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REVIEW

Urological Manifestation of Mpox Virus: A Scoping Review

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Background: Mpox primarily presents with systemic and cutaneous symptoms. However, it can also lead to urological complications, necessitating specialized attention. The aim of this scoping review is to summarize the current evidence regarding the urological manifestations of Mpox, possible complications, and available treatments.

Methods: An electronic systematic search of the current literature was conducted through the Medline and NCBI PubMed and Scopus databases on 18th August 2024. Our study search and inclusion criteria were in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. 9 The search terms and keywords used were: "monkeypox; Mpox" (MeSH Terms), combined with different terms: "urology", "kidney", "ureter", "bladder", "prostate", "genitals", "penis", "testicles", "urethra", in all different possible combinations.

Results: A total of 32 articles included in the scoping review. A total of 116 patients were included, all males. The genitals were the most interested organs, associated with urethritis, while bladder and kidneys seemed to be not impacted by the disease. Patients were usually young, with a mean age of 36 years [31.5–40 years]. The most prevalent risk factor was sexual intercourse in the days/weeks before the appearance of symptoms. All patients had a molecular confirmatory diagnosis by a polymerase chain reaction (PCR) test. Five articles out of 32 (15.6%) reported the need for surgical debridement of penile and genital lesions due to their clinical worsening. However, in most reports, patients experienced spontaneous resolution of the lesions and symptoms.

Conclusion: Awareness of Mpox and timely diagnosis are crucial for ensuring appropriate treatment and reducing the need for surgical management and the possible risk of long-term sequelae. Collaboration among dermatologists, infectious disease specialists, and urologists is pivotal to effectively managing Mpox patients.

Keywords: mpox, monkeypox, urology, UTIs, infections

Introduction

Mpox virus, formerly known as Monkeypox, is an emerging zoonotic viral disease caused by the Monkeypox virus, a member of the Poxviridae family, which has been traditionally confined to central African countries, with only sporadic cases outside this region.[1,2] However, Mpox has recently spread worldwide, making it a global health concern.[3,4] Usually, the clinical presentation of Mpox includes fever, headache, lymphadenopathy, and a characteristic rash that progresses through several stages (from macules to papules, vesicles, pustules, and crusts), affecting inoculum areas (eg mucosae and genitalia). Although Mpox primarily presents with systemic and cutaneous symptoms, it can also lead to urological complications, necessitating specialized attention. Furthermore, this symptomatology, which is often initially non-specific, can delay diagnosis and treatment.[5–8] Correct knowledge of the possible clinical manifestations of the virus also by urologists is pivotal, not only for Mpox patient care, but also for its prevention, prompt diagnosis and reduction of contagion.

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Materials and Methods

Literature Search Strategy

An electronic systematic search of the current literature was conducted through the Medline and NCBI PubMed and Scopus databases on 18th August 2024. Our study search and inclusion criteria were in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[9] The search terms and keywords used were: "monkeypox; Mpox" (MeSH Terms), combined with different terms: "urology", "kidney", "ureter", "bladder", prostate", "genitals", "penis", "testicles", "urethra", in all different possible combinations. References from commentaries, editorials, conference publications, review articles, and included studies were hand-searched and cross-referenced to ensure completeness. The research was performed independently by two Authors (GM and GD), and any disagreement was resolved by a third independent researcher (GG). The initial screening was done on the base of titles and abstracts. Any duplicates were screened, identified, and removed by Endnote (Version 9.2; Clarivate Analytics, Philadelphia, PA, USA) automated tools. The research focused on the urological manifestations of Mpox virus. Non-urological manifestations concerning kidney transplant patients were not considered relevant for this review. As regards genital lesions, only those relating to the male genitals were considered in the review.

Inclusion and Exclusion Criteria

Due to the paucity of literature in this field, also case series and case reports about "urological" clinical manifestations of Mpox virus were considered for the review. Other publications such as reviews and editorials were excluded, but screened in order to identify possible articles missed by our search strategy. The most recent publication was considered if the same patient cohort was used in more than one study. Only studies published in English were included.

Data Extraction Design

When available, the following data were extracted from each eligible study: article information (authors, study design, year), objectives, study cohort, sample size, patients' characteristics, clinical manifestations, involved organs, follow-up, risk factors, and outcomes.

Results

The flow diagram in Figure 1 depicts the number of publications selected or excluded through the different phases of our electronic literature search. After electronic search, we identified 284 studies (118 from PubMed and 166 from Scopus). After duplicates removal we found a total of 193 studies for screening. After careful evaluation we excluded 157 articles for a total of 32 articles included in the systematic review.[10–41]

Type of Articles and Origin

Almost all articles were case reports or small case series, of which only 2 had more than 10 cases described. Most of articles came from US (31.2%) and Italy (18.7%). However, cases were reported from all continents apart from Oceania.

Clinical Data

A total of 116 patients were included, all males. The genitals were the most interested organs, associated with urethritis, while bladder and kidneys seemed to be not impacted by the disease (Table 1). Patients were usually young, with a mean age of 36 years [31.5–40 years]. The most prevalent risk factor was sexual intercourse in the days/weeks before the appearance of symptoms in males who have sex with males (MsM) group. Seventeen studies reported previous sexually transmitted diseases (STDs), while 14 did not report previous comorbidities. Forty patients (34.4%) had HIV co-infection. Fourteen studies reported a genital onset, 17 systemic symptoms before the appearance of genital signs, and two a concomitant onset of both genital and systemic symptoms. In those who reported subsequent genital presentation, this usually occurred after a mean 5 days [4–7 days] after the

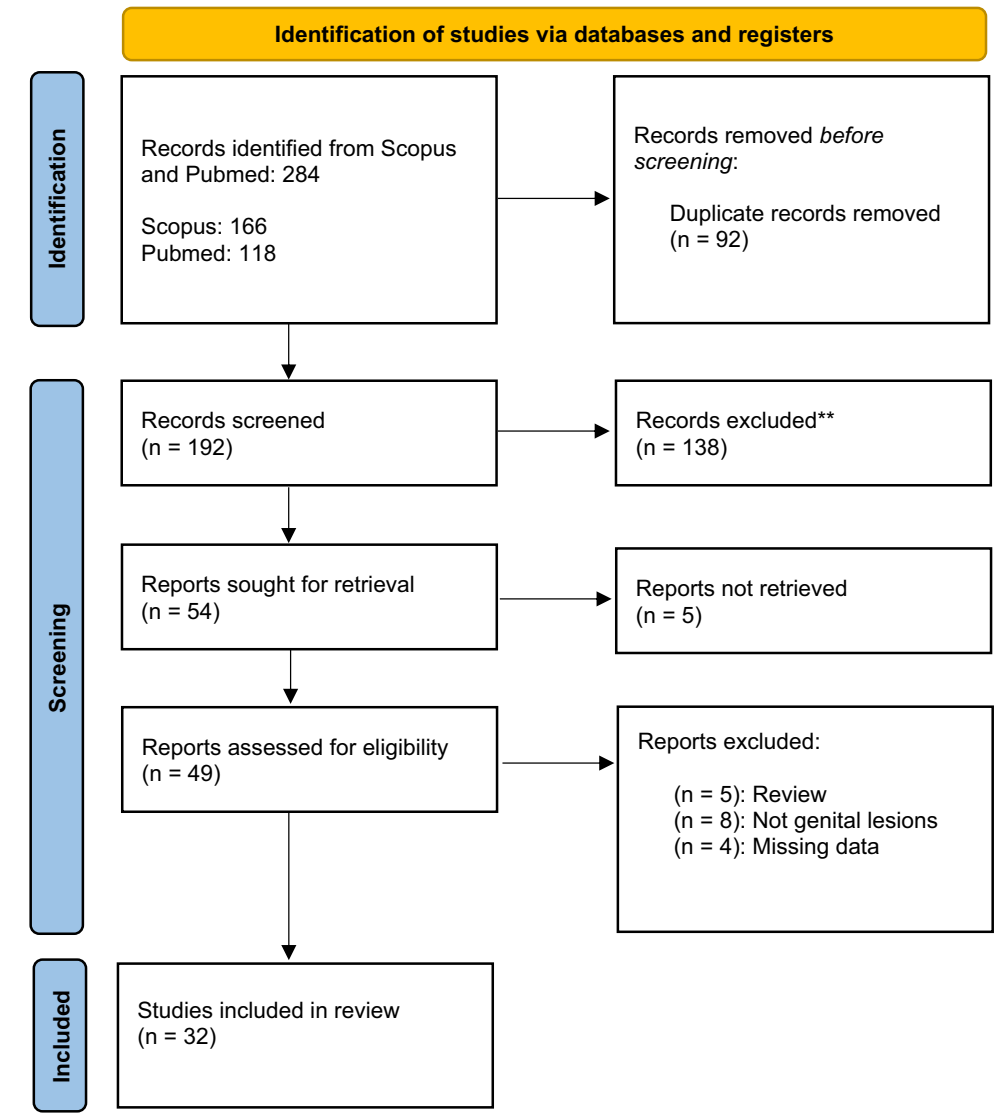

Figure 1 Flow diagram of publications explored.

systemic one. In most cases, the urological presentation was a genital lesion (often penile/foreskin umbilicated pustules or a vesicular/macular lesion) accompanied by swelling. Groin/inguinal mono or bilateral lymphadenopathy could be present. Fever, headache, arthromyalgia, diarrhea and skin lesions were the most commonly associated signs and symptoms. In some patients, urethritis could be concomitant (see Table 1).

Management and Follow-Up

When reported, all patients had a molecular confirmatory diagnosis by a polymerase chain reaction (PCR) test, obtained on swab or biopsies taken from the lesions/pustules. Five articles out of 32 (15.6%) reported the need for surgical debridement of penile and genital lesions due to their clinical worsening. However, in most reports, patients experienced spontaneous resolution of the lesions and symptoms, generally within a month of the onset of signs of the disease. Isolation and contact-tracing were fundamental to decrease disease spreading. Furthermore, in 9 studies (28.1%) patients were managed with tecovirimat, in all cases with a complete resolution. In 13 studies antibiotic prophylaxis or therapy was administered in order to avoid superinfections or to treat concomitant infections such as bacterial urethritis. All patients recovered but one who died due to multiple organ failure.

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Table 1 Overview of Included Studies

Author	N°	Age	Gender	Comorbidities	Timing from Systemic to Urological Symptoms	Urological Clinical Presentation	Other organs Involved	Diagnosis	Therapy	Outcomes
Moreno-Matson et al[10]	1	36	M	HIV and HBV	3 days	Pox-like papules, lymphadenopathy, penile edema, penile necrosis	Facial rash an papules; fever	PCR	Surgical debridement; Vancomycin, piperacillin/ tazobactam, amphotericin B	Died after Multiple Organ Failure
Kerkemeyer et al[11]	1	41	M	None	4 days	Distal penile ulceration and paraphimosis	None	PCR	Tecovirimat, clindamycin, piperacillin tazobactam Circumcision and debridement	Healed with atrophic scarring
Wegrzyn et al[12]	1	23	M	HIV	7 days	Ulcerative "punched out" lesions at the penis, bilateral inguinal lymphadenopathy	Pustules with central pitting on bilateral upper extremities, chest, back and the left lower face. Bilateral cervical lymphadenopathy.	NA	Tecovirimat; sulfamethoxazole/ trimethoprim; amoxicillin/ clavulanate potassium; Bictegravir/emtricitabine/ tenofovir	Resolutions of symptoms 3 weeks
Milano et al[13]	1	30	M	Urethral chlamydia trachomatis; HPV-59	Concomitant	Skin lesions; paraphimosis	Diffused skin lesions; laterocervical lymphadenopathy	PCR	Penile dorsal slit; azithromycin; HPV vaccination	Resolution of symptoms after 26 days
Urban et al[14]	1	42	M	Mycoplasma genitalium	NA	Umbelicated/ulcerated pubic lesions; painful lymphadenopathy	Ulcerated lesions at the neck and back	PCR	Doxycycline +moxifloxacin	Resolution of symptoms after 42 days
Sturgis et al[15]	1	28	M	HIV; Chlamydia trachomatis; HSV-2	Concomitant	Penile swelling and ulcerative lesions of shaft; dysuria; urinary frequency; malodorous urine; bilateral inguinal lymphadenopathy	Lesions on palms; lower extremities; oral mucosa; anus	PCR	Ampicillin; Cefdinir; Fluconazole; Penicillin G Benzathine; Valacyclovir; Doxycycline; Topical nystatin; Bactrim; Tecovirimat	Resolution after treatment
Garberi et al[16]	14	mean: 42	M	8: HIV 6: STDs	mean: 3–4 days 6: genital lesions onset	6: Penile edema; 10: ulcerative lesions of genitals; 7: bilateral inguinal lymphadenopathy	14: Malaise, fever; 3: perianal lesions; 14: skin ulcerative lesions	PCR	2: surgical debridement; 12: antihistamines, analgesics, and nonsteroidal anti-inflammatory drugs	NA
Chen et al[17]	1	40	M	Treponema Pallidum; HSV-I; HSV-II; HIV	Genital lesion onset	Ulcer at corona sulcus of penis; bilateral inguinal lymphadenopathy	Lesion at neck, trunk, and knee	PCR	Tecovirimat	Total recovery after 2 weeks

Lee et al[18]	68	mean: 34,9	M	22: HIV 20: Concomitant STDs	NA	Penile shaft lesion	NA	PCR	Tecovirimat; debridement with collagenase for severe lesions.	Resolution of symptoms at (mean) 20.3 days follow up
Fazal et al[19]	1	37	M	HIV; treponema pallidum	Genital lesion onset	Penile lesions	Whole body lesions	PCR	Tecovirimat	NA
Pipitò et al[31]	1	33	M	None	9 days	Non itching, painless, pustular and vesicular lesions on the penis	Non itching, painless, pustular and vesicular lesions on face, limbs, back and soles. Inguinal limphadenopathy	PCR	Isolation	Complete resolution in 3 weeks
Oliveira et al[32]	1	40	M	None	5 days	Lesions in the genital area, edema of the penis with local pain	Lesions at the upper and lower limbs.	PCR	NA	NA
Quattri et al[34]	2	35,29	M	HIV; None	1° 4 days; 2° 2 days	Single, umbilicated vesico-pustular lesion on the foreskin in patient n° 1 and on the penis shaft in patient n° 2	None	PCR	Self-isolation for 3 weeks	No new lesions appeared within 3 weeks
Li et al[35]	1	37	M	None	2 weeks	The dorsal side of penis was swollen, and a yellowish-white patch of coin size	None	PCR	Self-isolation observation	Resolution in 2 weeks
Miše et al[36]	1	34	M	None	2 days	Soft painless dark pigmented circular lesion with a crust and a hypopigmented halo on the penile shaft	None	PCR	Ceftriaxone, azithromycin self-isolation	Anorectal bleeding few days after discharge
Potthoff et al[37]	1	45	M	None	Genital onset	Painful pustule on the penis	Intensely pruritic vesicles on the hands and arms and oral mucosa; cervical and inguinal lymphonodes swelling	PCR	NA	NA
Contag et al[38]	1	36	M	HIV	1 week	Painless penile lesions and unilateral scrotal pain. acute right-sided epididymitis.	Headache, fevers, chills, and night sweats	PCR	Tecovirimat	Resolution in 4 days
Ramoni et al[29]	1	44	M	HCV; HIV	5 days	Cutaneous eruption on his external genitalia	Cutaneous eruption on the fingers. Fever, headache.	PCR	Isolation	Complete resolution in 7 days

(*Continued*)

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Table 1 (Continued).

Author	N°	Age	Gender	Comorbidities	Timing from Systemic to Urological Symptoms	Urological Clinical Presentation	Other organs Involved	Diagnosis	Therapy	Outcomes
Kreuter et al[40]	2	36; 40	M	None	NA	Umbilicated pustules and ulcerations on the mons of pubis, penile shaft and scrotum. Paraphimosis	Several vesicles on face, arms and legs	PCR	Ibuprofen, cold packs	Clinical improvement within 5 days
Turco et al[41]	1	46	M	None	6 days	Umbilicated Vesicular penile lesions + bilateral inguinal lymphadenopathy	Umbilicated Vesicular lesions on left hand and nose	PCR	/	/
Ciccarese et al[21]	1	33	M	Syphilis	NA	Ulcerative penile lesions; inguinal lymphadenopathies	Cervical lymphadenopathies	PCR	Isolation	Complete resolution after 1 month
Poole et al[21]	1	27	M	None	NA	Tender induration over the scrotum, penile shaft, pubis, and perineum in association with mild erythema and without crepitus or fluctuance. A yellow crusted papule was also present on the right penile sulcus	No systemic symptoms	PCR	Self-resolution	NA
Manoharan et al[22]	1	35	M	Marijuana and methamphetamine use	Few days	Raised penile vesicle lesion	Lymphadenopathy, fever, facial lesions	PCR	Vancomycin + Tecovirimat + Doxycycline	Complete resolution in few weeks
Perez-Martin et al[23]	1	40	M	None	Genital onset	Vesicular penile lesions and inguinal lymphadenopathy	Arthromyalgia	PCR	Paracetamol + Dexketoprofen	Complete resolution in 1 month
Davido et al[24]	2	37	M	One patient had previous Syphilis	6 days; Genital onset.	Macular penile lesion; Vesicular penile lesions	Fever, with headaches and mild diarrhea. Fever and concomitant Urethritis.	PCR	IsolationAntibiotics for urethritis (ceftriaxone plus azithromycin)	Complete resolution in 14 days; TC Scan: Fournier's gangrene.
Remington Farley et al[25]	1	33	M	HIV	Genital onset	Penile ulcerative lesion with edema	No systemic symptoms	NA	Vancomycin + Ceftriaxone, + Flagyl + Tecovirimat. The patient underwent surgical debridement	Complete resolution after 10 weeks

Miyazaki et al[26]	1	20	M	None	6 days	Penile swelling and pain	Fever, redness of the oropharynx and enlarged tonsils	PCR	Dimethyl isopropylazulene for the penile lesion	At 28 days completely resolved
Oiwoh et al[27]	1	30	M	None	Genital onset	Painful penile ulcer, and lymphadenopathy	Body rashes	PCR	Ceftriaxone + Metronidazole + Acyclovir + Contact tracing	Complete resolution at discharge
Bociąga-Jasik et al[28]	1	47	M	HIV, Syphilis, HCV	Genital onset	Foreskin papules + inguinal lymphadenopathy	None	PCR	Benzylpenicillin	Improved symptoms in 5 days
Ortiz-Martínez et al[30]	1	36	M	None	4 days	Painless umbilicated pearly colored penile lesions	Night sweats, sore throat, enlarged tonsils, and painful axillary	PCR	Amoxicillin/clavulanate + Isolation	Resolution in 10 days
Mahtani et al[33]	1	38	M	None	Genital onset	Foreskin and penis shaft vesicular lesions. Penile swelling	Pustular lesions on lower extremities, back and neck.	PCR	Clindamycin + Valacyclovir + paraphimosis reduction	Resolution in 7 days
Lopes et al[39]	2	28; 28	M; M	Previous syphilis	8 days; 7 days	Umbilicated pustules penile shaft; Inguinal lymphadenopathy	Mouth lesions, cervical lymphadenopathy, myalgia, headache, and fever;Mouth lesions.	PCR	Isolation	Spontaneous resolution in 14 days

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Discussion

Most urologic Mpox cases were reported as case reports or small case series, with the majority originating from the United States and Europe, while cases were reported from all continents except Oceania. These results suggest that the disease is not limited to specific geographic regions, but is a current global health issue. Although it is more prevalent in sub-Saharan Africa, reporting may be biased towards more developed countries, where healthcare infrastructures allow for better diagnosis and data reporting. Efforts should prioritize surveillance and widespread reporting systems to better characterize the real burden of the urological manifestation of Mpox.

In terms of patient demographics, it is notable that all cases involved were males, mainly with genital involvement. The disease predominantly affects the genital area, while the bladder, kidneys, and organs of the genito-urinary system are spared, possibly underlines the localized nature of the Mpox and its route of infection, at least in its early stages. MsM with a recent sexual activity were found to be at higher risk of urological Mpox. The observed median age of 36 years reflects a relatively young patient population, which may have implications for public health and sexual health education strategies. Systemic symptoms, including fever, headache, and arthromyalgia, were commonly reported prior to genital involvement, with genital symptoms occurring after a median of approximately five days from the onset of systemic signs. This temporal relationship between the onset of systemic and genital signs highlights the need for early recognition of systemic symptoms, which can aid in the diagnosis and management of the disease before genital symptoms fully manifest. However, in several cases the genital manifestation occurred before the systemic symptoms. A serious problem could also lie in the lack of ability of urologists to recognize this pathology, a problem already encountered with other uncommon infectious pathologies uncommon in developed countries, such as genitourinary tuberculosis (GUTB).[42] The genital lesions observed were predominantly penile or foreskin umbilicated pustules, with vesicular or macular lesions and associated swelling being the most common clinical findings. Lymphadenopathy, particularly in the inguinal area, was also frequently noted, adding to the characteristic presentation of the disease.

The management for these patients focused primarily on confirming the diagnosis by PCR testing of lesion smears or biopsies, with treatment strategies varying depending on the severity of symptoms.

A small proportion of patients (15.6%) required surgical intervention, such as debridement of genital lesions, due to clinical worsening. In the majority of patients, however, the symptoms and lesions resolved spontaneously within a month. This underlines that the disease is self-limiting in most cases, although monitoring and early intervention remain crucial in more severe cases and/or in case of multiple comorbidities. In addition to supportive care, tecovirimat was used in a significant number of cases (28.1%), with all patients experiencing complete symptoms resolution. This highlights the potential role of antiviral therapy in managing more severe or prolonged cases. WHO recommends the use of antiviral treatment with tecovirimat in case of extensive genital lesions. However, the availability of the antiviral is limited to some expanded access program; a second choice is cidofovir i.v.[43] The early initiation of the treatment is associated to a better outcome, so the early diagnosis is crucial. Antibiotic treatment may be of help in case of bacterial urethritis, with a comprehensive approach to patient management, addressing not only the primary disease but also the risk of superinfections, co-infections with other sexually transmitted diseases and proactive screening for HIV, HPV and viral hepatitis. The co-occurrence of HIV and MPOX presents unique challenges due to the potential for immunosuppression in people living with HIV (PLWH) and the impact this may have on disease severity. PLWH, especially those with a low CD4 count (<350 cells/μL) or uncontrolled HIV, are at a higher risk of developing severe MPOX.

Despite the generally favorable outcomes, there was one reported death due to multiple organ failure, despite surgical debridement and broad-spectrum antibiotic treatment. The World Health Organization (WHO) expressed global concern about the spread of Mpox and based on the recent experience with the COVID-19 pandemic, in order to alert about the potential impact of Mpox outbreaks on healthcare systems, including medical education and surgical training.[44]

Study Limitations

Most of the data on urologic Mpox cases came from case reports or small case series, leading to potential publication bias. The lack of large, systematic studies limits the ability to generalize findings. Differences in healthcare systems and

resources across regions may influence treatment strategies and outcomes, making it difficult to compare clinical treatment methods. In addition, the true burden of the disease in underserved areas may be overlooked. The lack of longitudinal studies limits understanding of the long-term impact of urologic Mpox, including potential sequelae or recurrence. The indirect impact of Mpox outbreaks on healthcare systems, including surgical training, was not consistently addressed in the literature reviewed, leaving a gap in understanding its wider impact.

Conclusions

The current available literature provides few insights into the clinical characteristics, management, and outcomes of patients with urological manifestation of Mpox. Known risk factors such as recent intercourse in the MsM population should drive clinical suspicion. The predominance of genital involvement, the clinical course with systemic symptoms preceding genital lesions, and the need for comprehensive MST screening are key takeaways. Additionally, the role of sexual health education and public health interventions in preventing transmission, particularly in high-risk populations, should be prioritized. Awareness of Mpox and timely diagnosis are crucial for ensuring appropriate treatment and reducing the need for surgical management and the possible risk of long-term sequelae. Finally, collaboration among dermatologists, infectious disease specialists, and urologists is pivotal to effectively managing Mpox patients.

Disclosure

The authors report no conflicts of interest in this work.

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