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Evaluation of erectile dysfunction in the ageing men using colour Doppler sonography

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Abstract

Background: Erectile dysfunction (ED) is common among ageing men because of associated underlying risk factors which are peculiar to this category of patients. Endothelial dysfunction and replacement of cavernosal smooth muscles by collagen fibres are common in older men, making them prone to ED. It is either vasogenic, neurogenic, hormonal, cavernosal or psychogenic in origin, but vasogenic causes are the commonest. This study was aimed at establishing vasogenic causes among patients being evaluated for ED using Doppler ultrasound as this category of ED is amenable to either medical and/or surgical treatment.

Methods: The study was conducted from July 2015 to January, 2017 at Federal Medical Centre Abuja. Nineteen consecutive patients with clinical diagnosis of erectile dysfunction were evaluated with Doppler ultrasound scan using a high-frequency linear array transducer. The penile scan was done before and after intracavernosal injection of 20 µg of Prostaglandin E_1 (PGE_1). B-mode scan of the penis was done prior to intracavernosal injection of PGE_1, and the spectral waveforms as well as peak systolic velocity (PSV) of the CA were recorded at 5 min interval, from 5 to 50 min post-intracavernosal injection of PGE_1, using angle of insoation $\leq 60°$.

Results: The age range of the patients was fifty to sixty-six years (mean: 57.4 ± 4.3 years), while the PSV of CA varied between 21.4 and 104.4 cm/s (mean: 46.2 ± 19.2) among the entire patients, between 21.4 and 22.3 cm/s (mean: 21.9 ± 0.7) among patients with arteriogenic ED, and between 25.0 and 74.9 cm/s (mean: 45.0 ± 15.5) among those with venogenic ED. Arteriogenic ED was found in two patients (10.6%), while venogenic ED was observed in seven patients, which constituted 36.8% of the entire research participants. None had Peyronie's disease, penile fracture, penile tumour or mixed arteriogenic and venogenic ED.

Conclusion: 47.4% of the patients had vasogenic ED and venogenic ED was more common than arterioegenic ED in the age range considered. This categorization of ED with Doppler study is imperative before initiating therapy as treatment protocol for vasogenic ED is aetiologic specific.

Keywords: Erectile dysfunction, Ageing men, Doppler ultrasound

1 Background

Erectile dysfunction (ED) is consistent inability to maintain erectile turgidity required for normal sexual performance [1, 2]. It could arise from neurogenic, vasogenic, hormonal, psychogenic or iatrogenic origin [3], but vascular causes are the commonest [1, 3, 4].

ED is commoner in the older men when compared with the young because of the age-related risk factors such as systemic hypertension, diabetes mellitus, hyperlipidaemia and obesity which are more frequently seen among the aged population [1]. Medical treatment for prostatic enlargement, hypertension and psychosomatic

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disorders is also known to affect erectile function in view of the effects of the drugs on the endothelial health which ultimately affects dilatation of the cavernosal arteries and fibrosis of the corporal smooth muscles [5]. Also, age-related changes are observed in the erectile tissues because α_1- adrenergic receptor subtypes are modulated by ageing [6]. Induction of vascular smooth muscle by phenyllephrine is reduced particularly in the cavernosum of those above 60 years which ultimately affects the expected expansion of cavernous sinusoids hence, reduction in their compressive effects on the emissary veins against the tunica albuginea. These changes result in venous leak and ultimately venogenic erectile dysfunction.

Reduced Nitric Oxide (NO) production by endothelial tissues of the penis is another contributory factor to ED in the elderly. Endothelial health is greatly maintained by normal plasma concentration of NO, and this is largely depleted with ageing [5]. In the elderly also, there is presence of reactive oxygen species (ROS) which causes inflammation of the endothelium hence, predisposition to atherosclerosis of the cavernosal arteries with attendant reduction in blood inflow to the erectile tissues. This ultimately leads to arteriogenic erectile dysfunction [1].

The morphological and vasculogenic changes that could result in ED are amenable to sonographic diagnosis [2]. Internal iliac Angiography with selective internal pudendal artery angiography is the gold standard imaging method used in the evaluation of arteriogenic ED. It is however invasive, not readily available and cannot demonstrate the morphological changes of the corporal bodies, hence the preference for the triplex Doppler sonographic assessment [2], which is the major thrust of this study.

2 Methods

This prospective study was conducted between July 2015 and January, 2017, at the Department of Radiology, Federal Medical Centre, Abuja, Nigeria following an approval by the Research and Ethics committee of the hospital (protocol number: FMCABJ/HREC/2017/003). Nineteen consecutive patients with clinical diagnosis of erectile dysfunction referred by urologist were evaluated using Doppler sonography. The Doppler study was performed on all the patients with ED in this study irrespective of the degree of erectile dysfunction or earlier response to treatment with $PGDE_5$ inhibitor. Those smoking cigarette among them were instructed to stop 72 h prior to the study as smoking causes penile vasospasm and increased sympathetic nervous system tone thus affecting penile erection [7, 8]. The procedure was explained in detail to the patients at booking and on the examination date. After obtaining an informed consent, they were assessed with colour Doppler ultrasound scan (Mindray DC 7, 2014 China) using high-frequency (5.0–12.5 MHz) linear transducer. The study was performed with patients in supine position, and penis in normal anatomical position. Following the application of ultrasound coupling gel to the ventral surface of the penis, the scan of the penis was done on Doppler mode before and after injection of PGE_1. Pre-injection scan was done to assess the echopattern of the penis in the flaccid state for the presence of plaques, fibrosis, or tunica albuginea defect/fracture. The diameter, spectral waveform and peak systolic velocity of the cavernosal arteries were also assessed prior to intracavernosal injection.

Under aseptic technique, 20 μg of PGE_1 was injected into one of the corpora cavernosa laterally at the proximal third of the penis with a 30-guage needle. The waveforms were obtained alternately by using an angle of insonation $\leq 60°$. Following intracavernosal injection of PGE_1, the diameter of each cavernosal artery, peak systolic velocities of the cavernosal arteries and spectral waveforms were documented each at 5 min interval, from 5 to 50 min with the probe at the junction of the proximal third and distal two-third of the penile shaft [3]. The PSV of CA was determined electronically with the software package of the ultrasound machine (Fig. 1).

The patients were kept in the departmental observation room for two hours after the procedure to check for possibility of complications such as priapism or penile haematoma, but none had these complications.

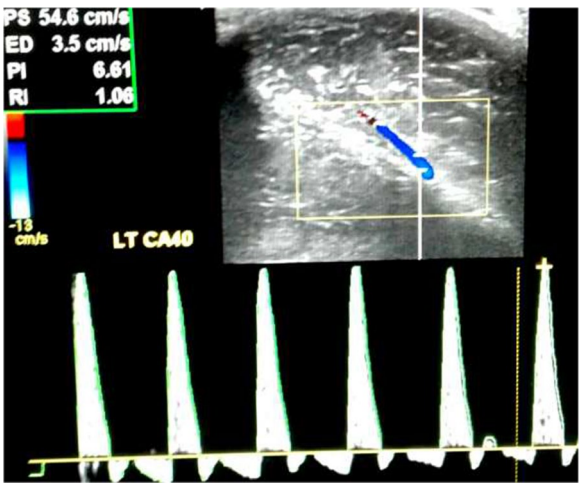

Fig. 1 Spectral waveform of the left cavernosal artery of a patient at 40 min showing normal arterial inflow with PSV of 54.6 cm/s, holo-diastolic flow reversal and good venous competence

Table 1 Frequency distribution of the entire patients with their respective CA PSV

Age (years)	*N*	Mean PSV (cm/s)	SD	Minimum (cm/s)	Maximum (cm/s)
50–54	8	41.1	10.3	27.1	50.4
55–59	5	57.4	24.3	31.1	104.4
60–64	5	48.2	22.3	22.1	74.9
65–69	1	21.6	0.3	21.3	21.9
Total	19	46.2	19.2	25.4	104.4

Table 2 Frequency distribution of the patients with arteriogenic ED and their respective Cavernosal artery PSV

	N	Minimum	Maximum	Mean	SD
Age (years)	2	62.0	66.0	64.0	2.83
Right CA PSV (cm/s)	2	21.4	22.3	21.9	0.64
Left CA PSV (cm/s)	2	21.8	21.9	21.9	0.07

2.1 Ethical consideration

This study was approved by the Research and Ethics committee of Federal Medical Centre Abuja (protocol number: FMCABJ/HREC/2017/003). Anonymity was maintained on all the information obtained and the patients had the choice to deny consent or opt out of the study at any stage with no direct effect on the quality of care obtained in the hospital.

2.2 Data analysis

The results were reported as mean ± (SD), and the collected data were analyzed using Statistical Package for Social Science (IBM SPSS) version 23. All test of significance were two-tailed, and *P* values less than 0.05 were considered statistically significant.

3 Results

The data of nineteen (19) consecutive patients with clinical diagnosis of erectile dysfunction (ED) were analyzed with SPSS version 23; (the age range of the patients was fifty to sixty-six years (mean age; 57.4 ± 4.3 years)), Table 1. Analyses tests used were independent samples t test, ANOVA and Pearson correlation. Following intracavernosal injection of Prostaglandin E_1 (PGE_1), the PSV of all the patients varied between 21.4 and 104.4 cm/s (Table 1), between 21.4 and 22.3 cm/s among patients with arteriogenic ED (Table 2) and between 36.8 and 74.9 cm/s among those with venogenc ED (Table 3).

Normal response to PGE_1 (Fig. 1) was observed in 10 patients (53%), while abnormal response to PGE_1 (arteriogenic ED) was found in two patients (10.6%), and

Table 3 Frequency distribution of the patients with venogenic ED and their respective cavernosal artery PSV

	N	Minimum	Maximum	Mean	SD
Age (years)	7	54.0	62.0	58.9	3.0
Right CA PSV (cm/s)	7	36.8	74.9	46.7	14.6
Left CA PSV (cm/s)	7	25.0	74.1	43.3	16.3

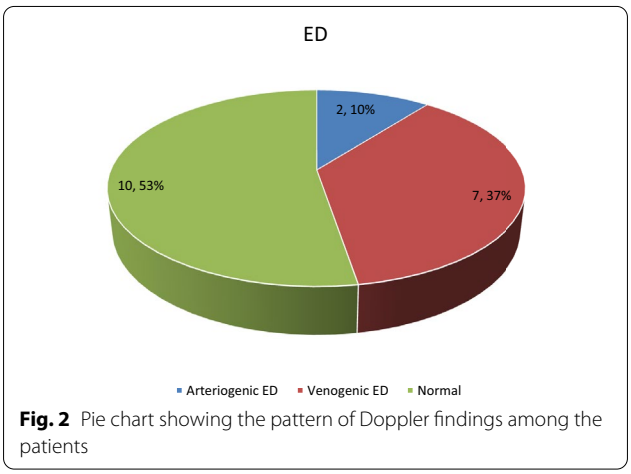

Fig. 2 Pie chart showing the pattern of Doppler findings among the patients

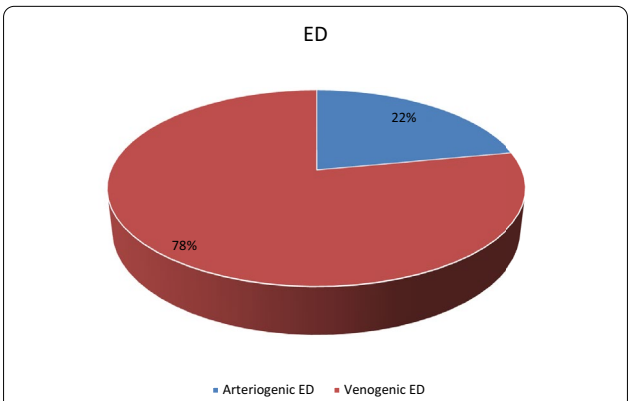

Fig. 3 Pie chart showing the pattern of Doppler findings among patients with vasogenic erectile dysfunction

Venogenic ED was noted in seven patients, which constituted 36.4% of the entire patients (Fig. 2). 78% of the patients with vasogenic erectile dysfunction had venous leak (venogenic ED), while 22% had arteriogenic ED. The pattern of vasogenic ED among the participants is shown in Fig. 3. None of the patients had mixed arteriogenic ED and veno-occlusive ED in the index study.

The mean PSV of CA of the entire patients was 46.2 ± 19.2 cm/s (Table 4), and that with normal response (Fig. 1) was 51.9 ± 20.1 cm/s, while those with

Table 4 Relationship between age and PSV of the CAs among the entire participants (ANOVA)

Age (years)	*N*	Mean CA PSV (cm/s)	*F* (df)	*P* value
50–54	16	41.1 (10.3)	5.211 (7,62)	< 0.001
55–59	10	57.4 (31.1)		
60–64	10	48.2 (22.1)		
65–69	2	21.6 (0.3)		
Total	38	46.2 (19.2)		

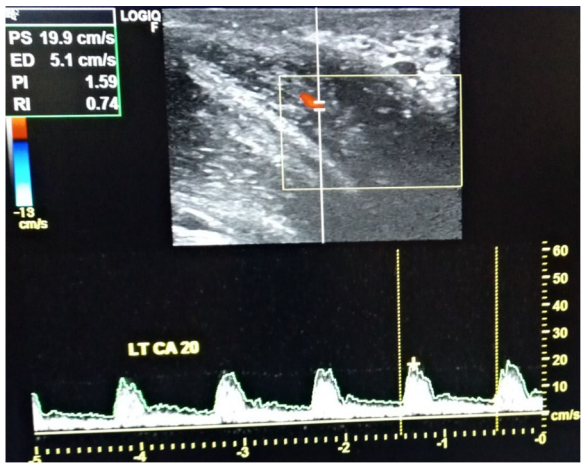

Fig. 4 Spectral waveform of the left cavernosal artery of a patient at 20 min showing reduced arterial inflow with a PSV of 19.9 cm/s, feature connoting arteriogenic ED

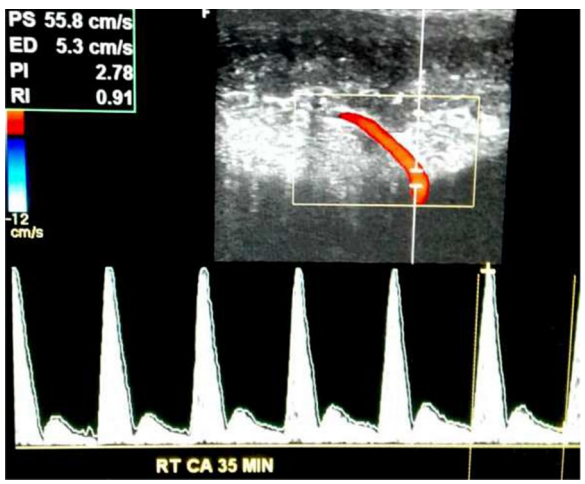

Fig. 5 Spectral waveform of the right cavernosal artery of a patient at 35 min showing normal arterial inflow with PSV of 55.8 cm/s, but the diastolic flow is persistent, features connoting venous leak (venogenic erectile dysfunction)

Table 5 Frequency distribution of the patients based on sonographic findings

Age (years)	Arteriogenic ED (*N*)	Venogenic ED (*N*)	Normal cases (*N*)	Total
50–54	–	1	7	8
55–59	–	3	2	5
60–64	1	3	1	5
65–69	1	–	–	1
Total	2	7	10	19

arteriogenic ED (Fig. 4) was 21.9 ± 0.7 cm/s and venogenic ED (Fig. 5) was 45.1 ± 15.5 cm/s. The mean age of patients with venogenic ED was 58.9 ± 3.0 years (Table 3), while the mean age of patients with arteriogenic ED was 64.0 ± 2.8 years (Table 2).

The PSV of the entire participants had a strong positive relationship with age, $P < 0.001$ (Table 4). The frequency distribution of the patients based on sonographic findings is shown in Table 5; most of the patients with arteriogenic ED were above 60 years of age while those with venogenic ED ranged between 55 and 64 years and no one aged 65 years and above had normal arterial inflow and good venous competence in our study. There was no case of penile fracture, penile tumour or Peyronie's disease among the research participants & none of the patients had priapism or haematoma following intracavernosal injection of PGE_1. No penile anatomical arterial variants were noted among the research participants.

4 Discussion

Erectile dysfunction is prevalent in ageing men because they are often affected with several diseases that could negatively influence sexual function; this includes systemic hypertension, diabetes mellitus and obesity [1, 9] Some also engage in polypharmacy for prostatic diseases, diabetes mellitus, systemic hypertension and psychosomatic illnesses with some of the drugs acting centrally and affecting sexual performance particularly libido [9, 10]. In a large US study, the proportion of sexually active males declined from 83.7% in the age group 57–64 years to 38.5% in the age group 75–85 years as a result of the aforementioned age-related changes [11]. Some studies have also shown increased probability of erectile dysfunction from 40 years of age and peaks in men above 70 years [12, 13]. This is consistent with the observation of Aiyekomogbon et al. [14] where they observed that peak systolic velocity (PSV) of cavernosal arteries (CAs) decreases with age and by extension, ED of vascular origin was observed to increase with age.

Erectile dysfunction is either due to arterial obstruction, venous insufficiency, psychogenic or iatrogenic

causes and cavernosal diseases such as Peyronie's disease, penile fracture or tumour [15]. Of the enumerated causes, vascular causes predominate [16]. This observation is in agreement with the outcome of our study where about half of our patients had ED of vasogenic origin; 36.8% venogenic and 10.6% arteriogenic. The study of Quam et al. [17] also had similar findings as a good number of their patients had ED of vascular origin. It is worthy of note that none of our patients had combined arteriogenic and venogenic erectile dysfunction although, Doppler study has limitation in diagnosing venogenic ED (veno-occlusive disorder) when arterial inflow is poor. This may explain why mixed arteriogenic and venogenic ED was not diagnosed in any of the patients. The submission of previous authors indicated that PSV of CA less than 25 cm/s post-ICI of active pharmacologic agent(s) is consistent with arteriogenic ED, while persistent end diastolic flow > 5 cm/s of CA post-ICI and persistent dorsal vein flow are diagnostic of venogenic ED [2–4]. A patient is considered normal if the PSV of cavernosal arteries is greater than 25 cm/s post-ICI of active pharmacologic agent coupled with diastolic flow reversal in the CA [4]. These parameters formed the basis of patients' categorization to normal, arteriogenic and venogenic ED in the index study.

Vasogenic erectile dysfunction is amenable to either medical or surgical management based on the type of vascular pathology that is identified on colour Doppler sonography. This explains why its categorization as ED of arterial or venous origin is important in the treatment outcome.

Majority of the patients with vasogenic erectile dysfunction in this study had venous leak and many reasons for this observation were adduced by previous authors. The percentage of smooth muscle in the corporal bodies steadily decreases while deposition of collagen fibres increases with ageing which results in corporal fibrosis and consequently, poor expandability of corporal sinusoids. In this circumstance, the expected compressive effects of the distended sinusoids on the emissary veins against the tunica albuginea are lost and this results in venous leak. Also, Androgen deficiency is a common scenario in the elderly and it results in significant deposition of connective tissues and fat in the corporal bodies, leading to veno-occlusive disorder [18]. The observations of previous authors revealed that 86% and 89% of vasogenic erectile dysfunction in their respective studies were due to cavernosal veno-occlusive disorders (CVOD) [19, 20]. This is consistent with the outcome of the index study where majority of the vasogenic ED was due to venous leak. High-resolution images of the venous drainage using a 3D-Computed Tomography cavernosography when available, should further help in the localization of the actual vein(s) that is (are) responsible for the leakage and this investigative approach will ultimately lead to better strategies in venous leak treatment [21–25].

Arterial occlusion is also a contributory factor to erectile dysfunction in the elderly and this was found in 10.6% of the entire patients in the index study, and 22% of those with vasogenic ED. Endothelial dysfunction is common in the aged men as a result of significant reduction in the plasma concentration of Nitric Oxide (NO). In addition, some ageing men are prone to compromised arterial supply due to atherosclesosis of the cavernosal artery which among other things, results from presence of reactive oxygen species (ROS) [26]. A low testosterone level in the elderly also causes increased rigidity and atherosclerosis of the entire arterial systems [27]. These ultimately cause arteriogenic erectile dysfunction, which was observed in some of our patients, and those affected were those above 60 years of age. Associated cardiovascular risks and mortality were noted in patients with cavernosal arterial inflow stenosis as the changes enumerated above affect the entire arterial systems. Consequently, the findings of atherosclesrosis of the cavernosal arteries are a 'blessing in disguise' as it guides the attending physician to further evaluate the patients for a more sinister life threatening sequalae of cardiovascular diseases such as cardiac arrest and thrombo-embolic stroke [27]. Confirmation of the arterial blockage or stenosis and location of such are usually achieved with angiographic technique. This was not done in the index study as such facility is not available in our health institution. Referral could however be made to a nearby health institution when such is desired by the primary Clinicians (urologists) or the patients themselves.

The treatment protocol for these specific causes of vasogenic ED differs. Patients with arteriogenic ED are either treated with oral phosphodiesterase inhibitors, intraurethral alprostadil (prostaglandin E_1), topical alprostadil which is applied 5–30 min prior to coitus, or intracavernosal alprostadil [28, 29]. The more advanced therapy includes penile prosthesis, low intensity shock wave therapy and then Zotarolimus-Eluting peripheral stent treatment in those with severe inflow stenosis [30, 31]. On the other hand, the treatment protocols for CVOD are venous stripping procedure and retrograde embolization of the insufficient veins, using Histoacryl-Lipidol solution [32]. In these categories of patients, medical treatment with phosphodiesterase inhibitors will amount to efforts in futility and as such, categorizing ED to the various specific causes is imperative, which is the major thrust of this study. Some of the patients with sonographic diagnosis of arteriogenic ED responded well to medical treatment with oral phosphodiesterase inhibitors but those with venous leak required surgical venous

stripping procedure and interventional Radiological care such as retrograde embolization of the insufficient veins, using Histoacryl-Lipidol solution. Those in the latter category which form the majority of our patients were counselled for the aforementioned surgical and/or interventional radiological procedure but they were largely constrained by finance and logistics of such care.

5 Limitation

The small sample size used in this study despite the study duration of 18 months was a major limiting factor observed. A larger sample size is advocated for future studies. Also, clinical categorization of the severity of the patients' ED based on international index of erectile function (IIEF) 15 scores was not employed in the index study. Efforts shall be made to circumvent such omission in future studies.

6 Conclusion

The usefulness of penile Doppler sonography in the evaluation of ED in ageing men is corroborated in this study as about half of the patients studied had vasogenic ED. As the treatment protocols of arteriogenic and venogenic ED differ, patients with ED should benefit from this radiological procedure before instituting management to avert treatment failure. It is also advocated that when available, patients with identified venous leak should have the benefit of 3D-Computed Tomography cavernosography to localize the actual vein(s) that is (are) affected as this will go a long way to aid targeted treatment of CVOD. This is a pilot study which should serve as stimulus for future studies using larger population samples.

Abbreviations

ED: Erectile dysfunction; PGE_1: Prostaglandin E_1; ICI: Intracavernosal injection; PSV: Peak systolic velocity; EDV: End diastolic velocity; CA: Cavernosal artery; NO: Nitric oxide; ROS: Reactive oxygen species; FMC: Federal Medical Centre; ABJ: Abuja; HREC: Health Research and Ethics Committee; SD: Standard deviation; SPSS: Statistical package for social science; ANOVA: Analysis of variance; CVOD: Cavernosal veno-occlusive disease.

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Authors' contributions

JOA: A Consultant Radiologist who carried out the Doppler study on the patients. He also contributed substantially to the conception, design and writing of the manuscript. He is the corresponding author of the article. DUI: She is a Consultant Radiologist who made substantial input to the writing of the manuscript. She reviewed and corrected the entire article before submission. TA: A Consultant Urologist who contributed substantially to the design and writing of the manuscript. He made an invaluable contribution to the aspect of medical and surgical management of the patients. JBI: He is a consultant Radiologist who contributed immensely to the aspect of data collection and writing of the manuscript. He also reviewed and corrected the manuscript before submission. All authors read and approved the manuscript.

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The authors bore the cost of this research.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Research and Ethics committee of Federal Medical Centre Abuja (protocol number: FMCABJ/HREC/2017/003), and a written consent to participate in the study was obtained from the research participants before recruiting them.

Consent for publication

Consent for publication was obtained on the condition that anonymity is maintained on all the information obtained from the patients.

Competing interests

None.

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