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ORIGINAL RESEARCH

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Minimizing bleeding of dorsal venous complex by artificial erection in a rat model

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Abstract

Background: Bleeding due to dorsal venous complex (DVC) injury is generally regarded as the main cause of stress for the surgeon during radical retropubic prostatectomy (RRP) and radical cystoprostatectomy (RSP). Despite its significance, previous studies have not adequately explored preventive strategies for DVC bleeding. This study aimed to determine whether applying an artificial erection (AE) before transecting the DVC in a rat model could effectively reduce bleeding. **Methods**: This study was conducted using 10 male Wistar albino rats, aged 16 weeks and weighed between 300 and 350 grams. These rats were randomly divided into two groups: one group underwent artificial erection (AE) before transecting the dorsal venous complex (DVC) (AE+, n = 5), while the other group did not (AE−, n = 5). At the end of the study, we compared the volume of aspirated blood around the transected DVC between the two groups. **Results**: In the AE− group, an average of 4.28 mL of blood was aspirated (range: 3.8 mL to 4.7 mL), while in the AE+ group, an average of 1.54 mL of sero-hemorrhagic fluid was aspirated (range: 1.4 mL to 1.7 mL). The difference between the two groups was statistically significant ($p = 0.009$). **Conclusions**: The results of this study suggest that DVC bleeding caused by DVC transection can be significantly reduced by inducing penile erection using the AE technique in rats. This study lays the groundwork for a novel approach to minimizing DVC bleeding and offers an original contribution to the field, enhancing the understanding and management of DVC bleeding.

Keywords

Artificial erection; Bleeding; Corpus cavernosum; Dorsal venous complex; Rat model

Minimizar la hemorragia del complejo venoso dorsal mediante erección artificial en un modelo de rata

Resumen

Antecedentes: La hemorragia debido a una lesión del complejo venoso dorsal (DVC) generalmente se considera la principal causa de estrés para el cirujano durante la prostatectomía radical retropúbica (PRR) y la cistoprostatectomía radical (CPR). A pesar de su importancia, los estudios anteriores no han logrado abordar las estrategias preventivas para la hemorragia por DVC. Nuestro objetivo era determinar si la hemorragia del DVC podría minimizarse aplicando una erección artificial (AE) antes de seccionar el DVC en un modelo de rata. **Métodos**: El estudio se realizó con 10 ratas albinas Wistar macho, de 16 semanas de edad y con un peso entre 300 y 350 gramos. Estas ratas se dividieron aleatoriamente en dos grupos: un grupo se sometió a una erección artificial (AE) antes de seccionar el DVC (AE+, n = 5), mientras que el otro grupo no (AE−, n = 5). Al final del estudio, comparamos el volumen de sangre aspirada alrededor del DVC seccionado entre los dos grupos. **Resultados**: En el grupo AE− se aspiraron una media de 4.28 mL de sangre (rango: 3.8 mL a 4.7 mL), mientras que en el grupo AE+ se aspira una media de 1.54 mL de líquido serohemorrágico (rango: 1.4 mL a 1.7 mL) fue aspirado ($p = 0.009$). **Conclusiones**: Los resultados de este estudio sugieren que el volumen de hemorragia del DVC debido a la transección del DVC se puede reducir significativamente induciendo la erección del pene con la técnica AE en ratas. Este estudio sienta las bases para un nuevo enfoque para minimizar el hemorragia de DVC y ofrece una contribución original al campo, mejorando la comprensión y el manejo del hemorragia de DVC.

Palabras Clave

Erección artificial; Hemorragia; Cuerpo cavernoso; Complejo venoso dorsal; Modelo de rata

1. Introduction

Santorini's venous plexus was first described in 1724 by Domenico Santorini [1]. In radical retropubic prostatectomy (RRP) and radical cystoprostatectomy (RCP), one of the most critical steps of the operation is controlling the dorsal venous complex (DVC) due to its high bleeding potential and retropubic location [2]. With the increasing use of laparoscopic and robotic-assisted laparoscopic approaches, DVC control can be achieved more effectively and easily compared to traditional open surgery [3]. However, open RRP and open RCP, which offer similar surgical and functional outcomes, are still widely recommended and practiced in many centers worldwide due to financial and technical limitations [4, 5]. In the literature, several recommendations for controlling DVC have been proposed, including the use of compression after transecting the urethra and DVC, as described by Memmelaar *et al*. [6]. The ligation of DVC by passing a right-angled clamp below it was described by Chute *et al*. [7], and the ligation of the DVC using a method described by Reiner and Walsh in 1979 [8]. However, even when attempting to apply these methods, bleeding from DVC can still occur at a high flow rate, complicating the surgical procedure and can increase morbidity.

Penile erection results from increased arterial flow due to vascular changes controlled by the autonomic nervous system, which fills the corpus cavernosum with blood while decreasing venous return through a veno-occlusive mechanism. In this study, considering the physiology of penile erection, we hypothesized that the bleeding from transected DVC could be minimized using a saline-induced artificial erection (AE) technique before transection, thereby reducing the venous return from the penis. We examined whether this bleeding could be controlled by inducing an erection with the AE technique in a rat model with DVC bleeding.

2. Materials and methods

2.1 Surgical procedure

A total of ten healthy male Wistar albino rats, 16 weeks old and weighing between 300 and 350 grams, were utilized. These rats were obtained from the Medipol University Animal Experiments Laboratory in Istanbul, Turkey. The rats were kept at a temperature of 22 ± 1 °C with humidity level around 50 ± 10%. They lived individually ventilated cages that allowed for 10 to 15 ventilations per hour and were maintained on a regular 12-hour night and 12-hour day cycle. The animals had unrestricted access to water and were provided with a standard laboratory diet (Mucedola 4RF21, Milan, Italy). The water was changed, and the cages were cleaned weekly. The cages were lined with aspen chip bedding (Tapvei, Finland). The rats were sedated using intramuscular injections of 4 mg/kg xylazine, and 50 mg/kg ketamine, administered at a body temperature of 37 °C. The subjects were randomly divided into two groups based on whether AE was applied before transection of the DVC: AE+ (n = 5) and AE− (n = 5). The retropubic approach was not considered, as we found that the dorsal vein of rat could be more easily located at the root of the penis, allowing for easier access to the dorsal venous system from this site. In the AE− group, DVC was dissected and transected without AE. Blood from the transected DVC was aspirated, and the total bleeding volume and duration were recorded. The endpoint of the study was defined as a 20% loss of the estimated total volume of blood (4–4.5 mL), calculated as 0.06 × body weight [9]. This amount is approximately equivalent to 750–1000 mL in humans and reflects the average blood loss reported in studies on open RRP [2, 10]. In the AE+ group, AE was initiated by injecting 0.4–0.5 milliliters of sterile saline into the corpus cavernosa using a 28-gauge insulin injector, and then DVC was dissected and transected. Aspiration was used to determine the quantity of blood from the transected DVC. Additional saline injections were administered to maintain it. In two of the five rats, an additional 0.4 mL of saline was given, with the total volume not exceeding 1 mL. On average, 0.6 mL of saline was required per rat to maintain the erection throughout the procedure. The volume and duration of bleeding were recorded. In the AE+ group, aspiration lasted eight minutes, as this was the time required for the AE− group to reach the endpoint. After the procedure, rats were sacrificed by intraperitoneal administration of pentobarbital (R-45Somnopentyl, Kyoritsu Seiyaku Co., Ltd., Tokyo, Japan) at a dose of 200 mg/kg. One penis each from AE+ and AE− groups was excised for histological examination (Fig. 1).

2.2 Microscopic examination

Rat penile tissues were fixed in 10% formaldehyde, and transverse sections were obtained in successive full-thickness slices. Following standard tissue processing procedures, 4-micron thick sections were taken from the paraffin blocks and the slides were stained with hematoxylin and eosin (Fig. 2).

2.3 Statistical analysis

The data were evaluated using the Mann-Whitney U test with SPSS version 26.0 (IBM, Armonk, NY, USA). A power analysis was performed, setting the type I error at 0.01 and the type II error at 0.10, focusing on the differences in bleeding volume between the groups. This analysis determined that at least four subjects in each group were necessary to achieve a statistically significant difference. A p-value of less than 0.05 was deemed statistically significant.

3. Results

The duration of aspiration and mean aspirated blood volumes of both groups are given in Table 1. Statistical analysis revealed significant differences in mean blood loss between the two groups during the measurement period.

According to our histological examination, in the AE− group, DVC was normal in size and its lumen was congested. The corpora cavernosa exhibited normal volumes and the lumens of the venous structures around the penis were congested. In contrast, in the AE+ group, the corpora cavernosa were dilated, and the DVC and peripheral vascular structures were collapsed. There was no congestion inside the lumens of the venous structures, and the lumens were observed to be empty.

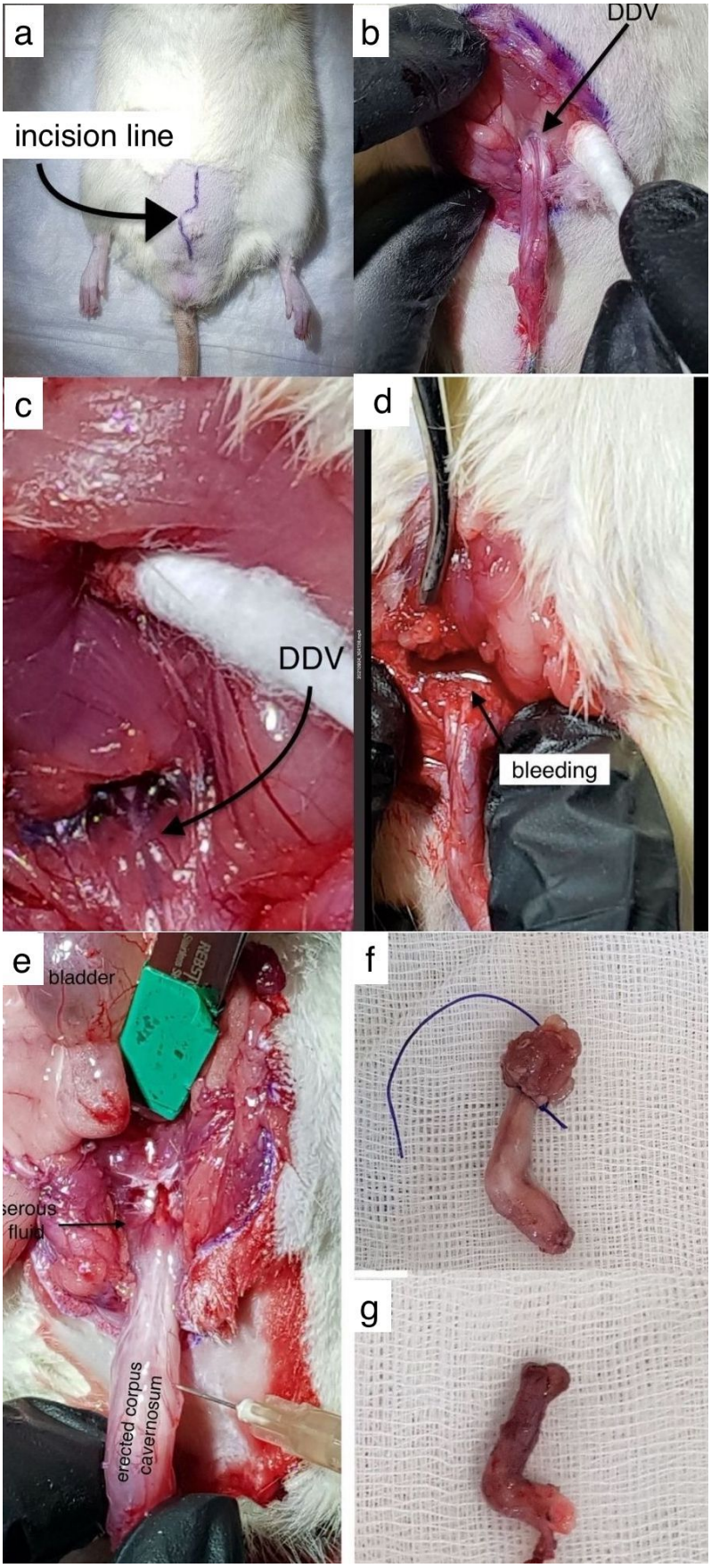

FIGURE 1. Surgical dissection of the penis and Deep Dorsal Vein (DDV). (a) Incision line. (b) Dissected penis and DDV. (c) DDV and its proximal bifurcation. (d) Bleeding that occurred in the penis of a rat in the group in which artificial erection (AE) was not applied. (e) Serous fluid coming from the dorsal vein in the penis of a rat in the group in which AE was applied, which shows minimal bleeding. (f) Excised state of the AE−applied penis after the procedure. (g) Excised state of the penis in which AE was not applied.

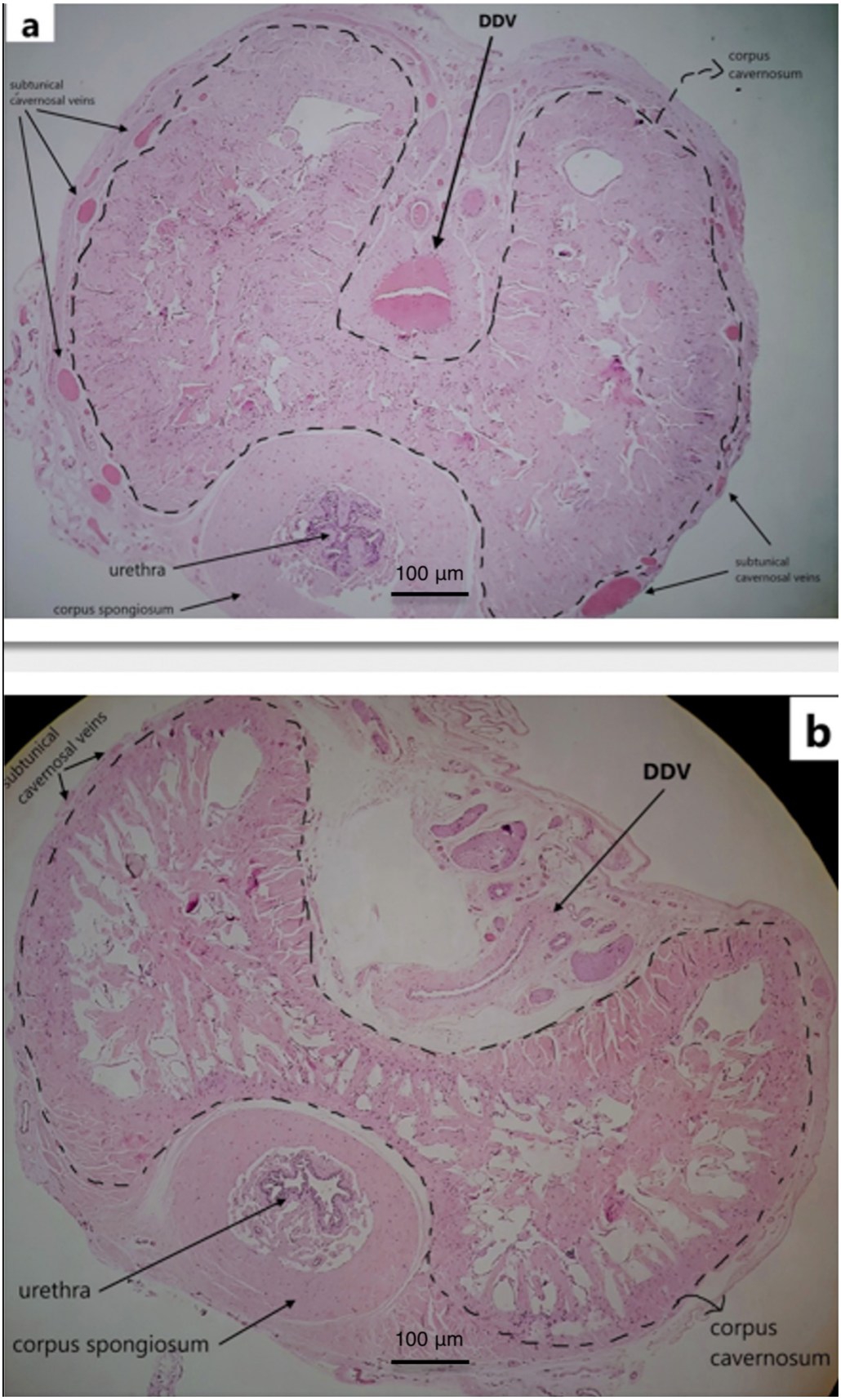

FIGURE 2. Microscopic examination of the penis without (a) and with Artificial Erection (b). (a) Significant congestion in the dorsal vein and other venous structures in the non-erectile tissue (H&E, ×4 magnification). (b) Dilated corpus cavernosum, significantly decreased blood flow and collapse in the dorsal vein and other venous structures in the erectile tissue H&E, ×4 magnification (scale bar = 100 μm) Deep Dorsal Vein (DDV).

4. Discussion

In men, prostate cancer is the second most common cancer, while bladder cancer ranks as the seventh most common cancer [11]. At the time of early diagnosis, approximately 25% of bladder cancer patients present with the muscle-invasive stage [12]. Current guidelines strongly recommend RCP in selected cases of T1 and T2 stage bladder cancer cases [13], as well as RP for locally advanced prostate cancer [5]. Therefore, RP and RCP procedures play an important role in urooncology practice. One of the most critical steps common to both surgical procedures is management of the DVC. Even among experienced surgeons, bleeding that requires transfusion can occur during open RP [14, 15].

Since the introduction of Santorini's venous plexus and the application of radical surgery to the prostate and bladder, various modifications have been proposed to control the DVC. However, a study by Herranz Amo reviewing these methods concluded that there remains no ideal technique to minimize blood loss [16]. In this study, we explored whether bleeding could be reduced using a fundamentally different method. We hypothesized that saline-induced AE, could increase pressure in the subtunical veins could by elevating intracavernous pressure. This, in turn, could decrease blood flow to the dorsal venous plexus by reducing venous return from the corpora cavernosa (Fig. 3).

In the AE+ group, clear liquid rather than blood was aspirated from the transected DVC, resulting in less bleeding and a clear view of the surgical field. Furthermore, the volume of aspirated fluid in the AE+ group was significantly lower than the volume of aspirated blood in the AE− group. One reasonable explanation for this decrease is that diminished venous return due to saline-induced AE. Furthermore, the decrease in arterial blood flow to corpora cavernosa, caused

TABLE 1. Comparison of the amount of bleeding between the study groups.

	AE− mean blood loss ± std. deviation, mL (min–max)	AE+ mean blood loss ± std. deviation, mL (min–max)	*p*
Second 30	0.52 ± 0.08 (0.4–0.6)	0.26 ± 0.05 (0.2–0.3)	0.008
Minute 1	0.94 ± 0.11 (0.8–1.1)	0.56 ± 0.10 (0.4–0.7)	0.009
Minute 3	2.12 ± 0.25 (1.8–2.5)	0.90 ± 0.15 (0.7–1.1)	0.009
Minute 5	3.34 ± 0.23 (3.0–3.6)	1.26 ± 0.11 (1.0–1.4)	0.009
Minute 8	4.28 ± 0.37 (3.8–4.7)	1.54 ± 0.12(1.4–1.7)	0.009

AE−, group in which artificial erection was not performed; AE+, group in which artificial erection was performed. AE: artificial erection; std. deviation: standard deviation; min: minimum; max: maximum.

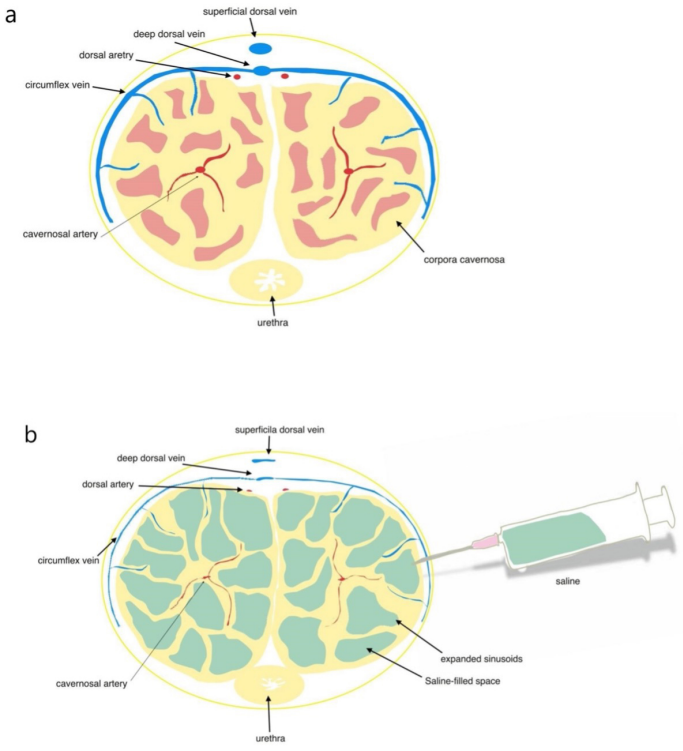

FIGURE 3. Schematic representation of vascular changes in the penis without (a) and with (b) Artificial Erection. (a) Flaccid penile anatomy. (b) Saline injected penile figure, expanded cavernosal sinusoids, and compressed arterial and venous system.

by an increase in intracavernosal pressure that exceeds the rat's systemic blood pressure, may also contribute to the reduction in bleeding. Unfortunately, the blood pressure and pulse values of the rats could not be recorded due to technical limitations. As a further limitation, additionally, could not measure intracavernous pressure during saline injections. However, the volume of saline used to maintain erection aligns with the findings reported by Dai [17]. Despite these limitations, the histological examination revealing the collapse of the DVC and subtunical veins in the AE+ group supports our hypothesis.

5. Conclusions

Our preliminary findings indicate that the AE technique effectively reduces hemorrhage from the transected DVC in rats. While the applicability of these results to human subjects remains uncertain, we believe that this research offers a novel perspective on potential strategies for DVC control during surgical procedures in the future.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and analyzed throughout this study are accessible from the corresponding author upon submission of a reasonable request.

AUTHOR CONTRIBUTIONS

AE and HSG—mainly prepared the study, performed the experiments, and performed the surgery. HSG and AK—write the article. IT—performed the histopathological examination. RS, VC and AI—edited the article. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was conducted following approval from the Medipol University Animal Experiments Local Ethics Committee (approval date: 01 June 2021, reference number: E-38828770-772.02-2456).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Dietrich H. Giovanni Domenico santorini (1681–1737). Charles-Pierre Denonvilliers (1808–1872). First description of urosurgically relevant structures in the small pelvis. European Urology. 1997; 32: 124–127.

[2] Salciccia S, Rosati D, Viscuso P, Canale V, Scarrone E, Frisenda M, *et al*. Influence of operative time and blood loss on surgical margins and functional outcomes for laparoscopic versus robotic-assisted radical prostatectomy: a prospective analysis. Central European Journal of Urology. 2021; 74: 503–515.

[3] Scarcella S, Castellani D, Gauhar V, Teoh JY, Giulioni C, Piazza P, *et al*. Robotic-assisted versus open simple prostatectomy: results from a systematic review and meta-analysis of comparative studies. Investigative and Clinical Urology. 2021; 62: 631–640.

[4] Wang Y, Cheng X, Xiong Q, Cheng S. The progress of dorsal vascular complex control strategy in radical prostatectomy. The Journal of International Medical Research. 2023; 51: 3000605231152091.

[5] Mottet N, van den Bergh RCN, Briers E, Van den Broeck T, Cumberbatch MG, De Santis M, *et al*. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer-2020 update. Part 1: screening, diagnosis, and local treatment with curative intent. European Urology. 2021; 79: 243–262.

[6] Memmelaar J. Total prostatovesiculectomy; retropubic approach. The Journal of Urology. 1949; 62: 340–348.

[7] Chute R. Radical retropubic prostatectomy for cancer. The Journal of Urology. 1954; 71: 347–372.

[8] Reiner WG, Walsh PC. An anatomical approach to the surgicalmanagement of the dorsal vein and Santorini's plexus duringradical retropubic surgery. The Journal of Urology. 1979; 121: 198–200.

[9] Lee HB, Blaufox MD. Blood volume in the rat. Journal of Nuclear Medicine. 1985; 26: 72–76.

[10] Carvalhal GF, Griffin CR, Kan D, Loeb S, Catalona WJ. Reducing blood loss in open radical retropubic prostatectomy with prophylactic periprostatic sutures. BJU International. 2010; 105: 1650–1653.

[11] GBD 2019 Adolescent Young Adult Cancer Collaborators. The global burden of adolescent and young adult cancer in 2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet Oncology. 2022; 23: 27–52.

[12] Lobo N, Afferi L, Moschini M, Mostafid H, Porten S, Psutka SP, *et al*. Epidemiology, screening, and prevention of bladder cancer. European Urology Oncology. 2022; 5: 628–639.

[13] Alfred Witjes J, Max Bruins H, Carrión A, Cathomas R, Compérat E, Efstathiou JA, *et al*. European association of urology guidelines on muscle-invasive and metastatic bladder cancer: summary of the 2023 guidelines. European Urology. 2024; 85: 17–31.

[14] Friederich PW, Henny CP, Messelink EJ, Geerdink MG, Keller T, Kurth KH, *et al*. Effect of recombinant activated factor VII on perioperative blood loss in patients undergoing retropubic prostatectomy: a double-blind placebo-controlled randomised trial. The Lancet. 2003; 361: 201–205.

[15] Chang SS, Duong DT, Wells N, Cole EE, Smith JA III, Cookson MS. Predicting blood loss and transfusion requirements during radical prostatectomy: the significant negative impact of increasing body mass index. The Journal of Urology. 2004; 171: 1861–1865.

[16] Herranz Amo F. Radical retropubic prostatectomy: control of Santorini's venous plexus. Actas Urologicas Españolas. 2020; 44: 417–422. (In Spanish)

[17] Dai YT, Stopper V, Lewis R, Mills T. Effects of castration and testosterone replacement on veno-occlusion during penile erection in the rat. Asian Journal of Andrology. 1999; 1: 53–59.

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