

**Erectile Dysfunction after Sickle Cell Disease-Associated
Recurrent Ischemic Priapism:
Profile and Risk Factors**

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Acknowledgments

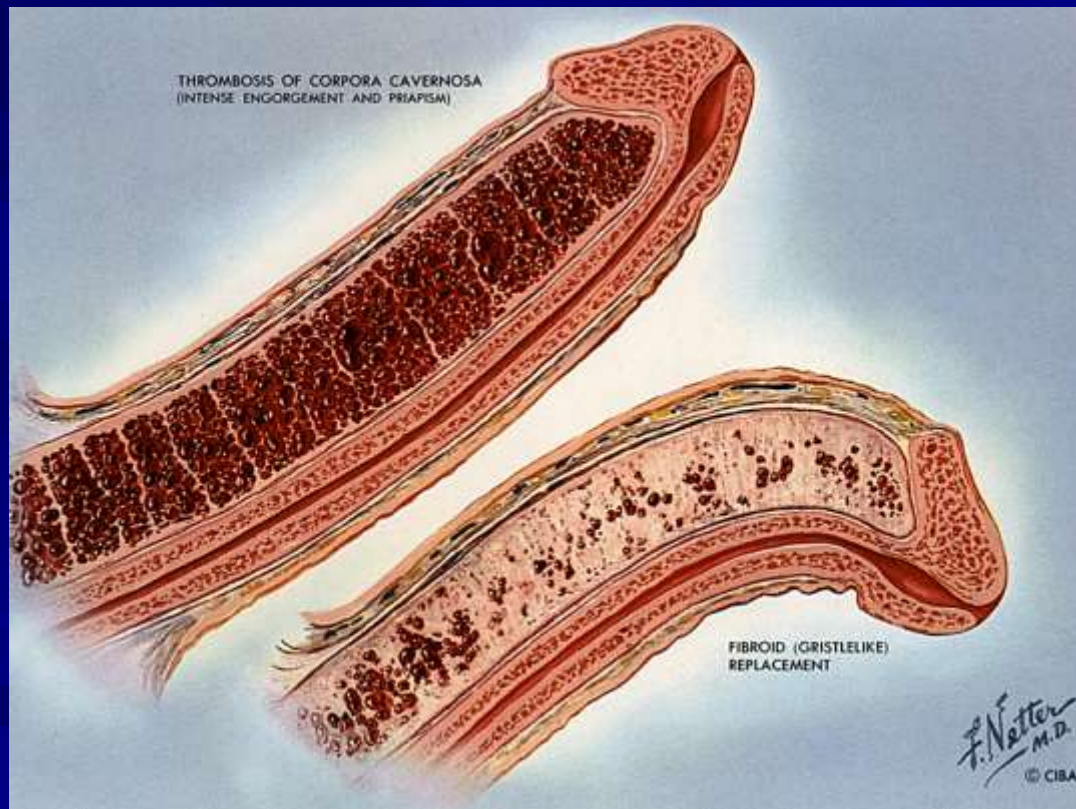
Uzoma Anele MD, Post-Doctoral Clinical Fellow 2013-2015

Disclosures

- American Medical Systems (AMS)
- Auxilium Inc.
- Endo Pharmaceuticals
- Lilly
- Pfizer Inc.
- Reflexonic LLC
- VIVUS
- National Institutes of Health

Definition

“Priapism is a pathological condition of a penile erection that persists beyond or is unrelated to sexual stimulation.”



Types of Priapism

- Ischemic (veno-occlusive or low flow) - 95% prevalence
 - Stuttering (intermittent) = recurrent ischemic priapism
- Non-ischemic (arterial or high flow) – 5% prevalence

Significance of Priapism

- Afflicts 40% of males with sickle cell disease
- Threatens sexual health
- Exerts negative impact on physical and mental health of affected individuals
- Urges comprehensive health programmatic efforts

Priapism-Associated Erectile Dysfunction

- Commonly associated with major ischemic priapism
- Irreversible, time-dependent erectile tissue ultrastructural changes occur after 6 hours of ischemia¹
- Erectile tissue necrosis and fibrosis (with ED rates >90%) occur after 24 hours of ischemia²

1. Spycher MA, Hauri D. J Urol 1986; 135: 142-7.

2. Bennett N, Mulhall J. J Sex Med 2008; 5: 1244-50.

Erectile Dysfunction after Recurrent Ischemic Priapism?

- ED prevalence reported at 29-36%^{1,2}
- However, earlier studies did not clearly define ED or how it was assessed
- Prolonged durations of priapism do not solely account for the risk of ED

1. Emond AM et al. Arch Intern Med 1980; 140: 1434-7

2. Adeyoku AB et al. BJU Int 2002; 90: 898-902

Aim

- To determine and compare ED risk factors associated with sickle cell disease (SCD) and non-SCD related “minor” recurrent ischemic priapism (RIP)

(“Minor” RIP was defined as having ≥ 2 episodes of ischemic priapism within the past 6 months with the majority ($>75\%$) of episodes lasting < 5 hrs)

Methodology

- Retrospective study of RIP in SCD and non-SCD patients presenting to the urology and hematology clinics of the JHMI from June 2004 to March 2014 (n=124)
- Prospectively managed database consisting of priapism-specific, International Index of Erectile Function (IIEF) and IIEF-5 questionnaires
- RIP categories: “Minor” = 2-5 hr; “Very minor” = < 2 hr; “Major” = > 5 hr
- Excluded ED risk confounding factors, e.g., surgical shunts, penile prosthesis surgery, androgen ablative therapies
- ED definitions
 - Any ED: IIEF EF Domain <26, IIEF-5 <22
 - Excluding mild ED: IIEF EF Domain <22, IIEF-5 <17

Patient Demographic and Medical Comorbidities

Characteristic	SCD Patients (n=40)	Non-SCD Patients (n=19)	P-Value
Mean Age, yrs (SD)	28.2 (8.9)	32.6 (11.7)	0.0943
Race, n (%)			
Caucasian	0 (0)	10 (52.6)	0.0001
African American	40 (100)	7 (36.8)	0.0001
Other	0 (0)	2 (10.5)	0.0999
Married, n (%)	6 (15)	7 (36.8)	0.0916
Hypertension, n (%)	8 (20)	5 (26.3)	0.7381
Dyslipidemia, n (%)	1 (2.5)	1 (5.3)	0.5441
Diabetes, n (%)	0 (0)	1 (5.3)	0.3220
Stroke, n (%)	4 (10)	0 (0)	0.2945
Kidney Disease, n (%)	4 (10)	0 (0)	0.2945
Tobacco Use, n (%)	6 (15)	8 (42.1)	0.0460

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Clinical Characteristics

Characteristic	SCD Patients (n=40)	Non-SCD Patients (n=19)	P-Value
Mean Age of RIP Onset, yrs (SD)	19.5 (8.2)	29.1 (13.8)	0.0024
Mean RIP Duration, yrs (SD)	9.2 (6.9)	4.6 (5.0)	0.0042
Episode Onset, n (%)			
Sleep	37 (92.5)	15 (78.9)	0.1030
≤2 hr Episode Duration, n (%)	30 (75)	10 (52.6)	0.1351
≥ Weekly Episode Frequency, n (%)	28 (70)	14 (73.7)	1.0000
Major Episodes, n (%)	14 (35)	11 (57.9)	0.0963
Erectile Dysfunction (includes mild ED), n (%)	19 (47.5)	4 (21.1)	0.0516
Erectile Dysfunction (excludes mild ED), n (%)	13 (32.5)	3 (15.8)	0.1773
Perceived Penile Deformity or Scarring, n (%)	n = 36 7 (19.4)	n = 8 1 (12.5)	1.0000

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ED Risk Associations for RIP Variables

Subgroups		SCD Patients	Non-SCD Patients	P-Value
Including Mild ED		n = 19	n = 4	
	Mean Age of RIP among ED patients, yrs (SD)	18.5 (6.3)	22.8 (5.0)	0.0944
	Mean RIP Duration among ED patients, yrs (SD)	9.5 (6.7)	3.8 (4.2)	0.0807
		n = 30	n = 10	
	≤2 hours Duration, n (%)	14 (46.7)	0 (0)	0.0075
		n = 10	n = 9	
	2-5 hours Duration, n (%)	5 (50)	4 (44.4)	1.0000
		n = 28	n = 14	
	≥Weekly Frequency, n (%)	13 (46.4)	2 (14.3)	0.0404
		n = 12	n = 5	
	≤Monthly Frequency, n (%)	6 (50)	2 (40)	1.0000
		n = 19	n = 4	
	Major Episodes among ED patients, n (%)	7 (36.8)	2 (50)	1.0000
Excluding Mild ED		n = 13	n = 3	
	Mean Age of RIP among ED patients, yrs (SD)	16.1 (2.5)	25.0 (2.6)	0.0120
	Mean RIP Duration among ED patients, yrs (SD)	11.1 (7.1)	2.1 (3.0)	0.0221
		n = 30	n = 10	
	≤2 hours Duration, n (%)	10 (33.3)	0 (0)	0.0428
		n = 10	n = 9	
	2-5 hours Duration, n (%)	3/10 (30)	3 (33.3)	1.0000
		n = 28	n = 14	
	≥Weekly Frequency, n (%)	9 (32.1)	1 (7.1)	0.1249
		n = 12	n = 5	
	≤Monthly Frequency, n (%)	4 (33.3)	2 (40)	1.0000
		n = 13	n = 3	
	Major Episodes among ED patients, n (%)	5 (38.5)	2 (66.7)	0.5500

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Odds Ratios* for Developing ED for SCD Patients

- 4.7 x more likely than non-SCD patients (95% CI: 1.06 – 20.96, $p=0.041$), after controlling for RIP duration, presence of major episodes, episode duration, and episode frequency
- 3.6 x more likely than non-SCD patients (95% CI: 0.69 – 18.35, $p=0.131$), when using the alternative ED definition

*Based on logistic regression analysis

Conclusions

- ED is associated with RIP, occurring in nearly 40% of affected individuals overall and nearly 50% of patients with SCD
- RIP variables associated with the development of ED in SCD patients include duration of priapism recurrences, priapism episode frequency and presence of “very minor” episode durations (≤ 2 hours)
- SCD patients with RIP are nearly 5 times more likely to develop ED compared with those having RIP associated with non-SCD etiologies