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Original Article

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Clinical implications of the superficial uterine vein pattern for the dissection of the anterior layer of the vesicouterine ligament in radical hysterectomy

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ABSTRACT

Objective: To describe anatomic patterns of the superficial uterine vein (sUV) and assess their association with aspects of the dissection procedure of the anterior layer of the vesicouterine ligament (aVUL) by retrospectively reviewing surgical videos.
Methods: We analyzed patients who underwent laparoscopic radical hysterectomy for early-stage cervical cancer from 2014 to 2019. The primary endpoint was the time required for aVUL dissection. Multiple linear regression analyses were performed to identify factors influencing the time required for aVUL dissection.
Results: Fifty-three Japanese patients were included. Two sUV configurations were observed: type 1 (the vein ran ventral to the ureter along the uterine artery) and type 2 (the vein did not run along the usual ventral course; it ran dorsal to the ureter or was absent). Approximately 30% of the sUVs were type 2. The total time for dissection of both sides of the aVUL was significantly shorter for type 2 sUVs than for type 1 sUVs. The number of hemostatic interventions during dissection of each side of the aVUL was significantly lower for type 2 sUVs than for type 1 sUVs. In the multivariate analysis, the sUV configuration was the factor significantly influencing the duration of aVUL dissection on each side (right side: β=−143.4; left side, β=−160.4).
Conclusion: We demonstrated that the sUV had 2 types of courses, ventral and others, and its course affected the time required for dissection and the number of hemostatic interventions. Our results provide information supportive of improved radical hysterectomy outcomes.

Keywords: Cervical Cancer; Hysterectomy; Vessels; Vesicouterine Ligament; Superficial Uterine Vein

Synopsis

Approximately 30% of superficial uterine veins (sUVs) did not run ventral to the ureter. Anterior vesicouterine ligament dissection was faster when the sUV did not run ventral to the ureter. Anterior vesicouterine ligament dissection needed less hemostasis when the sUV did not run ventral to the ureter.

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
Conceptualization: F.A., K.H.; Data curation: K.M., N.S., O.M.; Formal analysis: F.A., K.H.; Investigation: F.A., K.M., N.S., O.M.; Methodology: F.A., A.A., N.H.; Project administration: K.H.; Supervision: A.A., N.H.; Validation: K.H., O.M.; Visualization: F.A.; Writing - original draft: F.A.; Writing - review & editing: K.H., A.A., N.H.

INTRODUCTION

The standard treatment for patients with early-stage uterine cervical cancer is radical hysterectomy [1,2]. Wertheim et al. [3] described radical hysterectomy in 1911, establishing the indications for radical surgery to treat cervical cancer, and the technique of radical hysterectomy has improved over the years [4,5]. Currently, radical hysterectomy comprises 2 concepts, as follows: (i) extensive removal of the parametrial tissue and (ii) division of the vesicouterine ligament (VUL) into anterior and posterior layers, resulting in the separation of the gynecologic (uterus and vagina) and urologic (bladder and ureter) organs. Therefore, understanding the anatomy and precise dissection of the VUL is critical in radical hysterectomies.

Previous studies have shown that the anterior layer of the VUL (aVUL) consists of vessels and avascular connective tissue [6,7]. The arterial components of the aVUL, called the cervicovesical vessels, originate in the superior vesical artery [7]. However, even with this knowledge, the dissection of the aVUL is challenging, and we often observe injury to small vessels in the aVUL, resulting in some bleeding. In the worst-case scenario, ureteral injury occurs. Urogenital fistulas following radical hysterectomy, including vesicovaginal or ureterovaginal fistulas, have been reported to occur in 0.3%–3.0% of the patients and are very serious complications that gynecologists want to avoid, leading to higher rates of reoperation and rehospitalization, development of depression and anxiety, reduction in quality of life, and delay in the induction of adjuvant therapy by the patient [8-13]. In previous reports, some veins in the aVUL could not be delineated, and their patterns remain unclear. Description of the veins in the aVUL will help reduce the complication rate related to aVUL dissection, resulting in a safer surgical procedure.

Based on clinical and embryological observations, it would be useful to focus on veins related to the uterus to describe venous patterns in the aVUL. Although there are some variations of the uterine vein, there are 2 primary types, the superficial uterine vein (sUV) and the deep uterine vein (dUV). These types have the following features: (i) the sUV usually runs parallel to the uterine artery ventral to the ureter, and the dUV runs dorsal to the ureter, and (ii) some veins from the bladder that run in the posterior VUL, called the inferior vesical veins, are connected to the dUV [6,7,14-16]. Focusing on the ventral/dorsal network of the uterine vein demarcated by the ureter, we hypothesized that the sUV patterns could relate to other veins in the aVUL. The ability of laparoscopic surgery to improve intraoperative visibility and reach deep surgical areas can provide details of the venous system in the aVUL.

Thus, this study aimed to investigate sUV patterns by reviewing surgical videos in which radical hysterectomy was performed. We also evaluated the significance of the sUV patterns in terms of the dissection of the aVUL.

MATERIALS AND METHODS

1. Study design

We performed this retrospective study to describe the anatomic patterns of the sUV and assess associations between the patterns and details of the dissection procedure of the aVUL. The Institutional Review Board at Cancer Institute of Hospital of Japanese Foundation for Cancer Research approved this study (approval date: October 12, 2022, protocol No. 2202-GB-070). Given the anonymized nature of the data, the requirement for informed consent was waived. This study was conducted in accordance with the principles of the Declaration of Helsinki. Surgical videos of eligible patients were reviewed independently by 2 surgeons (AF and HK) to evaluate the outcomes described below. In cases of disagreement, the final interpretation was decided based on mutual agreement between the surgeons. The first and second authors take responsibility for the accuracy of the data analysis.

2. Participants

Patients who underwent laparoscopic radical hysterectomy with pelvic lymphadenectomy for early-stage uterine cervical cancer at the Japanese Foundation for Cancer Research from 2014 to 2019 were included. The patients had clinical stage IA2, IB1, IB2, or IIA1 tumors based on the revised 2018 International Federation of Gynecology and Obstetrics staging [17], had histologically confirmed cervical cancer, and had not been previously treated except for diagnostic conization. All included patients underwent type III radical hysterectomy and pelvic lymphadenectomy (per the Piver–Rutledge–Smith classification) using the no-look no-touch technique (NLNT) performed by a single board-certified gynecologic oncologist with over 20 years of surgical specialty training (HK). Avoidance of tumor spillage is of high concern during laparoscopic radical hysterectomy, and the NLNT is representative of the techniques used to address this [15,18-20]. To ensure the uniformity of aVUL dissection, patients were excluded if laparoscopic radical hysterectomy was performed without the NLNT, the surgery was performed by a surgeon other than HK, or the surgery was not performed in the order of the protocol described below.

3. Endpoints

The primary endpoint was the time for aVUL dissection (seconds), defined as the interval from the start of uterine artery transection to the end of aVUL dissection. The secondary endpoint was the number of hemostatic interventions, defined as the mechanical methods performed using an electrocautery device, given that the blood loss volume was expected to be too small to measure.

4. Surgical procedure

The patients were positioned in a 10° Trendelenburg lithotomy position. Four trocars were used: a 12-mm camera port placed at the umbilicus and 3 in the lower abdomen. During laparoscopic radical hysterectomy using the NLNT, dissection of the aVUL was performed as follows [15]:

(i) the uterine artery was transected, and the position of the sUV was confirmed;
(ii) the superior vesical vein was transected, and the ureter was unroofed; and
(iii) the cervicovesical vessels were dissected.

Before these steps, preparatory procedures, including dissection of the paravesical and pararectal spaces and pelvic lymphadenectomy, were completed. The procedures were performed from right to left. The surgeon used an electrothermal ultrasonic coagulation device (e.g., Harmonic ACE®, Ethicon Endo-Surgery Inc., Johnson & Johnson Company, Cincinnati, OH, USA or Sonicision™, Covidien, Mansfield, MA, USA) or a bipolar vessel sealing system (LigaSure™, Covidien) at his discretion.

5. Patient variables

We evaluated the following variables: age, body mass index (kg/m^2), histological subtype, tumor size, history of conization, intraoperative and postoperative complications, disease-free survival, overall survival, energy devices used during surgery, time for aVUL dissection,

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and number of hemostatic interventions during aVUL dissection. Abdominal organ injuries, whether to the ureters, bladder, colon, greater vessels, or nerves, were recorded as intraoperative complications. Postoperative complications were defined based on the Clavien-Dindo classification [21] as grade ≥2 events (requiring pharmacological treatment beyond that for grade 1 events) that occurred up to postoperative day 30.

6. Evaluation of the sUV and dissection of the aVUL

We examined the location of the vessels, including the uterine artery, sUV, and superior vesical artery, and classified the sUV patterns as follows: type 1, where the vein accompanies the uterine artery ventral to the ureter in the usual manner; and type 2, where the vein does not run ventral to the ureter along with the uterine artery, either because it runs dorsally or because it is absent. Based on this classification, we compared the continuous variable times for the dissection of the aVUL and the number of hemostatic interventions during the dissection between the groups.

7. Statistical analyses

We evaluated continuous variables using the Mann-Whitney U test and categorical variables using Pearson's χ^2 test. Single and multiple linear regression analyses were performed to identify factors influencing the time required for the dissection of an aVUL. Variables considered to be associated with outcomes based on clinical experience, including age, body mass index, history of conization, tumor diameter, type of surgical device used in surgery, and sUV pattern, were included in the linear regression analyses. Statistical software EZR (R Foundation for Statistical Computing, Vienna, Austria) was used. These p-values ≤0.05 were considered to indicate statistical significance.

RESULTS

1. Patient characteristics

Fifty-three Japanese patients who underwent laparoscopic radical hysterectomy using the NLNT were included in our study (**Table 1**). The median follow-up time was 36.4 (range 11.4–63.0) months. Patients' clinicopathological characteristics are presented in **Table 1**. No patients in our study received adjuvant radiation or concurrent chemoradiotherapy. No patients developed local pelvic recurrence. Overall, 1 of the 53 patients developed a relapse with lung metastases at 12 months and died 27.3 months postoperatively. There were no intraoperative complications. Six patients had postoperative complications as follows: ileus (n=1, grade II), delayed ureteral injury (n=1, grade IIIa), symptomatic lymphatic cysts (n=3, all grade IIIa), and hydronephrosis (n=1, grade IIIa).

2. Patterns of the sUV

The 2 observed sUV patterns are shown in **Fig. 1**. They were type 1, where the sUV ran ventral to the ureter accompanied by the uterine artery (**Fig. 1A**), and type 2, where the sUV did not run ventral to the ureter, because it either ran dorsal to the ureter or was absent (**Fig. 1B**). In type 1, a pattern of sUVs leading to the internal iliac vein and a pattern leading to the dUV were observed. The type 1 pattern was observed on the right side in 37/53 (69.8%) cases and on the left side in 35/53 (66.0%) cases.

We categorized each case into one of 4 groups based on the sUV type on the patient's right and left sides, where group A had type 1 sUVs on both the right and left, group B had type 2

Table 1. Clinicopathological characteristics of all patients

Characteristic	Patients (n=53)
Age (yr)	
Mean ± SD	43.9±8.2
Range	29–65
BMI (kg/m^2)	21.4±3.4
Histological subtype	
SCC	32 (60.4)
AC	16 (30.2)
ASC	5 (9.4)
Tumor size (cm)	
Mean±SD	1.73±1.25
Range	0–3.9
Post-conization	
No	43 (81.1)
Yes	10 (18.9)
pT	
1a1	3 (5.7)
1a2	1 (1.9)
1b1	42 (79.1)
1b2	3 (5.7)
2a1	3 (5.7)
2a2	1 (1.9)
pN	
N0	48 (90.6)
N1	5 (9.4)
Lymphatic invasion	
Negative	29 (54.7)
Positive	24 (45.3)
Venous invasion	
Negative	41 (77.4)
Positive	12 (22.6)
Stromal invasion	
<1/2	35 (66.0)
≥1/2	18 (34.0)
Cut margin	
Negative	53 (100.0)
Positive	0 (0.0)
Adjuvant therapy	
None	31 (58.5)
Chemotherapy	22 (41.5)
Radiation/CCRT	0 (0.0)
Operative time (min)	
Mean±SD	283.5±40.0
Range	218.0–377.0
Blood loss (mL)	
Mean±SD	79.6±55.4
Range	5.0–210.0
Device	
Ultrasonic	21 (39.6)
Bipolar	32 (60.4)

Values are presented as number (%).
AC, adenocarcinoma; ASC, adenosquamous carcinoma; BMI, body mass index; CCRT, concurrent chemoradiation therapy; SCC, squamous cell carcinoma; SD, standard deviation.

on the right and type 1 on the left, group C had type 1 on the right and type 2 on the left, and group D had type 2 on the right and left (**Table 2**). The patients with delayed ureteral injury and hydronephrosis complications both had sUV patterns falling into group A.

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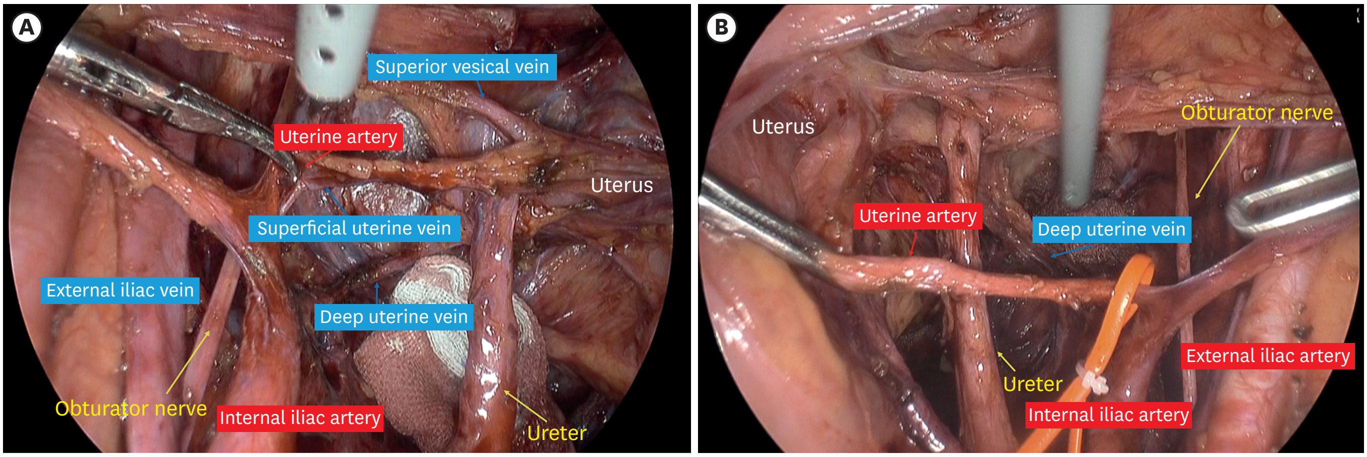

Fig. 1. Superficial uterine vein patterns. (A) The uterine artery and superficial uterine vein running ventral to the ureter (type 1), after meticulous dissection (left side). (B) The uterine artery running ventral to the ureter, but no superficial uterine vein is seen running along with it (type 2), after meticulous dissection (right side).

Table 2. Observed configurations of the superficial uterine vein

Side/Type	R type 1	R type 2	Total
L type 1	A: 28	B: 7	35 (66.0%)
L type 2	C: 9	D: 9	18 (34.0%)
Total	37 (69.8%)	16 (30.2%)	53 (100.0%)

L, left; R, right.

3. Relationship between sUV patterns and the aVUL dissection procedure endpoints

Table 3 shows the time and number of hemostatic interventions during the aVUL dissection. The total duration of dissection on the right and left sides of the aVUL was significantly different among the 4 groups (p=0.002). In subgroup analyses, the time for aVUL dissection on both the right and left sides was shorter for type 2 patterns than for type 1 patterns (right: 998 vs. 823 seconds, p=0.007; left: 876 vs. 717 seconds, p=0.002). The number of hemostatic interventions during dissection on both the right and left sides of the aVUL was significantly lower for the type 2 pattern than for the type 1 pattern (right: 4.9 vs. 2.3, p<0.001; left: 5.5 vs. 2.7, p<0.001).

4. Single and multiple linear regression analyses

Age (years), body mass index (kg/m^2), history of conization (no or yes), tumor size (cm), type of surgical device used (ultrasonic coagulation device or bipolar vessel sealing system), and sUV pattern on each side (type 1 or 2) were included in the regression analyses. History of conization (β=350.8, p=0.004), tumor size (β=90.5, p=0.023), and pattern of the right-

Table 3. Procedure duration and number of hemostatic interventions during dissection of the anterior layer of the vesicouterine ligament

Condition	Mean time (sec)	p-value	Mean number of interventions	p-value
Group A	1,894.2	0.002	10.3	0.004
Group B	1,604.1		6.4	
Group C	1,819.4		8.8	
Group D	1,456.6		4.8	
R type 1	998.9	0.007	4.9	<0.001
R type 2	823.6		2.3	
L type 1	877.0	0.002	5.5	<0.001
L type 2	717.8		2.7	

L, left; R, right.

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Table 4. Single and multiple linear regression analyses for the duration of dissection of the anterior layer of the vesicouterine ligament

Variable	Unit	Single linear regression analysis			Multiple linear regression analysis		
		Beta coefficient	95% CI	p-value	Beta coefficient	95% CI	p-value
Age	yr	−7.4	−18.7, 4.0	0.199	0.6	−9.7, 10.8	0.911
BMI	kg/cm^2	12.0	−15.7, 39.6	0.389	2.6	−21.4, 26.6	0.829
Conization	0 = no, 1 = yes	231.4	−0.2, 463.0	0.050	350.8	116.2, 585.3	0.004
Tumor size	cm	46.6	−28.2, 121.5	0.216	90.5	12.9, 168.1	0.023
Device	0 = ultrasonic, 1 = bipolar	4.8	−187.6, 197.2	0.960	−24.4	−187.7, 138.8	0.764
Right sUV	0 = type 1, 1 = type 2	−354.9	−534.0, −175.8	<0.001	−274.3	−464.6, −84.0	0.006
Left sUV	0 = type 1, 1 = type 2	−198.2	−389.9, −7.4	0.042	−110.3	−293.1, 72.5	0.231

BMI, body mass index; CI, confidence interval; sUV, superficial uterine vein.

side sUV (β=−274.3, p=0.006) were significant influencing factors for aVUL dissection times (**Table 4**). In the subgroup analysis where aVUL dissection procedures on each side were examined separately, sUV patterns were significant influencing factors for the duration of aVUL dissection on each side (β=−143.4, p=0.030 on the right, and β=−160.4, p=0.004 on the left) (**Table S1**).

DISCUSSION

In this study, we reviewed surgical videos to assess the anatomic routes of sUVs and their influence on aVUL dissection during surgery. Our data showed that the sUV might not always run ventral to the ureter along with the uterine artery, despite this being its most common route. In addition, a relationship was observed between the sUV pattern and the details of aVUL dissection (the time of the procedure and the number of hemostatic interventions). To our knowledge, this is the first study to address the venous system in the aVUL, giving important information to gynecologic oncologists who perform radical hysterectomies.

Previous studies have attempted to clarify the structure of the aVUL; however, all of them mainly focused on the arteries of the aVUL [6,7]. To dissect the aVUL, the ureter is separated laterally from the cervix, and the cervicovesical vessels, originating from the superior vesical artery, are isolated and transected [14,15]. A previous report showed that a venous branch from the bladder, called the superior vesical vein, is connected to the sUV ventral to the ureter [6]; however, there are veins in the aVUL that cannot be explained by the superior vesical vein alone. There are complicated venous patterns, including veins from the cervix, the upper area of the vagina, and the bladder, that run in the aVUL, and there is some risk of injury to these veins during dissection. Hemostasis at this site is challenging because of the high risk of ureteral injury [8-13,22-24]. Understanding the position of the arteries in the aVUL, as previously reported, is not sufficient; understanding the features of the veins is also important in performing aVUL dissections.

In this study, we analyzed the characteristics of aVUL vessels by reviewing surgical videos. The novel idea of our study was to focus on the possibility that the sUV pattern could be related to the orientation of other vessels in the aVUL and to analyze their association. The environment surrounding the uterus is occupied by the urological system—the bladder and ureters—which has a different embryological origin than the uterus, resulting in the division of the uterine venous network into ventral and dorsal elements. Additionally, the dUV, the dorsal part of the uterine venous network, is related to the inferior vesical vein that runs in the posterior layer of the VUL [14-16]. Therefore, we hypothesized that the sUV, the ventral part of the uterine venous network, might be related to veins in the aVUL. The ability of laparoscopic surgery to provide better intraoperative visibility and reach deep surgical areas enables the visualization of the venous pattern in the aVUL in detail. This is the first study to analyze uterine vessels based on this idea.

Some of the findings of our study are quite noteworthy. First, we detected variations of the sUV course, some of which did not run ventral to the ureter alongside the uterine artery; approximately 30% of the sUVs did not run ventral to the ureter in this study. Knowledge of these variations makes it possible to be aware of where the sUV runs during surgery, thus preventing unexpected vascular injury.

Second, the duration of the aVUL dissection procedure and the number of hemostatic interventions during the procedure were associated with the sUV pattern. Because all of the dissections analyzed in the study were performed by a single, well-experienced surgeon, variability based on the surgeon's experience and skill level was not a factor in this result. In type 2 cases, where the sUV did not run ventral to the ureter, the time was up to 20% shorter and the number of hemostatic interventions was up to 50% lower than those in type 1 cases, where the sUV ran ventral to the ureter. In the multivariate analysis that considered factors that could influence the time of dissection, the sUV pattern had as large an impact on the dissection of the aVUL as the history of conization. This is biologically plausible based on the relationship between the uterine venous network and urological organs described above. In type 2 cases, the venous system is mainly supplied from the dorsal, or posterior, layer of the VUL, and there are probably also fewer veins in the aVUL. Since the course of the sUV is usually confirmed before the dissection of the aVUL, the running pattern of the veins can provide clues about the vessels in the aVUL.

The fact that the duration of the dissection of the aVUL was shorter on the left side than on the right side could be influenced by the performance of the surgical procedure in order from right to left. Dissection on the left followed completion of the procedure on the right, which involved both right and left uterine artery transection. The resulting reduction in blood flow to the uterus may have resulted in a shorter time of dissection on the left side. This fact may underlie our observation in the multivariate analysis that the running pattern of the sUV on the right but not the left was a significant factor in the time required for the total dissection of the aVUL on both sides. However, this effect did not influence the number of hemostatic interventions. In addition, in a subgroup analysis focusing only on the left side, the pattern of the sUV course on the left was a significant factor for the time required to dissect the aVUL on the left. We believe that, clinically, the running pattern of the sUV on both the left and right sides may affect aVUL dissection.

Since all the dissections analyzed in the study were performed by a single, well-experienced surgeon, variability based on the surgeon's experience and skill level would not have created bias. Moreover, since this result was obtained by a well-experienced surgeon, this trend may be even more pronounced when applied to other less experienced surgeons, resulting in complications, such as massive bleeding and ureteral injury. Taking them into consideration, our study suggests to gynecologic oncologists that knowledge of the sUV's venous pattern could have a meaningful effect on the outcome of the aVUL dissection. Normally, sUV patterns are known prior to aVUL dissection based on the normal radical hysterectomy procedure. The gynecologic oncologist can anticipate the appropriate caution needed beyond the dissection of the cervicovesical arterial vessels, thus eliminating the need for excessive precautions against ureteral injury from poor understanding of the aVUL anatomy.

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Some limitations of this study should be acknowledged. First, our study was a retrospective analysis with a small sample size. Second, our study did not evaluate an anatomical body; thus, we could not identify the veins among the aVUL as anatomical structures. In addition, while the uniformity of studying dissections performed by a single, well-experienced surgeon using the NLNT exclusively provided highly accurate information about the vein in the aVUL, the results are possibly not applicable to radical hysterectomy performed by other surgeons using other methods. Future prospective studies with larger sample sizes and the inclusion of multiple surgeons are needed to validate our anatomical and procedural findings.

In conclusion, we conducted this retrospective analysis by reviewing the surgical videos of patients who underwent laparoscopic radical hysterectomy to investigate the running pattern of the sUV and its correlation with the features of dissection of the aVUL. Our study demonstrated that the sUV ran in 2 alternate routes, ventral and dorsal to the ureter. It also suggested that the sUV patterns may be related to the distribution of other veins in the aVUL. The finding that the running pattern of the sUV is associated with aVUL dissection performance, including time and blood loss, indicates that surgeons should pay attention to this during radical hysterectomies. Further studies are needed to evaluate the anatomical and clinical features of the blood vessels in the aVUL.

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SUPPLEMENTARY MATERIAL

Table S1

Multiple linear regression analysis for the duration of dissection of each side of the anterior layer of the vesicouterine ligament

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