the distinct nature of these iatrogenic erections, several important factors relating to management strategies remain poorly defined, including duration requiring intervention and what constitutes a persistent erection, the impact of underlying ICI medication selection, and the efficacy of conservative treatments.

The duration of a persistent erection requiring intervention is not clearly defined. Broadly, the current panel's expert opinion was that an erection lasting <1 hour post injection would not require intervention, while those lasting >4 hours would warrant treatment, regardless of underlying etiology. The decision to intervene in the time-period between 1 and 4 hours would depend on several clinical factors which are discussed in greater detail below.

One factor which may be used to determine whether intervention is appropriate is the extent of penile rigidity. As an example, a mild erection (i.e., not sufficient to penetrate without assistance) would not require treatment, whereas a fully rigid erection might, depending on other factors. Similarly, an intermittently rigid erection is considered differently than a fully rigid erection, which has remained persistent since the original injection.

The use of pain as an indicator for treatment is not relevant in many scenarios, as the intracavernosal medications themselves are often associated with penile pain. Additionally, the ICI itself may directly cause pain from needle trauma or subsequent bleeding, or pain may result from subsequent interventions after ICI (e.g., other injection therapies for Peyronie's disease).

The specific medication used for ICI may also be used in the clinical decision-making process. Specifically, given the known mechanisms of action, the use of alprostadil alone is likely associated with shorter durations of erections and likely has a lower risk of ischemic priapism compared to combination therapies, which include papaverine and/or phentolamine. The dosage selected is also important, as higher dosages are empirically more likely to result in a prolonged erection compared to lower ones.

Several other factors should be considered in deciding whether treatment is warranted for a prolonged erection including the patient's age, baseline erectile function, reliability/capacity, and comorbid conditions, among others.

Incorporating all of the above criteria would suggest that a 23 year-old male who received a large dose of Trimix and has a fully rigid erection for 3 hours may be managed differently than a 73 year-old male with baseline ED who received alprostadil and has an intermittently rigid erection with standing.

20. **In patients presenting with a prolonged erection of four hours or less following intracavernosal injection pharmacotherapy for erectile dysfunction, clinicians should administer intracavernosal phenylephrine as the initial treatment option. (*Expert Opinion)***

21. **Clinicians should utilize intracavernosal phenylephrine if conservative management is ineffective in the treatment of a prolonged erection. *(Moderate Recommendation; Evidence Level: Grade C)***

In contrast to true acute ischemic priapism, prolonged erections, which are <4 hours in duration and occur following ICI pharmacotherapy for ED, are arguably much more common and may be managed differently than acute ischemic priapism. The physiology of prolonged erections versus acute ischemic priapism is also distinct, as the latter often represents conditions where clotting has occurred and true tissue ischemia (with impaired

smooth muscle function and impaired oxygenation) has begun. Prolonged erections frequently occur following deformity assessments, following PDUS for ED, following ICI training for ED therapy, or following one of several intracavernosal therapies. It is important to recognize that there are very few studies which have been published on this topic, with no high-level studies (i.e., RCTs) available to inform recommendations or guidelines.

Prior to initiating treatment, it is important to differentiate conditions which require therapy versus those which may be reasonably observed. Men with prolonged erections that are not fully rigid are less likely to later progress to acute ischemic priapism compared to those with fully rigid erections. As such, partial erections should likely not be counted towards the four-hour time criteria. Similarly, the specific medication used to achieve the erection is an important factor to consider. Men treated with alprostadil alone are less prone to progress to ischemic priapism compared to those treated with papaverine and phentolamine, which may counteract normal pathways of detumescence. Pain is also not likely a helpful indicator, as many men may experience pain relating to the injection medication or pain from full engorgement. Ultimately, clinical judgment is required to determine if any specific therapy is warranted versus additional observation.

The optimal management strategy for a persistent erection following iatrogenic ICI administration is not clear. Several randomized, controlled studies have evaluated the use of oral therapies, including terbutaline, pseudoephedrine, and midodrine in this setting.[12, 13, 105, 106] Results from these small series demonstrated either modest or inconsistent responses. Specifically, oral midodrine as a single dose was not more effective than placebo, whereas in a repeat-dosing protocol, it was modestly more effective (36-41% versus 12-15%). Similarly, oral pseudoephedrine (60 mg) was found to be mildly more effective than placebo, although not statistically significant (28% versus 12%). In a case series of 14 men receiving midodrine 15-30 mg, all men achieved detumescence, although side effects included increased blood pressure and heart rate.

Other potential conservative treatments include applying ice to the penis, ejaculation, exercise, laying supine, and penile compresses. It is notable that none of these therapies have any high-level evidence and that most are based on clinician experience and physiologic mechanism. Given the non-emergent nature of prolonged iatrogenic erections, the Panel felt that these treatments were reasonable and could be done at the clinician's discretion. However, these should never be used in place of, or prolong effective treatments, if more emergent detumescence is required (i.e., if a fully rigid erection > 4 hours).

In contrast to the above therapies, the use of ICI phenylephrine is highly effective in this population. Four specific case series (n=126 combined) with phenylephrine doses ranging from 200-1000 mcg achieved detumescence in 100% of men.[26, 43, 107, 108] Although other therapies, including multi-step protocols, cold saline infusions, and others have been described with some efficacy, if invasive treatments are required, ICI phenylephrine is recommended, given their clear efficacy and favorable safety profile.[33, 109]

Men with prolonged erections <4 hours who are deemed candidates for treatment should be considered for an injection of intracavernosal phenylephrine; see Supplementary Materials A for guidance on dosing and administration of phenylephrine. Rationale for the use of phenylephrine over other sympathomimetic agents and specific dosing are discussed in Statement 8. Intracavernosal aspiration and irrigation likely represents too aggressive of a therapy for this specific clinical scenario to be used as a first-line therapy. Additionally, the physiologic rationale for aspiration and irrigation is to remove intracavernosal clots and permit entry of fresh blood in an attempt to restore smooth muscle function and vascular drainage. As the pathologic state of intracavernosal clotting and ischemia likely is not present with prolonged erections <4 hours, aspiration and irrigation is rarely warranted. However, persistent, prolonged erections may be considered for aspiration and irrigation if phenylephrine alone is unsuccessful. See Supplementary Materials B for guidance on aspiration and irrigation.

In contemporary practice, prolonged erections often present in distinct 'virtual' clinical settings, including during telephone conversations, text messages, and other similar scenarios. It is the Panel's opinion that these must be managed using the clinician's best judgment and may lead to recommendations of observation with status updates, oral or topical therapies (e.g., pseudoephedrine,

ice), urgent return to clinic with anticipated phenylephrine injection, or referral to the emergency department.

**22. Clinicians should instruct patients who receive intracavernosal injection teaching or an in-office pharmacologically-induced erection to return to the office or Emergency Department if they have an erection lasting >4 hours. (*Expert Opinion)***

The Panel felt that it was important to highlight a clinician's responsibility in managing office-based erectogenic therapies. In cases of prolonged erections resulting from in-office intracavernosal erectogenic injections, the treating physician should make appropriate efforts to achieve adequate detumescence prior to dismissal from the office. Patients should also be counseled as to appropriate management strategies if a fully rigid erection were to recur after leaving the office. In general, the Panel felt that it was not appropriate for clinicians who administer in-office erectogenic medications to refer the patient to the emergency department as a matter of routine following an in-office injection, rather, the patient should return to the office for detumescence whenever possible. Similarly, it is the Panel's opinion that clinicians who lack the expertise, facilities, hospital privileges, or other factors which preclude them from fully managing ischemic priapism (including surgical management if required) should not administer intracavernosal injection therapies.

All patients should be instructed at the time of ICI training, or after receiving an in-office erectogenic therapy, that they should return to either the office or emergency department if they experience an erection lasting longer than 4 hours. If a patient experiences a prolonged erection 1-4 hours after home ICI or following an in-office injection, they may be treated with conservative options (in the case of home ICI) or in-office phenylephrine. However, if the erection persists >4 hours they should be treated according to the ischemic priapism algorithm.

## Non-Ischemic Priapism

**23. Clinicians should counsel patients that non-ischemic priapism is not an emergency condition and should offer patients an initial period of observation. (*Expert Opinion)***

Diagnosed NIP is not a medical emergency. In contrast to acute ischemic priapism, NIP results in an erection with fully oxygenated corporal blood, and thus, no immediate erectile tissue damage occurs.

All diagnosed NIP patients should undergo a period of at-home observation to determine if the fistula will close spontaneously resulting in penile detumescence. It is worth noting that many men with NIP will have observed themselves at home for extended periods of time before clinical presentation, and therefore, may have already fulfilled their period of observation.

In the absence of any rigorous data pertaining to the optimal duration of observation, the Panel suggest that a 4-week period is reasonable, unless the patient is severely bothered by the tumesced penis. This 4-week monitoring period will permit the clinician to define if the fistula has started to close, supporting a further period of close observation. After the 4-week mark, the patient's fistula can be re-evaluated using PDUS; the patient's sexual function and degree of bother can be further quantified. In cases where the fistula is unchanged and/or where patient bother is significant, intervention may be considered.

It has been suggested that prolonged periods of observation may have deleterious effects on the structure and function of the cavernosal smooth muscle and/or sinusoid endothelium. It remains unclear what duration of such observation is required for tissue damage to occur.

**24. In a patient with diagnosed non-ischemic priapism, the clinician should consider penile duplex ultrasound for assessment of fistula location and size. (*Expert Opinion)***

PDUS may be performed in a non-urgent fashion in a patient with NIP to help with screening for anatomical abnormalities and identification of cavernous artery fistula (turbulent flow may be detected) or pseudoaneurysm location and size. Presence of normal to high velocities in the cavernous arteries should be expected in the setting of NIP. Ultrasonography should be performed in the lithotomy or frogleg position, scanning the perineum first and then along the entire shaft of the penis. Ultrasonography is of particular benefit in a patient with NIP being considered for fistula embolization. This allows for communication between the urologist and radiologist prior to intervention regarding fistula location, size, and eventual choice of vascular access. Ultrasonography may also potentially help with the follow-up of a patient with

NIP opting for observation through tracking of fistula and its size. If a urologist with ultrasound experience and/or radiologist is not immediately available, then follow-up with an experienced ultrasound urologist and/or radiologist can be performed non-emergently.

**25. In patients with persistent non-ischemic priapism after a trial of observation, and who wish to be treated, the clinician should offer embolization as first-line therapy. (*Moderate Recommendation, Evidence Level: Grade C)***

For patients with persistent NIP who have failed a period of observation and are bothered by persistent penile tumescence, and who wish to be treated, first line therapy should be percutaneous fistula embolization.

Prior to consideration for embolization, the fistula should be readily visible on a PDUS. The ultrasound should be performed in the erect state and both penile shaft and perineum should be scanned. Embolization should only be attempted by an experienced interventional radiologist. Where the latter is not available, further conservative management (observation) should be conducted or the patient should be directed to a facility which has an interventional vascular radiologist who is experienced in this form of intervention.

While heterogeneity in technical details and patient follow-up undermined the reliability of studies published on embolization, pooled analysis suggest that embolization resulted in penile detumescence in 85% of patients, with 80% of men retaining functional erections.[4, 28, 110-152]

Both resorbable (e.g., gel foam, autologous clot) and non-resorbable (e.g., microcoils, PVA particles) materials can be used. Similar rates of detumescence, preservation of functional erections, and recurrence were found among studies assessing resorbable and non-resorbable agents. While no direct head-to-head studies of resorbable and non-resorbable agents were conducted evaluating detumescence, erectile function, and recurrence, it appears that PVA particles were associated with the best erectile function recovery, while the use of autologous clot was associated with the highest recurrence rate.

In patients who have failed an initial attempt at embolization, patients should be offered a second attempt at an embolization procedure with non-resorbable PVC particles, if available, especially if the first attempt was performed using a resorbable embolizing agent. The Panel recommends this approach, as it is likely to be more effective and safer than an attempt at surgical ligaton, given the lack of experience in the latter approach for most urologists and the poor data supporting ligation.

**26. Non-ischemic priapism patients should be informed that embolization carries a risk of erectile dysfunction, recurrence, and failure to correct non-ischemic priapism. (*Moderate Recommendation, Evidence Level: Grade C)***

Embolization of visualized fistulae or similar vascular anomalies represents a viable therapeutic option in men with NIP. Success rates of embolization in appropriately selected individuals remain high, however, as with all interventions, embolization carries risks of potential adverse effects, including ED, recurrence, and primary failure, among others.

To determine potential risks of embolization, a summary evidence document was created from 42 studies reporting outcomes of embolization in men with NIP.[4, 28, 117-152] All reports represented small series, with a median of 5 patients and the largest being 27 patients. The studies also represented very heterogeneous cohorts and included men with fistulae from prior trauma, surgical procedures, and cases of recurrence following failed prior embolizations. Disease and treatment characteristics were also variable, with widely varying durations of symptoms, location of fistulae, patient ages, and embolization techniques and materials varied significantly. The studies themselves were also of variable quality, with the majority being retrospective in nature and failing to include standardized measures (e.g., IIEF for erectile function).

Overall, in summarizing the combined results from these studies, successful correction of NIP occurred in 85% of individuals undergoing embolization, with 15% experiencing priapism recurrences over time. However, it is notable that approximately 1/3 of studies failed to report on recurrences, and those with longer-term follow-up generally reported higher rates compared to those with shorter follow-up. The range of reported recurrences also varied widely (0-100%), which underscores the poor reliability of the data overall.

The impact on erectile function was also inconsistently described, with only 5/42 studies using the standardized

IIEF questionnaire. Overall, ED occurred in 15% of men post-treatment (17% when only including studies which used IIEF questionnaires) with the range being 0-50%. Although inadequately reported, it is likely that repeated attempts at embolization would be associated with increasing risks of ED.[109]

The specific technique and materials used for embolization have evolved over time, with super-selective embolization being preferentially used in contemporary practices. In reviewing outcomes of studies published between 1960-1999 and 2000-2020, detumescence rates, erectile function, and recurrences are nearly identical. Similarly, the success rates in adults versus children are also similar, with the exception of erectile function, which was preserved in all children under the age of 18. Resorbable materials were reported in the majority of studies (n=29 versus n=15 studies of non-resorbable agents), with comparative outcomes suggesting an approximately 10% lower detumescence rate, ~10% higher ED rate, and ~10% lower recurrence rate with non-resorbables.

Overall, the data on embolization outcomes are too limited to draw any firm conclusions on specific complication rates, or to provide guidance on the optimal method or material used with embolization. The data are sufficient to indicate that complications do occur in a percentage of individuals, including failure, ED, and recurrences. Despite these adverse events, embolization represents a viable therapeutic option in men with NIP men and vascular fistulae, with results suggesting high initial success rates and relatively low complications.

27. **In non-ischemic priapism patients who have failed an attempt embolization of the fistula, the clinician should offer repeat embolization over surgical ligation.** ***(Moderate Recommendation, Evidence Level: Grade C)***

The Panel recommends that the clinician perform repeat embolization in patients who are refractory to embolization. This should be done in the context of shared decision making after the patient is aware of the surgical options. While surgical ligation of the corporo-cavernosal fistula following failed attempts at embolization (or when embolization is not available at the center treating the patient) is an option for patients with NIP, the lack of familiarity of most urologists with this surgical approach makes the procedure particularly challenging. Furthermore, while fistula ligation has historically been performed, it is an outdated procedure and there is inadequate evidence to quantify the benefit of the procedure.

There is not published data to provide a direct comparison between ligation and embolization; however, individual pooled patient data across studies indicate that penile detumescence occurs in approximately 85% of both surgical ligation and embolization patients,[4, 28, 110-152] while erectile function preservation appears to be better with embolization over ligation surgery (85% versus 50% respectively). These comparisons need to be taken cautiously, given the heterogeneity in reporting on erectile function. The majority of studies that reported erectile function as an outcome did not use standardized measures (e.g., IIEF); however, in studies that did report on erectile function using IIEF, 83.3% of patients reported good erectile function after embolization.[122, 125, 128, 130, 137]

# Future Directions

Priapism remains an understudied area of sexual medicine, with several areas of future research required:

- Basic translational science of the pathophysiology of priapism to identify the most effective therapeutic targets.
- Preventative medical and interventional strategies for stuttering priapism, especially in the sickle cell population.
- Identifying the timeline of acute ischemic priapism and permanent corporal fibrosis with subsequent ED in various clinical and etiologic settings.
- Defining risks and benefits of penile prosthetics placement in acute ischemic priapism, including patient reported outcomes, complications, prosthesis durability, and role of malleable versus inflatable devices.
- Methods of controlling thrombosis, including preserving shunt patency.
- Comparisons of surgical techniques: distal versus penoscrotal approaches to distal shunts; distal shunting with or without tunneling.

- Comparison of embolization techniques and materials, including short- and long-term outcomes including patient reported outcomes.
- Comparative, prospective protocols for both acute ischemic and NIP management to better identify optimal management strategies.
- Identifying a role of sexual health counselor in patients with acute ischemic priapism undergoing surgery and how this affects short- and long-term mental health.

As noted above, there are numerous areas where additional research is warranted to improve our understanding and treatment of priapism. Fundamental basic science investigations are necessary to identify pathophysiologic mechanisms and potential treatment targets. The enhanced understanding of mechanisms and pathways of priapism would allow for new pharmacologic treatment strategies to prevent and terminate priapism early in its course. Although a base-level understanding of disease mechanisms currently exists with priapism in general, more nuanced evaluations and research separating subtypes of priapism (e.g., ICI-induced, oral medication-induced, sickle-cell, idiopathic) may provide for a more customized treatment approach. This is particularly relevant with cases of stuttering priapism, where management includes not only the acute phase but also long-term prevention strategies. Research in this area may expand to include the study of the sleep cycle, neurologic perturbations, and 'backward engineering' from medications which have shown some efficacy, including baclofen, anti-androgens or anxiolytics, among others.

Another critical question which remains outstanding relates to the timeline and progression of irreversible corporal damage related to priapism. The issue is further challenged by inaccuracies of estimated duration, possibility of intermittent periods of complete or partial priapism, underlying health of the corporal tissue (i.e., patient age, prior ED, comorbid conditions), prior episodes of priapism, various subtypes (e.g., sickle cell), and interventions performed. This is particularly relevant as providers consider earlier definitive interventions such as placement of a penile prosthesis, wherein confidence is required that spontaneous recovery of erectile function is not possible. Future research into imaging studies, biopsies, adjunctive laboratory testing, or other modalities may help to better inform these decisions. However, at the present time, data are clearly lacking to quantify the true risks and benefits of early, definitive surgical interventions including distal shunting and prosthesis placement in men with acute ischemic priapism.

A third area where future research may benefit outcomes is with anti-thrombotic therapies. As prolonged priapism is associated with cavernosal thrombosis, these therapies may have roles in both the early and late phases of treatment. Specifically, further research is required to determine if anti-thrombotics reduce the frequency of stuttering priapism, minimize the extent of ischemia in active priapism, and/or prevent closure of surgical shunts. Currently, there are very limited data on these topics, however, given the pathophysiology of priapism, the ability to control or regulate corporal thrombosis has inherent appeal.

Finally, significantly more research is required comparing various treatment strategies. Because priapism is an unpredictable and rare event, nearly all research reports are retrospective in nature and do not include comparison groups. Prospective, comparative protocols are warranted to better define optimal treatment approaches. These may include differing surgical techniques (e.g., proximal versus distal approaches, tunneling versus no tunneling, specific methods of shunting); preventative medications; agents and protocols for embolization; imaging modalities; customized algorithms based on etiology and clinical factors; and efficacy of conservative therapies. Outcomes-based assessments and longer-term follow-ups are also merited, as it is not uncommon to see restoration of excellent erection post priapism management in one setting, while another results in clustered recurrence of priapic episodes in another. Although the ideal research protocol would include development of a national priapism registry, in its absence, ambitious clinicians and scientists should consider beginning an institutional database tracking priapism patients and outcomes with pre-defined protocols and standardized follow-up assessments. The development of such protocols would be expected to greatly enhance our understanding of priapism and help provide the data necessary to further refine the next set of guidelines.

# ABBREVIATIONS

| | |
|---|---|
| AUA | American Urological Association |
| CBC | Complete blood count |
| CT | Computerized tomography |
| ECRI | Emergency Care Research Institute |
| ED | Erectile dysfunction |
| GRADE | Grading of Recommendations Assessment, Development and Evaluation |
| ICI | Intracavernosal injection |
| IIEF | International index of erectile function |
| MAOI | Monoamine oxidase inhibitors |
| MRI | Magnetic resonance imaging |
| NIP | Non-ischemic priapism |
| NPO | Nothing by mouth |
| PDE5i | Phosphodiesterase type 5 inhibitors |
| PDUS | Penile duplex Doppler ultrasonography |
| PGC | Practice guidelines committee |
| QUADAS | Quality assessment of diagnostic accuracy studies |
| RCT | Randomized controlled trial |
| SCD | Sickle cell disease |
| SMSNA | Sexual Medicine Society of North America |

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Appendix A

**Dosing and Administration of Phenylephrine**

The optimal regimen for phenylephrine dosing, frequency, and method of administration has not been clearly defined in the scientific literature. As such, the recommendations which follow are all based on expert opinion and recommendations. Clinicians should consider blood pressure monitoring in men undergoing repeated injections and in those with underlying, relevant comorbid conditions (e.g., hypertension). Monitoring seems especially prudent in patients with a history of cardiovascular disease, hypertension, prior stroke, and those using medications such as monoamine oxidase inhibitors (MAOI). Phenylephrine is a direct-acting sympathomimetic (alpha-1 selective) with end organ selectivity, and there are no reports of toxicity when used for priapism in men using MAOI. Potentiation of phenylephrine effects by prior administration of MAOI is most significant with use of oral phenylephrine, which is dissimilar from intracavernosal administration. When parental use of phenylephrine has been deemed necessary in patients on MAOI, recommendations have included use of low starting doses, thus gradual dose escalation may be reasonable when treating priapism in men using these medications. Should blood pressure spike, this would be detected by monitoring and appropriate medical intervention could be performed.

Although there is no upper limit to the number of injections which may be performed, injections should be stopped if blood pressure changes are detected. Similarly, if the erection persists despite repeated attempts with injections and aspiration/irrigation over a period of one hour or more, the panel recommends proceeding with more definitive therapy (i.e., shunting procedure). Indeed, some clinical scenarios may be more appropriate for a more rapid transition to surgical procedures, without prolonged attempts at phenylephrine and aspiration/irrigation (e.g., priapism >36 hours).

*Dosing and instructions*:

- Phenylephrine 100-500 mcg doses suspended in 1 ml of normal saline (optimally premixed by pharmacy to minimize risks of miscalculation/overdose)
- Doses administered ≥5 minutes apart
- Administered intracavernosally (not subcutaneously)
- Administered laterally (3 or 9 o'clock position) near the base of the penile shaft
- May be continued for up to 1 hour (see commentary above)
- Small needles may be used (e.g., 27G)
- Consider performing a penile block with local anesthetic prior to beginning
- In cases where the combination of phenylephrine and aspiration/irrigation are performed, aspiration should precede phenylephrine administration to permit fresh, oxygenated blood to fill the corpora and potentially improve the yield of phenylephrine administration

**Appendix B**

**Sample Protocol for Aspiration and Irrigation:**

The following protocol is one potential example of aspiration/irrigation with instillation of phenylephrine. However, this should not be considered the gold-standard approach, as there are currently no publications which have identified any method which is superior to another. Similarly, the decision as to when to stop performing aspiration/irrigation with phenylephrine will depend on clinical factors, including response to aspiration/irrigation and time since priapism onset, among others.

*Steps for aspiration/irrigation with phenylephrine administration:*

1. Perform a penile block with local numbing medication (if not previously performed).
2. Place a 16-18 gauge butterfly needle in the 3 or 9 o'clock position on the penis near the base.
3. Connect the butterfly needle to a 30-60 cc Luer Lock syringe.
4. Alternate between aspiration of blood clots and instillation of saline (chilled if available and if the patient does not have sickle cell disease) until some degree of detumescence can be achieved.
5. Instill phenylephrine.
6. Allow 3-5 minutes of time to pass.

7. Repeat steps 4-6 until detumescence is achieved or until the decision has been made to proceed with surgical shunting.
8. If temporary detumescence is achieved with aspiration followed by a rapid refilling of blood despite multiple attempts of phenylephrine instillation, consideration may be given to placement of a firm penile wrap at the time of aspiration to maintain detumescence.