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Application of dual-energy CT angiography in diagnosis of arterial erectile dysfunction: new scanning technology, new scanning area

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ABSTRACT

Objectives: To explore the value of dual-energy computed tomography (DE-CT) angiography in diagnosis of arteriogenic erectile dysfunction (ED) patients and feasibility of new scanning area that excludes the testis.

Materials and methods: Ninety-three patients suspected of suffering arterial ED and 40 health volunteers underwent penile duplex Doppler ultrasound and DE-CT angiography (DE-CTA). The scanning range of DE-CTA covered whole arterial system of pelvis and testis was excluded. Two blinded investigators independently evaluated the arterial system that supplies the penis.

Results: Finally, 1596 segments were evaluated and 470 segments were judged to be abnormal. The distribution was: 2 (0.4%) in common iliac artery, 7 (1.5%) in internal iliac artery, 82 (17.5%) in internal pudendal artery, 89 (18.9%) in penile artery, 120 (25.5%) in dorsal artery, and 170 (36.2%) in cavernosal artery. The specificity, sensitivity, positive predictive value, and negative predictive value of DE-CTA in diagnostic were 86.02%, 87.50%, 94.12%, and 72.92%. Besides, the new scan area allowed for effective evaluation of the arteries while excluding the testis.

Conclusion: DE-CTA can provide unbiased, safe evaluation of the vascular status of the penile bed in patients with ED.

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Dual-energy CT; erectile dysfunction; exposure control; peripheral arterial disease

Introduction

Erectile dysfunction (ED) is defined as the inability to obtain or maintain an erection sufficient for successful vaginal intercourse [1]. ED is often considered a potential harbringer of cardiovascular disease, based on the shared risk factors but is also severely affecting the couple's well-being [2]. It is supposed that more than 150 million men around the world suffer from ED [3], and 40.56% of men at least 40 years of age in China have various degrees of ED [4]. Several studies indicate that erection is affected by many factors including non-organic (intrapsychic and/or relational), neurogenic, vasculogenic, and endocrine [5,6]. Among the most important causes of organic ED, arterial insufficiency resulting in impaired penile perfusion ED is frequently mentioned [7,8].

A growing body of evidence supports the association between cardiovascular health and erectile function [9], with ED being a hallmark of potentially harmful lifestyles [10]: indeed, several health risk behaviors, such as malnutrition, obesity, alcohol abuse [5], and smoking [11], are considered risk factors for both ED and CVD. Moreover, ED is deemed to be the clinical manifestation of some vascular lesions affecting circulation in penile vessels [12]. Several angiographic studies indicate that vascular lesions of arterial system supplying the penis are among the reasons contributing to ED [13,14]. Based on these assumptions, it is unsurprising that adequate anatomical evaluation of penile artery appears vital in both diagnosis and treatment of ED [15].

Currently, penile duplex Doppler ultrasound (PDDU) is considered as the "gold standard" for diagnosing

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vasculogenic ED [16,17]. Peak systolic velocity (PSV), end diastolic velocity (EDV), and resistive index (RI) are useful parameters in evaluation of penile arterial blood flow with ultrasonography [18]. Importantly, PSV is the most accurate index in the assessment of penile arterial insufficiency, and it has a significant correlation with arteriography [19].

As a noninvasive imaging means, computed tomography angiography (CTA) is considered as an effective diagnostic tool in peripheral arterial lesions [20,21], and the quality of image is improving with the update of technology and machine. However, the effects of radiation are worrisome because the scanning area contains sensitive tissue such as testis. In addition, ionizing radiation negatively affects the penile corpus cavernosum, causing its levels of nitric oxide synthase to decrease, both in neurons and in the endothelium [22,23]. At the same time, ionizing radiation can cause damage to the cavernous blood vessels and nerves, thereby affecting the erectile function of the penis [24,25]. Up to half of prostate cancer patients report erectile dysfunction after radiotherapy [26]. Therefore, it is very important to minimize the effects of radiation on the sexual organs. Recently, dual-energy CT (DE-CT) has been increasingly applied in diagnosis and surveillance of abdominal and pelvic lesions and plays an important role in the detection for genitourinary tract diseases [27–29]. Iodine attenuation gains significantly on low-energy images, which allows images with adequate contrast to be obtained with iodine dose reduced. The important concomitant problem is that the noise of the resulting image will increase. However, the virtual monoenergetic images obtained by DE-CT by decomposed two basic materials can effectively optimize noise and improve the quality of low-energy images. The quality of virtual noncontrast images obtained by decomposing different materials is similar to that of true non-contrast CT images, and this advantage allows the real plain scanning process to be canceled and the radiation to be cut in half [29]. Compared to traditional single-energy CT, DE-CT effectively improve the effectiveness of iodine contrast agent, reduce the load of patients' kidneys, and reduce the cost of contrast agent [27–29]. As a novel technology, DE-CT potentially improves the diagnostic performance while contributing to the patient's safety [30]. The present work was undertaken to explore the value of DE-CT angiography (DE-CTA) in the diagnosis of arteriogenic ED and the feasibility of the new scanning area that can reduce the effect of radiation.

Materials and methods

Study population

The study was performed in our andrology clinical center. Between April 2017 and July 2021, 377 consecutive patients that complained of ED were evaluated for inclusion in the study based on the following criteria: age $\geq$18 years; difficulty in obtaining or maintaining erection for more than six months, as measured by International Index for Erectile Function (IIEF)-5. Exclusion criteria were the following: severe hepatic and renal impairment, hormonal disorders, contrast agent hypersensitivity, presence of a known neoplasia, serious psychological abnormalities, neurologic disease, and penile fibrosis. Furthermore, subjects who had taken drugs that may affect erectile within four weeks were excluded. Forty sexually active male health volunteers were also recruited to undergo the testing as a healthy control population.

Subjects were evaluated by a multidisciplinary team that was made up of experienced sonographers, radiologists and urologists. All subjects had been informed about the design of our study. This prospective study was approved by the research subject review board of Affiliated Hospital of Anhui Medical University.

Preliminary evaluation

The assessment included medical history, sexual history, physical examination, routine blood test (blood routine examination, blood coagulation function, fasting blood glucose, HbA1c, triglycerides, total cholesterol, hepatic and renal function tests), and sexual hormonal values (luteinizing hormone, follicle-stimulating hormone, estradiol, prolactin, and total testosterone).

NPTR and AVSS examination

Nocturnal Penile Tumescence and Rigidity (NPTR) was performed with the RigiScan Plus (Timm Medical Technologies, Eden Prairie, MN, USA) in our medical center. NPTR was carried out for three subsequent nights to obtain accurate measurements [31,32]. To ensure a peaceful sleep, all patients were required to avoid chemical sleep aids, alcohol intake, or caffeine before the test. The NPTR was performed as further confirmation of clinical and laboratory work-up suggestive for the presence of a non-organic form of ED [32].

Audiovisual sexual stimulation was performed in a dark and quiet room. RigiScan Plus was used to

monitor the erectile response after the patient had comfortably lain on the examination bed. Each patient watched a favorite pornographic video for 30 min [33,34].

The result of examination was considered as normal if at least one event indicated the rigidity of tip >70% for ≥10 min [32,34,35]. Patients with a normal response were considered to have a non-organic form of ED, based on the assumption that vascular impairment would result in inadequate spontaneous erections and/or in reduced response to a sexual stimulus. Therefore, patients with abnormal outcomes were qualified to undergo further tests.

PDDU examination

PDDU was performed following standard operating procedures (SOPs) by well-trained sonographers that were blinded to the clinical information [34]. Measurements were observed in the flaccid state, 20 min and 25 min after ICI. Left and right values were recorded separately. Cavernous artery with PSV above 30 cm/s was considered as arterial sufficiency [36,37]. The examination was carried out in a warm and quiet room with subjects being in a supine position. For ICI in the process of both PDDU and DE-CTA, erection of penis was induced by intracavernosal injection with 10 μg alprostadil (Alprostadil, Beijing Tide Pharmaceutical Co., LTD, Beijing), and a rubber tourniquet with appropriate tension was previously placed at the base of penis to generate dorsoventral pressure for 30 s to retain most of the alprostadil [38]. If the erection was not as hard as it would be during sexual intercourse, the redosing strategy would be performed. And if patient continued to exhibit an erection for more than 45–60 min, the reversal with phenylephrine would be performed to avoid priapism.

DE-CTA examination

To keep the physical and mental relaxation of patients, two examinations (PDDU and DE-CTA) were a week apart. The patients were fully acquainted with the result of PDDU before deciding to undergo DE-CTA examination. In order to avoid the adverse reactions to iodinated contrast media, patients underwent the test for allergies before DE-CTA. The penis was fixed in the position that dorsal side was close to the pubic symphysis. DE-CTA was performed by using Revolution CT with generation 256-slice scanner (GE Healthcare, Waukesha, WI, USA) at 20 min after ICI (alprostadil 10 μg), administered in order to ensure proper vasodilation. Scanning parameters were as follows: tube voltages, 140 kV and 80 kV; tube current, 260 mA; rotation time, 0.6 s; helical pitch, 0.992:1; scanning field of view, medium body; displaying field of view, 40.0 mm; image interval and image thickness, 5.0 mm; and pixel matrix, 512 × 512. The scanning range covered the whole arterial system of pelvis (from common iliac artery to the cavernous artery and penile dorsal artery). Nonionic iodinated contrast medium (iohexo, 350 mg/mL iodine, 1.3 mL per kilogram of body weight) was injected into the antecubital vein with flow rate of 4.5–5.0 mL/s, then 40 mL saline was injected with the same flow rate.

Image assessment

The date was transferred to the workstation (Advantage Workstation Version4.7; GE Healthcare) and evaluated independently by two experienced radiologists both were blinded to the clinical information. The evaluation was accomplished with Multiple maximum Intensity Projection (MIP) and Volume Rendering (VR).

Arterial reconstitution of concern was classified as macrovascular (common iliac arteries, internal iliac arteries, and internal pudendal arteries) and microvascular (common penile arteries, dorsal penile arteries, and cavernosal arteries). Arterial lesions contain stenosis, occlusion, poorly continuous and no adequate distal arterial reconstitution.

Statistical analysis

Statistical analysis was performed with SPSS version 24.0 software. Distribution of data was tested with Kolmogorov–Smirnov test. Descriptive statistics were applied to describe the characteristics of the subjects. All quantitative data were presented as means ± standard deviations (SDs). Categorical variables were summarized with percentages and compared using the Chi-square test. The t-test was used to analyze numerical variables with normal distribution, and the other was analyzed with Mann–Whitney U-test. The diagnostic sensitivity, specificity, accuracy, negative predictive value, and positive predictive value of DE-CTA were analyzed. Statistical significance was set at $p < .05$.

Results

Demographic information

Finally, 93 arterial ED patients and 40 health volunteers underwent DE-CTA (Figure 1), and the demographic

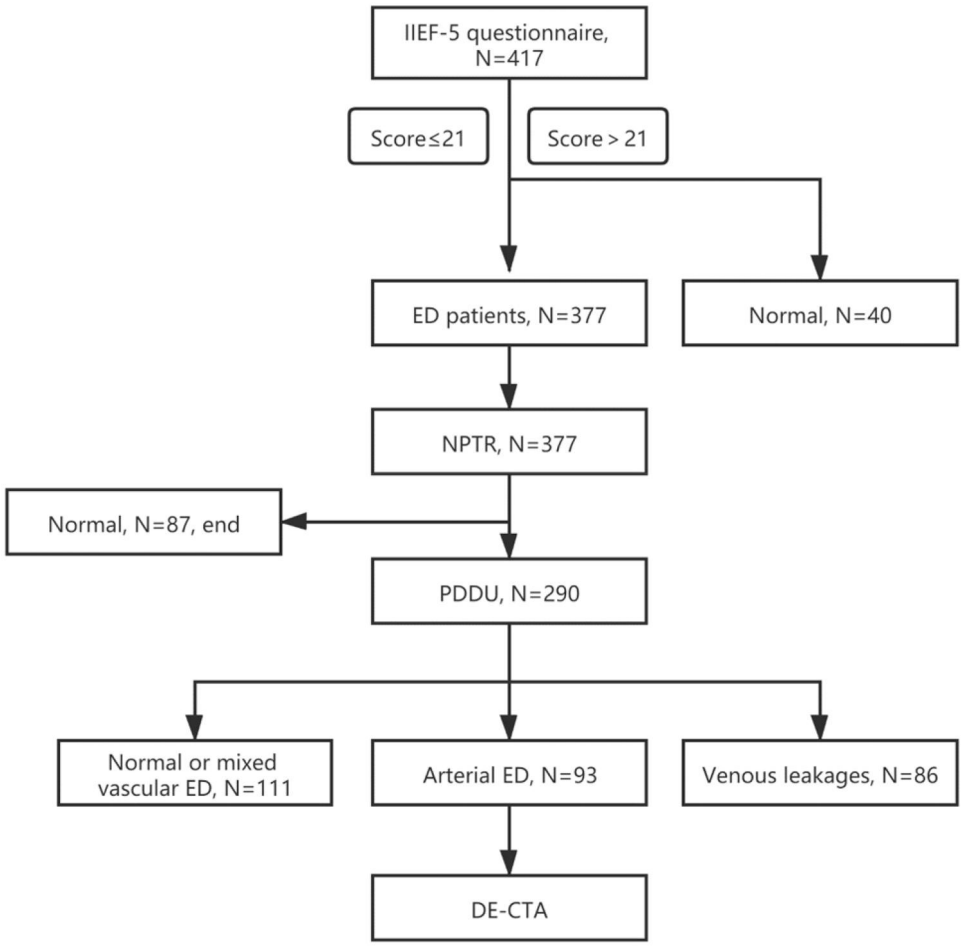

Figure 1. Flow chart of examination. Note: IIEF-5: International Index of Erectile Function; NPTR: Nocturnal Penile Tumescence and Rigidity; PDDU: penile duplex Doppler ultrasound; DE-CTA: dual-energy CT angiography.

Table 1. Demographic characteristics of all subjects.

Variables	Study population ($n = 133$)
Age (years)	31.47 ± 6.95
IIEF-5 score	15.15 ± 6.81
Hypertension	21 (15.8)
Diabetes mellitus	18 (13.5)
Smoking	43 (32.3)
Hyperlipidemia	27 (20.3)
Sedentary	44 (33.1)
LH (mIU/mL)	5.73 ± 2.20
FSH (mIU/mL)	7.56 ± 2.74
PRL (ng/mL)	8.19 ± 3.02
Progesterone (ng/mL)	0.46 ± 0.21
Estradiol (pg/mL)	49.18 ± 16.51
Testosterone (ng/dL)	5.00 ± 1.60
Fibrinogen (g/L)	3.09 ± 0.69
Fibrin degradation products (mg/L)	2.43 ± 1.08
D-dimer (mg/L)	0.26 ± 0.11

Notes: Categorical variables are presented as n (%). Continuous variables are presented as mean ± standard deviation. LH: luteinizing hormone; FSH: follicle-stimulating hormone; PRL: prolactin hormone; IIEF-5: International Index of Erectile Function.

information are shown in Table 1. According to IIEF-5 score, the number of severe ED patients was 20 (21.5%), moderate was 33 (35.5%), mild to moderate was 21 (22.6%), and mild was 19 (20.4%). The comparison between two groups is shown in Table 2. There were no significant differences between two groups in baseline characteristics except for IIEF-5 score, smoking, and LH. The mean IIEF-5 score in arterial ED group and control group was 11.50 ± 4.61 and 23.65 ± 0.95 ($p < .001$), the proportion of smokers was 39.8% and 15.0% ($p < .05$), and the mean LH was 6.01 ± 2.21 and 5.09 ± 2.06 ($p < .05$).

Ultrasonographic evaluation of erectile dysfunction

Significant differences in PDDU parameters between two groups as shown in Table 3: compared to arterial ED group, control group has a better arterial blood supply (PSV: 21.12 ± 3.86 vs 35.55 ± 2.85 cm/s, $p < .001$), lower diastolic blood flow (EDV: 2.40 ± 1.75 vs 1.04 ± 2.13 cm/s, $p < .001$) and stronger peripheral resistance (RI: 0.89 ± 0.08 vs 0.97 ± 0.06, $p < .001$).

DE-CTA evaluation of erectile dysfunction

A total of 1596 segments were obtained and 470 obstructive segmental lesions in total were observed.

Table 2. Demographic between two groups.

Variables	Arterial ED group ($n = 93$)	Control group ($n = 40$)	p
Age (years)	32.12 ± 7.54	29.98 ± 5.10	.103
Duration (years)	1.55 ± 0.60	–	–
IIEF-5 score	11.50 ± 4.61	23.65 ± 0.95	**< .001**
Hypertension	18 (19.4)	3 (7.5)	.120
Diabetes mellitus	15 (16.1)	3 (7.5)	.270
Smoking	37 (39.8)	6 (15.0)	**.005**
Hyperlipidemia	23 (24.7)	4 (10.0)	.062
Sedentary	34 (36.6)	10 (25.0)	.231
LH (mIU/mL)	6.01 ± 2.21	5.09 ± 2.06	**.026**
FSH (mIU/mL)	7.75 ± 2.77	7.12 ± 2.64	.228
PRL (ng/mL)	8.51 ± 3.10	7.44 ± 2.71	.060
Progesterone (ng/mL)	0.45 ± 0.22	0.49 ± 0.20	.250
Estradiol (pg/mL)	50.30 ± 17.37	46.58 ± 14.15	.253
Testosterone (ng/dL)	5.04 ± 1.65	4.91 ± 1.48	.678
Fibrinogen (g/L)	3.17 ± 0.71	2.91 ± 0.63	.055
Fibrin degradation products (mg/L)	2.52 ± 1.11	2.22 ± 0.99	.130
D-dimer (mg/L)	0.27 ± 0.12	0.25 ± 0.88	.502

Notes: Categorical variables are presented as n (%). Continuous variables are presented as mean ± standard deviation. $p < .05$ were shown in bold.

Table 3. Penile Doppler ultrasonography parameters between two groups.

Parameter	Arterial ED group ($n = 93$)	Control group ($n = 40$)	p
PSV (cm/s)	21.12 ± 3.86	35.55 ± 2.85	<.001
EDV (cm/s)	2.40 ± 1.75	1.04 ± 2.13	<.001
RI	0.89 ± 0.08	0.97 ± 0.06	<.001

Notes: Data are presented as mean ± standard deviation. PSV: peak systolic velocity; EDV: end diastolic velocity; RI: resistivity index.

The distribution was: 2 (0.4%) in common iliac artery, 7 (1.5%) in internal iliac artery, 82 (17.5%) in internal pudendal artery, 89 (18.9%) in penile artery, 120 (25.5%) in dorsal artery, and 170 (36.2%) in cavernosal artery. Macroangiopathic and microangiopathy were shown in Figure 2.

Compared with PDDU, the diagnostic sensitivity, specificity, positive predictive value and negative predictive value of DE-CTA were 86.02% (95% CI: 76.92%–92.06%), 87.50% (95% CI: 72.40%–95.31%), 94.12% (95% CI: 86.20%–97.81%), and 72.92% (95% CI: 57.91%–84.26%).

Figure 2. DE-CTA findings of the arterial system supplying the penis. (A) Normal penile dorsal artery (white arrowhead) and cavernous artery (black arrowhead). (B) Multiple calcification of internal pudendal artery (black arrowhead) and poor development of penile dorsal artery and cavernous artery. (C) Focal stenosis (black arrowhead) in the left internal pudendal artery. (D) Multiple calcification of common iliac artery and internal iliac artery.

Discussion

Penile erection depends on synergistic mechanisms between psychologic, neural, endocrine and vascular systems, and therefore ED can be caused by any defect in these systems [39]. Decreased perfusion of penile arteries caused by arterial lesions is an important cause of vasculogenic ED. Currently, penile duplex Doppler ultrasound (PDDU) is treated as the gold standard for diagnosis of vascular ED because of the high sensitivity in the assessment of penial hemodynamics and significant correlation with arteriography [16,17]. However, there are some obvious limitations to ultrasonography. First, the diagnosis is highly susceptible to the skill and experience of operator, and the value relies on Doppler cursor angle and anatomic location [40]. Second, the result is

considered to be affected by psychological disturbance such as anxiety and nervousness, especially in young patients [41]. Finally, it is unable to fully evaluate penile arteries, focusing only on selected vessels [36]. Additional diagnostic tests, such as cavernosometry and cavernosography, have also been used in the investigation of ED, but are considered "third line" options in the clinical setting, being invasive and complicated procedures [42].

In 2001, Y. Kawanishi et al. [43] first used CTA performed with multi-slice CT in the diagnosis of arterial ED, proving its high diagnostic accuracy. They considered CTA to be a potential method for the diagnosis of arterial ED, and with the development of machine and technology, the image quality was expected to improve manifolds. DE-CT has been employed in several clinical applications including peripheral arterial occlusive disease and genitourinary tract imaging as an advanced scanning mode [21,27,28]. Compared to single-energy CT, DE-CT acquires simultaneous acquisition of low-energy and high-energy datasets at two different kilovoltages by rapid peak kVp switching, thereby getting more material information [44]. The differentiation of iodine from calcification allows vessel calcification subtraction and provides preferable evaluation of vascular disease [45]. Acquisition of the low-energy monochromatic images results in the reduction of nephrotoxic contrast medium dose and improves contrast enhancement of vessels, and similarly, acquisition of virtual noncontrast images is able to reduce overall radiation exposure by displacing true noncontrast CT [46].

To the best of our knowledge, this study is the first to apply DE-CTA to arterial erectile dysfunction. Our findings suggested that DE-CTA is a promising method in the evaluation of patients with arterial ED, as it could depict pelvic vasculature from the distal aorta to the dorsal artery and cavernosal artery of penis clearly. Our results showed that arterial ED patients in the DE-CTA suffered from arterial lesions at various sites, and the lesions were mainly concentrated in cavernosal artery and dorsal artery. Compared to PDDU, DE-CTA offered complete anatomic evaluation of the arterial system supplying the penis. DE-CTA is expected to provide more detail information about extent and location of arterial lesions in ED patients, and it is critical in the surgical management of ED patients. When penile revascularization surgery is required for ED patients with pelvic trauma, arterial stenosis, etc., preoperative arterial disease information will guide the operation to be performed more safely and effectively [41,47,48]. On the other hand, obtaining anatomical information on arterial lesions is helpful for drug therapy strategies. Previous study has shown that cavernous artery intima-media thickness was a useful predictor of sildenafil efficacy in patients with arterial ED [49]. Severe penile arterial insufficiency was observed in most non-responders to sildenafil, and internal pudendal artery stenosis was common in these patients [13,50]. The same phenomenon was observed in alprostadil non-responders, of whom nearly two-thirds developed internal pudendal artery lesion [51]. Anatomical evaluation of the arterial lesions in these patients is important for the establishment of the next treatment plan [52]. In terms of diagnostic accuracy, DE-CTA possess high specificity and sensitivity value in arterial ED assessment. Compared to the previous study, DE-CT had a higher specificity than conventional single-energy CT, and the consistency of DE-CTA and PDDU findings were preferable, that indicated DE-CTA has potential in the diagnosis of arterial ED. In the clinical setting, PDDU would still be the preferable choice, being a relatively easier procedure; however, DE-CTA would provide objective measurement, whereas PDDU results are clearly influenced by the expertise and skill of the clinician performing the US examination [53].

Radiation is a crucial problem for traditional CT examination, due to the potentially increased risk of carcinogenesis,—a risk which is also increased for the gonads, because of higher sensitivity. In this study, a new scan area was set to minimize the effects of radiation for testis, therefore reducing exposure and subsequently the risk to the gonads as well. The process of CT scanning is continuous and dynamic, and the shape and position of penis are likely to change during this. To keep the high quality of images and reduce involuntary penis motion, penis was fixed in the scanning process. There are two common methods of fixation, ie fixing the penis between thighs or to the pubic symphysis. In the former fixation method, testis will inevitably be exposed in the scanning area for the purpose of obtaining the anatomical information of the dorsal and cavernous arteries, though the accessory sex glands are not included in the evaluation (Figure 3(A)). In our study, the penis was fixed to the pubic symphysis and testis was excluded from the scanning area. The method allows the information about arteries of concern to be obtained without exposing the testis to the scanning area (Figure 3(B)), most importantly, the result showed that the quality of images about penis artery was not affected (Figure 2(A)). We got the complete anatomical information of as well as protected gonad of patients.

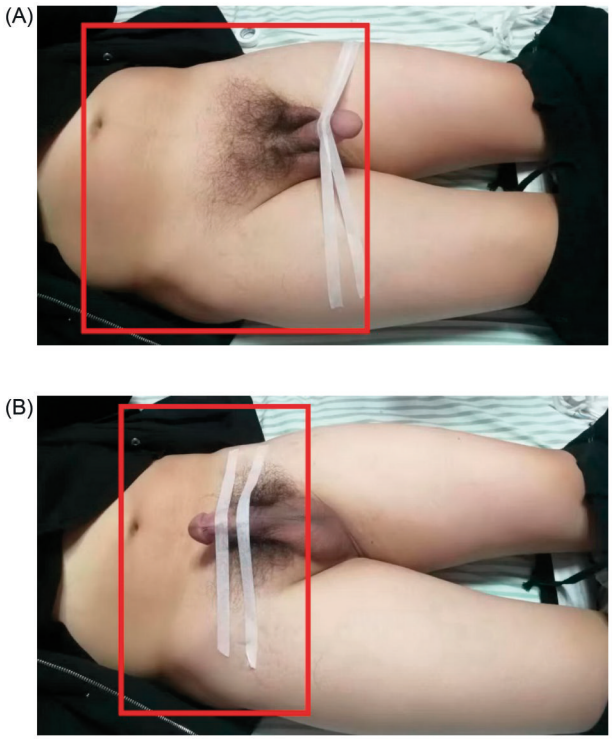

Figure 3. Two methods to fix the penis in the process of CT scanning. (A) The erect penis is fixed between thighs and testis is involved in the scanning area (box region). (B) The erect penis is fixed to the pubic symphysis and testis is excluded from the scanning area.

The findings in our study are subject to limitations. In this study, we did not compare the diagnostic efficacy of DE-CT with angiographic examination. Another limitation is that sample size was limited, in order to verify the results of this study, an expanded sample size is necessary for further investigations. At last, we did not measure testicular damage of these subjects, which should be explored in subsequent experiments.

Conclusion

DE-CTA is a is a novel, noninvasive and effective approach in the evaluation about pelvic arterial system supplying the penis and it exhibited high sensitivity and specificity in the diagnosis of arterial ED. Besides, the new scanning area can protect the gonad of patients from direct radiation as well as provide complete arterial information.

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Author contributions

XSZ and HJ formulated the idea of the article and supervised the research. MW, XSZ, and YTD performed the research, analyzed the data, and wrote the manuscript. AS and EJ reviewed the manuscript. All authors read and approved the final version of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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