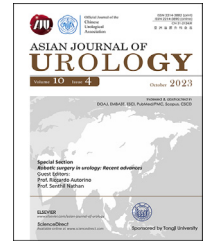


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Original Article

# Penile vascular anomalies: A retrospective single center study and cumulative analysis of studies from China

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## KEYWORDS

Hemangioma;  
Laser irradiation;  
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**Abstract** *Objective:* Penile vascular anomalies (PVAs) or hemangioma can arouse patient concern about aesthetics and cause symptoms like bleeding and sexual dysfunction. However, its low incidence and the deficiency of large-volume studies hinder urologists from making informed decisions. This study aimed to investigate the clinical features and treatment experience of PVAs at the Seventh Medical Center of PLA General Hospital, Beijing, China. Furthermore, by systematically analysis of studies on PVAs in Chinese people, we aimed to provide novel insights on the management of this condition.

*Methods:* We retrospectively investigated clinical features and pathology of surgery-treated PVAs at our center. Moreover, by systemically reviewing the literature from PubMed and the three largest medical databases (China National Knowledge Infrastructure, Wan Fang, and Chinese Medical Journal Database) in China, we analyzed the clinical features and various therapies of PVAs in Chinese people.

*Results:* Between March 1, 2018 and March 1, 2023, a total of 356 cases with vascular anomalies were treated with surgery at our center. Only seven (2.0%) cases had lesions involving the perineum and external genitalia. All the seven cases were pathologically benign and demonstrated no recurrence over a follow-up period of 1–52 months (median 14 months). A total of 410 cases from 44 studies were selected in the cumulative analysis. Most patients (92.4%) diagnosed with PVAs were asymptomatic, and 68.8% of the patients were treated with sclerotherapy. As to the pathology, 57.1% were venous malformation.

*Conclusion:* The most common PVA is venous malformation and the majority of patients are asymptomatic. Sclerotherapy and laser have emerged as viable options for treating small lesions. Surgery still has its role in treating large lesions and obtaining pathology. Although PVAs

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often relapse or demand multiple treatments, the prognosis is favorable.

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## 1. Introduction

Vascular anomalies (VAs), traditionally classified as hemangiomas, are considered rare in the external genitalia, taking only 3% of all male hemangiomas [1]. Since some patients without symptoms do not seek treatments and not all treated cases have been reported, the true incidence can be underestimated. According to the updated nomenclature, VAs can be stratified into vascular tumor and vascular malformation [2]. The most significant difference between them lies in the abnormal proliferation of endothelial cells in vascular tumors, whereas vascular malformations do not exhibit this feature [2]. The venous malformation is well known as “cavernous hemangioma”. Though most VAs are pathologically benign, when VA occurs in the penis, patients or their parents often have concerns about its negative impact on the appearance and sexual function [3,4]. Treatments such as sclerotherapy, laser irradiation, copper wire insertion, and surgery have been reported sporadically [1,4–8]. Nevertheless, no guidelines or systematic reviews have been published to compare different therapies and to help urologists make clinical decisions [5]. Most studies published in English on the penile vascular anomalies (PVAs) are case reports, which tend to describe large and complicated lesions [3,6]. Such a focus fails to capture the true clinical features and management strategies relevant to small and typical lesions. Noteworthy, quite a few valuable studies on PVAs have been published only in Chinese. In this study, we aimed to conduct a retrospective investigation into the clinical manifestation, pathology, and surgical outcome of PVAs treated at the Seventh Medical Center of PLA General Hospital, Beijing, China, describe our surgical techniques to treat a large PVA, and finally comprehensively review previous studies conducted in Chinese people. Given its large population, China’s experience is likely to offer informative insights on the understanding and management of PVAs.

## 2. Patients and methods

### 2.1. Retrospective study

To analyze the clinical manifestation, pathology, and surgical outcomes of cases involving the PVA treated at our center, we conducted a retrospective study using electronic medical records between March 1, 2018 and March 1, 2023. We have obtained permission from the dataset owner to use the information in databases or repositories for the purposes of this research. Patients were excluded if the pathology was unavailable. The outcomes were disease recurrence and metastasis. Written informed consent was

obtained from each patient for the treatment and data publication, including the use of medical images. Ethical approval for this study was obtained from the Institutional Review Board of the Seventh Medical Center of PLA General Hospital (No. 202345).

### 2.2. Systematic review

#### 2.2.1. Search strategy

The Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) protocol was used to facilitate the systematic review [9]. To identify as many relevant studies as possible, we searched PubMed and the three largest medical databases in China (China National Knowledge Infrastructure, Wan Fang, and Chinese Medical Journal Database). In addition, the clinical information of our case was included in the total statistics of the systematic review.

#### 2.2.2. Inclusion and exclusion criteria

Studies on Chinese patients with PVAs were included. Studies without necessary clinical information such as symptoms and treatments were not enrolled. Reviews, correspondences, editorial articles, and meeting reports were excluded.

#### 2.2.3. Data extraction and quality assessment

Two reviewers (Ma C and Gao F) independently assessed studies and extracted data. Disagreements were resolved by discussion. When multiple reports of one study were identified, only the publication with the largest volume was included. Major outcomes included age, symptoms and signs, radiology, treatments, and complications.

## 3. Results

### 3.1. Clinical features of VAs

Between March 1, 2018 and March 1, 2023, a total of 356 cases with 361 lesions had been treated via surgery with pathologically verified VAs at our center. Those patients had a wide age range of several months to 90 years, with a median age of 41 years at the time of pathological diagnosis. The male to female sex ratio in this cohort was 1.2:1. The systems and organs most frequently involved with VAs were the skin (31.8%), digestive system and liver (22.1%), and musculoskeletal system (21.5%). Notably, only seven cases (2.0%) had VAs involving the perineum or external genitalia, whose clinical manifestations, pathology, and outcomes were summarized. During a follow-up period of 1–52 months (median 14 months), no recurrence of the seven cases was observed (Table 1).

**Table 1** Vascular anomalies involving the perineum and external genitalia.

Patient	Sex	Age, year	Symptom	Lesion location, size (cm×cm)	Pathology	Follow-up, month	Outcome
1	Male	5	No	- Scrotum, 1.8×1.4	- Venous malformation	6	- No recurrence
2	Female	13	Tenderness, bleeding	- Perineum, 2.8×2.0	- Venous malformation	1	- Symptom relief, no recurrence
3	Male	19	No	- Scrotum, 2.0×1.0	- Lymphatic malformation	2	- No recurrence
4	Male	22	No	- Penis, 2.0×1.0	- Venous malformation	26	- No recurrence
5	Female	47	No	- Vulva, 1.0×0.6	- Venous malformation	52	- No recurrence
6	Female	64	No	- Perineum, 1.8×1.2	- Venous malformation	19	- No recurrence
7	Female	67	Bleeding	- Perineum, 1.2×0.8 - Vulva, 0.4×0.4	- Capillary malformation - Venous malformation	14	- Symptom relief, no recurrence

For the pathology, the vast majority (337/361, 93.4%) can be stratified into vascular malformation, with merely 6.6% (24/361) lesions into vascular tumor. The most common vascular tumor type was pyogenic granuloma (15/24, 62.5%) involving the skin, which is considered a benign tumor by the International Society for the Study of Vascular Anomalies [2].

### 3.2. The clinical features and treatment experience of PVAs

In the past 5 years at our center, only one case of VAs (0.3%) involving the penis required surgical intervention and had pathological result. The patient was a 22-year-old male presented with a gradually enlarged penile mass for over 10 years. He had no complaints of hematuria, hemospermia, or erectile dysfunction. The young man was in distress by the appearance of his penis with the lesion. Upon physical examination of the flaccid state, a purple irregular mass with a size of 2.0 cm×1.0 cm, was located under his glans penis and beneath the epithelium of the foreskin (Fig. 1A). Instead of oval forceps, we used iodine-soaked gauze held with gloved hands to gently disinfect the penis after

general anesthesia. This approach allowed for more effective disinfection of the ridges and grooves on the surface of the irregular mass without the risk of the hypervascular lesion rupture. Before the incision, a 23 Gauge syringe filled with normal saline was used to enlarge the space between the lesion and normal fascia by inserting the needle just under the stroma of the lesion (Fig. 1B). The resection of the mass was complete, and the corpus spongiosum was well protected (Fig. 1C). The operation took 20 min with about 5 mL blood loss. The pathology was venous malformation or cavernous hemangioma (Fig. 1D). The patient was satisfied with his penis appearance without compromising erectile function at 26-month follow-up.

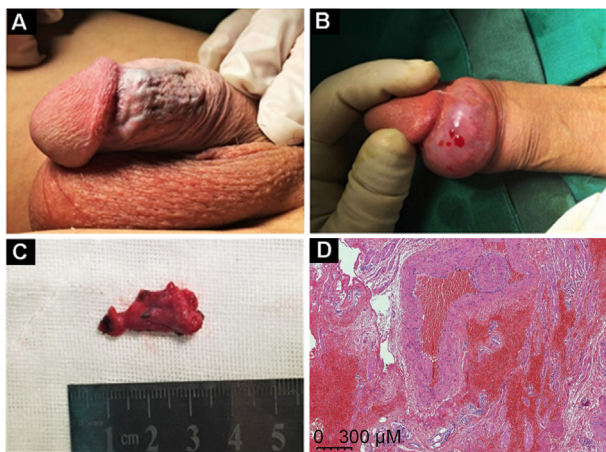
### 3.3. Systematic review

#### 3.3.1. Study characteristics

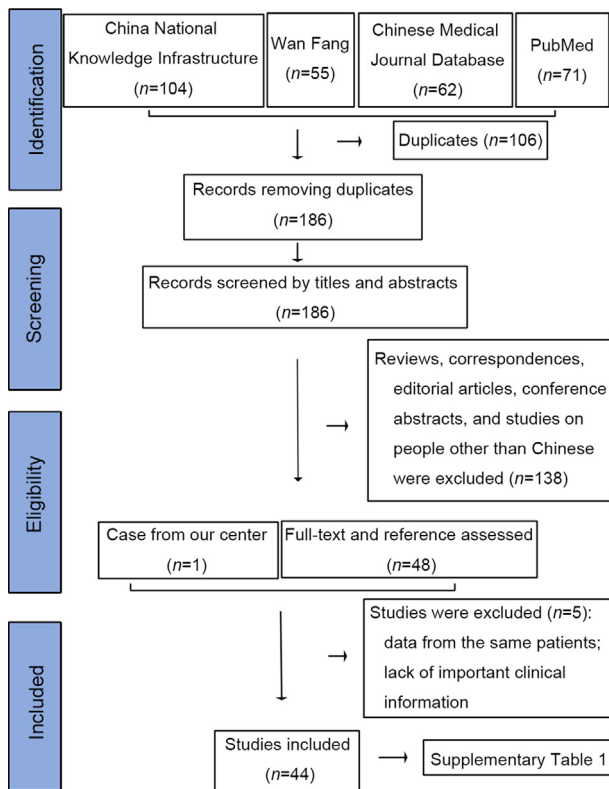
A total of 71, 104, 55, and 62 studies were identified respectively in PubMed, China National Knowledge Infrastructure, Wan Fang, and Chinese Medical Journal Database, respectively, until December 2022, using the search retrieval described in Supplementary Table 1. After removing duplicates and screening for eligibility, four more studies were excluded because the data from the same patients had been published later in larger cohorts [8,10–12]. Furthermore, one was ruled out for insufficient clinical information [13]. As a result, 44 studies with 410 cases (our case included) of PVAs were selected for further analysis [14–56]. Most studies included were case reports and only a small number of studies had large volume, making meta-analysis inappropriate. Fig. 2 demonstrates the process of literature search and review. The information of the included study is summarized in Supplementary Table 1.

#### 3.3.2. Epidemiology

The first case of PVAs in China was described in 1958 by Wei [14]. Most patients were aged 3–30 years when presented to the hospital [14–56]. The youngest patient ever described was only 10-month-old and the oldest 65-year-old [55,56]. Although there were cases that did not seek treatment or cases treated without reports, the PVA could be considered rare in China. Most high-volume teaching hospitals only treat one to three cases per year. We only notice one exceptional study reported 113 cases for 10 years [45].



**Figure 1** The venous malformation of the penis. (A) The lesion before surgery; (B) Injection of normal saline to facilitate isolation; (C) Complete resection of the lesion; (D) Venous malformation with hematoxylin-eosin staining on microscopy.



**Figure 2** Flow diagram of the study selection.

### 3.3.3. Natural course

PVAs are often identified during childhood, and tend to grow gradually. Only in a 21-year-old man, two lesions on his penis disappeared spontaneously after digital subtraction angiography (DSA) examination [16]. Only one case explicitly reported a history of penile trauma before the initiation of the lesion [20].

### 3.3.4. Symptoms and signs

Most patients with PVAs (379/410, 92.4%) did not have any symptoms. They or their parents usually sought treatment with concerns about the lesion's negative consequence on penile appearance or intercourse. After pooling previous studies, we identified that the most common complaints of PVAs were deflected or obstructive voiding (16/410, 3.9%) and bleeding (14/410, 3.4%). Only six patients (6/410, 1.5%) had reported a direct negative influence on their sexual function. All reported PVAs were not difficult to diagnose on physical examination. The largest PVA reported in China was 10 cm × 8 cm and involved the scrotum [55]. Moreover, 8.0% (33/410) cases were reported to have multifocal lesions or lesions involving the penis and the adjacent organs.

### 3.3.5. Imaging

A total of 133 cases had Doppler ultrasound examination. Venous malformation or cavernous hemangioma was often described as low echoed with vein phase on blood flow spectrum [52]. A total of 20 cases have been reported to have DSA [16,33,42,56]. Two cases had lesions showing a direct connection with the blood supply of the corpora cavernosum, one of which complained of erectile dysfunction [40,42]. The venous malformation or cavernous hemangioma often drainages into the dorsal vein of the penis [16].

### 3.3.6. Treatment

Various therapies have been described. We classified them into the following categories: sclerotherapy, laser irradiation, copper wire insertion, and surgery. The main parameters, like the complication rate and the recurrence rate of different treatments, are summarized in Table 2. Among the 407 cases (our case included) with treatment information, 280/407 (68.8%) were treated with sclerotherapy. Most patients (203/280, 72.5%) treated with sclerotherapy demanded multiple injections because VA recurred or a single injection was not enough. Infection

**Table 2** Results of different treatments for penile vascular anomalies.

Treatment	Pain or swelling	Recurrence or had $\geq 2$ operations	Infection or delayed healing
Sclerotherapy	28/280 (10.0)	203/280 (72.5)	7/280 (2.5)
40% urea solution	2/154 (1.3)	133/154 (86.4)	0/154 (0)
Bleomycin	8/76 (10.5)	60/76 (78.9)	5/76 (6.6)
95% ethanal	1/19 (5.3)	3/19 (15.8)	1/19 (5.3)
Polidocanol	2/15 (13.3)	5/15 (33.3)	1/15 (6.7)
2% phenol glycerin	14/14 (100.0)	2/14 (14.3)	0/14 (0)
5% sodium morrhuate	0/1 (0)	0/1 (0)	0/1 (0)
Liquid nitrogen	1/1 (100.0)	0/1 (0)	0/1 (0)
Laser irradiation	13/71 (18.3)	25/71 (35.2)	1/71 (1.4)
Nd:YAG	13/41 (31.7)	25/41 (61.0)	1/41 (2.4)
Semiconductor	0/15 (0)	0/15 (0)	0/15 (0)
Copper vapor	0/13 (0)	0/13 (0)	0/13 (0)
CO <sub>2</sub> laser	0/2 (0)	0/2 (0)	0/2 (0)
Copper wire insertion	2/15 (13.3)	15/15 (100)	0/15 (0)
Surgery	0/41 (0)	0/41 (0)	1/41 (2.4)
Total	43/407 (10.6)	243/407 (59.7)	9/407 (2.2)

Nd:YAG, neodymium:yttrium-aluminum-garnet.

Note: data are presented as n/N (%); N means total cases of specific treatment.

or delayed healing has been described with low incidence (7/280, 2.5%). Various sclerosants such as bleomycin (pingyangmycin in China), urea solutions, and ethanol have been reported to treat PVAs. Among them, 40% urea solution had the least complication rate (2/154, 1.3%), but had the highest recurrence rate or multiple operation rate (133/154, 86.4%). Laser irradiation has become more prevalent in recent years (71/407, 17.4%), especially neodymium:yttrium-aluminum-garnet (Nd:YAG) laser. More than one-third (25/71, 35.2%) of the laser-treated lesions relapsed or needed multiple operations, which was less than sclerotherapy. After treatment, the pain or swelling rate was higher (13/71, 18.3%) than that of the sclerotherapy. Copper wire insertion was not common and required removal of the wires 7–14 days after insertion. Though surgery accounts for only 10.1% (41/407) of all the treatments, it is often used in larger lesions or in cases that have failed with other therapies. No recurrence was reported after surgery. Two cases with extensive lesions underwent penectomy [19,27].

### 3.3.7. Prognosis

A total of 35 cases had pathological results. Consequently, 20.0% (7/35) were capillary hemangioma [16,18,37]. Furthermore, 17.1% (6/35) were racemose hemangioma [17,20,33,55]. Two cases could be classified as vascular tumor or true hemangioma, one of which was hemangioma with atypical proliferation and the other was verrucous hemangioma [26,43]. The remaining VAs treated with surgery (20/35, 57.1%) were venous malformation or cavernous hemangioma. No case ever reported had distant metastasis or died of PVAs.

## 4. Discussion

The PVA is rare in China and the rest of the world, and only accounts for a small proportion of all VAs. Patients without bothering symptoms may not seek treatment, and not all treated ones have been reported. Therefore, the true incidence can be underestimated. Though most of PVAs are pathological benign, delayed treatment could generate a dilemma between lesion removal and cosmesis or even horrible consequences like penectomy [4,19]. The scarcity of large-volume studies further complicates decision-making for urologists. To address this problem, we first analyzed our data and experience to treat VAs with 5-year follow-up and then systematically reviewed studies on PVAs in Chinese people.

### 4.1. Terminology

In 1995, the ISSVA stratified VAs into vascular malformations and proliferative vascular lesions or vascular tumors [2]. This classification is based on the lesion biological behavior and natural course rather than appearance. Therefore, it is considered more scientific and getting wider acceptance. According to the ISSVA scheme and its updated version in 2015, cavernous hemangioma without tumor-like proliferation should be categorized as venous malformation [2]. In contrast, capillary hemangioma belongs to capillary malformation, and racemose hemangioma is classified as

arteriovenous malformation. Since “penile cavernous hemangioma” has been well-known and is still being used, we think it is necessary to clarify the updated nomenclature here [57].

### 4.2. Mechanism and assessment

Some researchers argued that PVAs could be herniation of the cavernous body tissue or the re-vascularization of a previous penile trauma [58]. However, DSA did not show a connection between the lesion and the cavernous body in some cases. Moreover, most patients cannot recall any previous penile traumas. The exact genetic and molecular mechanisms underlying PVAs remain unknown. Nonetheless, the up-regulation of vascular endothelial growth factor-A/receptor-1 autocrine in hemangioma-derived stem cells is considered to enhance vasculogenesis [59]. Moreover, there is molecular evidence indicating the involvement of abnormal activation of the phosphatidylinositol 3-kinase/mammalian target of rapamycin signaling pathway in vasculogenesis [60].

### 4.3. Diagnosis

Almost all cases of PVAs were diagnosed by physical examination. More than 90% of the patients with PVAs do not complain of any symptoms. Only 3.9%, 3.4%, and 1.5% of the patients reported deflected or obstructive voiding, lesion bleeding, or sexual inconvenience, respectively. In their studies, Huang et al. [53] and Wu et al. [48] explained that large lesions on the glans penis could obstruct the external urethral orifice and cause voiding symptoms. Though the sexual problem is not commonly complained of as a separate symptom, we believe bleeding and the large lesion will surely hinder intercourse. Moreover, we realize that many patients were too young to have any sexual experience at diagnosis. Some of them could suffer from bleeding or sexual inconvenience if had not been treated. Though the size and location could differ, PVAs are usually not difficult to diagnose on physical examination. Typically, vascular malformation would shrink when compressed; true hemangioma or vascular tumor should be considered if this would not happen. Noteworthy, we identified that 8.0% of the cases with PVAs had multifocal lesions or lesions involving organs more than the penis, namely the scrotum, perineum, or even lower limbs. Therefore, we recommend that physical examinations should be taken carefully and systematically. No routine imaging examination is recommended for the simple PVA. If the lesion is deep beneath the foreskin or impacts erectile function, the Doppler ultrasound could help evaluate the lesion’s actual size and depth. DSA can offer more accurate information about the blood supply. MRI is not cost-effective unless malignancy cannot be excluded.

### 4.4. Management

Though its prognosis is quite well, PVAs can grow and become difficult to remove. We suggest treating at the time of diagnosis or at least regular follow-up before the lesion

becomes too large. Penectomy has been reported for delayed treatment [19]. Novel sclerosants and laser devices are evolving to treat PVAs. Sclerotherapy is easy to administer at the outpatient clinic, and sclerotherapy is less aggressive than surgery, with no scar left. Sclerotherapy is recommended for small and multifocal lesions. The major drawback is that more than 70% of the cases treated with sclerotherapy will recur or remain. Since different studies have various follow-up plans, ranging from 1 month to 6 months after the first treatment, assessing the actual recurrence time after the initial sclerotherapy is difficult. As heterogeneity existed among the studies using different sclerosants, we could not conclude which sclerosant is superior. Laser irradiation has attracted increasing interest with its lower complication and recurrence rate. Especially, Nd:YAG laser has been used in China and abroad [7,25]. Nevertheless, because of its thermocoagulation effect, insufficient thermocoagulation could facilitate recurrence, while over-irradiation would harm the normal tissue [53]. Copper wire insertion is a challenging operation. Nonetheless, a team in China is experienced and has published this creative method [8]. Surgery still has an indispensable role for some reasons. First, injection or fulguration cannot obtain intact tissue samples, which are materials for precise pathological diagnosis and essentials for scientific research. Immunohistochemistry, genetic sequencing, and drug sensitivity assay will be unfeasible without high-quality samples. The mechanisms underlying the lesions will remain veiled. Second, circumcision or other plastic surgery of the penis can be carried out simultaneously [28]. Third, some large VAs or complicated lesions with ulcers or infections may only be cured by surgery. Therefore, we believe the detailed description of our operative procedures and techniques is informative. Since most patients with PVAs are young men or teenagers, who or whose parents often worry about its negative impact on future sexual dysfunction, we recommend that urologists pay attention to the psychological state of the patient. We can interpret the disease natural course and good prognosis, and discuss in detail the potential benefits and risks before a specific operation.

#### 4.5. Limitations

Firstly, one obvious limitation is that the studies included have evident heterogeneity. Many were case reports with data from only one case, while the largest cohort reported had more than 100 cases. The heterogeneity reminds us to have a caring attitude toward the pooled results of both symptoms and treatment outcomes. The heterogeneity also makes meta-analysis inappropriate. Secondly, none of the studies identified was a randomly designed clinical trial. Some studies were of low quality with an insufficient description of clinical features. To compare different therapies, further studies designed randomly would be much more rigorous. Thirdly, we limited our investigation to Chinese people because of the paucity and publication bias in studies on PVAs in English. Therefore, the generalization of our results should be tentative.

## 5. Conclusion

PVAs are rare in China and account for only a small proportion of all VAs, with venous malformation or cavernous hemangioma representing the most common pathological subtype. Though most patients do not have any symptoms, obstructive voiding, bleeding, and sexual inconvenience were documented. Furthermore, patients often express concerns regarding the impact of these lesions on penile appearance and sexual function. Local injection with various sclerosants and laser irradiation have emerged as the prevailing treatment modalities. However, surgery continues to play an indispensable role in treating PVAs.

### Author contributions

*Study concept and design:* Xing Ai, Jingfei Teng.

*Data acquisition:* Chong Ma, Feng Gao.

*Data analysis:* Ran An, Yawei Guan.

*Drafting of manuscript:* Chong Ma.

*Critical revision of the manuscript:* Chong Ma, Jingfei Teng.

### Conflicts of interest

The authors declare no conflict of interest.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajur.2023.03.006>.

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