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Research Report

Anatomical location of the surgically identifiable bladder branch of the inferior hypogastric plexus for nerve-sparing radical hysterectomy

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ABSTRACT

Objective: We aimed to demonstrate the entire structure of the inferior hypogastric plexus in the female pelvis focusing on surgically identifiable nerve bundles to the urinary bladder.
Methods: Surgical videos of transabdominal nerve-sparing radical hysterectomy for 10 patients with cervical cancer at International Federation of Gynecology and Obstetrics (FIGO 2009) stage IB1–IIB were retrospectively analyzed. The paracervical tissue dorsal to the ureter was separated into the lateral component (dorsal layer of the vesicouterine ligament) and medial component (paracolpium) using Okabayashi's technique. Any bundle-like structures in the paracervical area were isolated and divided using cold scissors, and each cut edge was inspected to determine whether the bundle was a blood vessel or a nerve.
Results: In all cases, the surgically identifiable nerve bundle of the bladder branch was identified on the rectovaginal ligament running parallel and dorsal to the vaginal vein of the paracolpium. The bladder branch was revealed only after complete division of the vesical veins in the dorsal layer of the vesicouterine ligament where no definitive nerve bundles were observed. The bladder branch was derived laterally from the pelvic splanchnic nerve and medially from the inferior hypogastric plexus.
Conclusions: The surgical identification of the nerve bundle of the bladder branch is essential for a safe and secure nerve-sparing radical hysterectomy. The preservation of the surgically identifiable bladder branch from the pelvic splanchnic nerve as well as from the inferior hypogastric plexus can provide satisfactory postoperative voiding function.

1. Introduction

Since the first report of the radical hysterectomy surgical technique by Ernst Wertheim in 1911 (Wertheim, 1911); three major modifications were made by Latzko in 1919 (Latzko and Schiffmann, 1919); Okabayashi in 1921 (Okabayashi, 1921); and Meigs in 1954 (Meigs, 1958). Radical hysterectomy has become a standard treatment modality for early-stage cervical cancer; however; the conventional procedure is associated with postoperative bladder dysfunction and colorectal motility disorders. To reduce these complications, Kobayashi introduced a new radical hysterectomy technique to preserve nerve function in 1961 (Kobayashi, 1961). Since then; surgeons from Japan (Sakamoto and Takizawa, 1988; Kuwabara et al., 2000; Yabuki et al., 2000; Sakuragi et al., 2005; Fujii et al., 2007); Europe, and Asia (Possover et al., 2000; Trimbos et al., 2001; Höckel et al., 2003; Raspagliesi et al., 2004; Charoenkwan et al., 2006) have advocated nerve-sparing radical hysterectomy and published various surgical techniques and anatomical findings. In 2008; Querleu and Morrow proposed a new classification of radical hysterectomy (Querleu and Morrow, 2008); among which nerve-sparing radical hysterectomy was newly defined as type C1.

The bladder branch of the inferior hypogastric plexus (IHP) has two different described anatomical locations in the literature: one on the lateral wall of the cervix/vagina on the dorsal side of the vaginal blood vessels (paracolpium) (Kobayashi, 1961; Sakamoto and Takizawa, 1988; Sakuragi et al., 2005; Fujii et al., 2007; Raspagliesi et al., 2004; Charoenkwan et al., 2006), the other in the lateral ligament of the bladder (i.e., lateral part of the bladder pillar) (Kuwabara et al., 2000; Trimbos et al., 2001). These two contradictory descriptions cause confusion for

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surgeons and have produced various surgical division lines to the paracervical area under the name of nerve-sparing radical hysterectomy.

To solve this problem, here we aimed to demonstrate surgically identifiable nerve bundles of the bladder branch and IHP during radical hysterectomy.

2. Materials and Methods

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Ten patients with cervical cancer at International Federation of Gynecology and Obstetrics (FIGO 2009) stage IB1–IIB who underwent transabdominal nerve-sparing radical hysterectomy based on Okabayashi's technique were retrospectively enrolled in this study. In all cases, the surgeon could successfully reveal the bladder branch and IHP and record them on good-quality surgical videos. All patients had residual urine volumes of less than 50 mL, a sensation of bladder fullness, and micturition satisfaction by 15 days postoperative. The surgical videos were recorded using a wearable camera with an integrated headlight. IHP photos were collected as screenshots from the surgical videos.

The surgical videos were reviewed carefully with focus on the relationship between the IHP and blood vessels in the paracervical area. During the dissection, any bundle-like structures necessary for division were isolated and divided with scissors, and each cut edge was inspected to determine whether the bundle was a blood vessel or a nerve. Only definitively recognizable nerve bundles were included.

The brief surgical steps prior to the identification of nerve bundles were as follows: To detect the hypogastric nerve, the pararectal space was developed, and the ureter and hypogastric nerve were revealed on the rectal sidewall. Further development of the paravesical space created a connective tissue bundle between the cervix and the pelvic side wall ventrally containing the uterine artery and the superficial uterine vein and dorsally containing the deep uterine vein and the pelvic splanchnic nerve. Dividing the ventral blood vessels, the deep uterine vein was identified to detect the pelvic splanchnic nerve. To detect the bladder branch, surgical treatment was necessary to separate the paracervical tissue surrounding the ureter. The ventral side of the paracervical tissue from the ureter is called the roof of the ureter tunnel or the ventral layer of the vesicouterine ligament (Fig. 1A), which contains the divided superior vesical vein and cervicovesical vessels (Fig. 1B). The ventral side of the ureter was exposed at the insertion level into the urinary bladder and rolled laterally toward the pubic/inguinal side, revealing the paracervical tissue dorsal to the ureter (Fig. 1C). This connective tissue area is called the dorsal paracervix in the Q-M classification. The paracervical tissue dorsal to the ureter was separated into lateral and medial components based on Okabayashi's technique (see "IHP and bladder branch" section of the Results).

3. Results

3.1. Definite nerve bundles of the IHP

(1) Hypogastric nerve.

The definite nerve bundle of the hypogastric nerve ran on the lateral wall of the rectum 2–3 cm dorsal to the ureter (Fig. 2A) and was easily isolated from the rectal sidewall (Fig. 2B). Vessel tape is usually used as a marker to trace its course to the IHP (Fig. 2C). Tracing the definite nerve bundle of the hypogastric nerve as close as possible to the IHP (Fig. 2D) was the most important approach for nerve-sparing surgery because the ventral level of the hypogastric nerve was the search point for the uterine and bladder branches of the IHP.

(2) Pelvic splanchnic nerves.

In our study, a definite nerve bundle of the pelvic splanchnic nerve was usually observed on the dorsal side of the deep uterine vein. After division of the deep uterine vein, the definite nerve bundle of the pelvic splanchnic nerve was traced toward the uterus, showing dichotomous branching to the: (a) lateral wall of the vagina; and (b) uterus (Fig. 3A). The former branching nerve bundle ran parallel and dorsal to the vaginal vein of the paracolpium up to the urinary bladder (Fig. 3B–C) and was considered a bladder branch component. The latter was considered the uterine branch from the pelvic splanchnic nerve and divided. However, some nerve bundles of the pelvic splanchnic nerve remained connected to the IHP behind the divided nerve bundle (Fig. 5A). This observation suggests that the pelvic splanchnic nerve

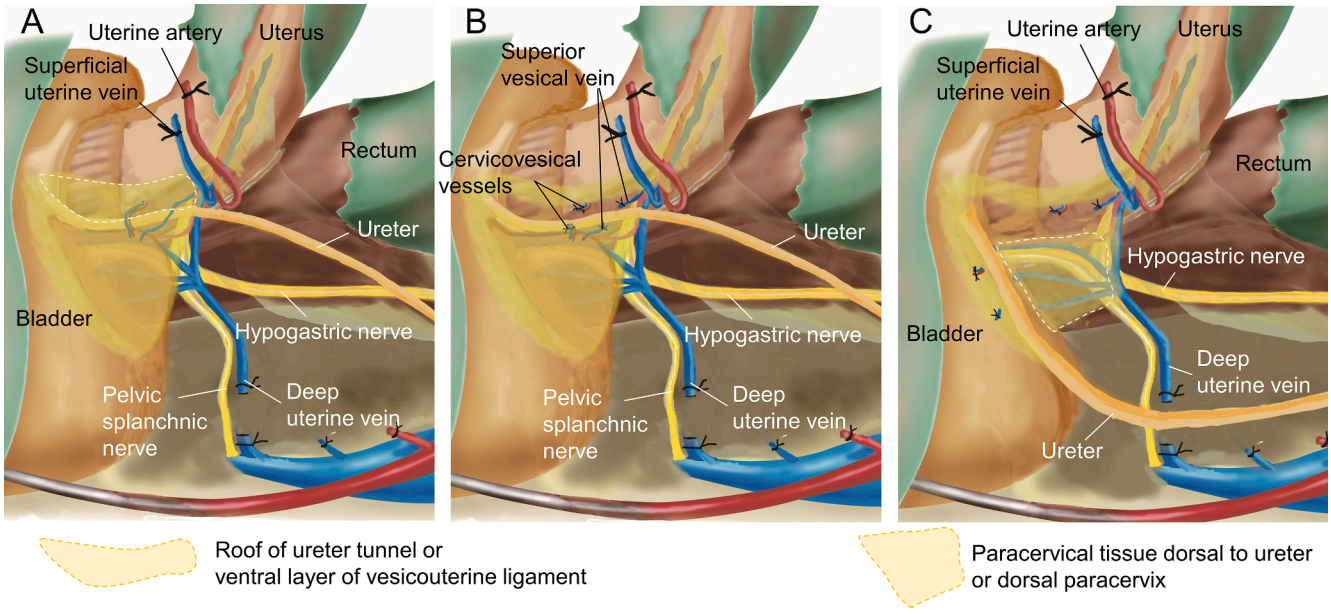

Fig. 1. Illustrations of the paracervical tissue during mobilization of the ureter. (A) Anatomical location of the ventral layer of the vesicouterine ligament (roof of the ureteral tunnel). (B) Separation of the ventral layer of the vesicouterine ligament by division of the superior vesical vein and the cervicovesical vessels. (B) Rolling of the ureter laterally toward the pubic/inguinal side exposing the paracervical tissue dorsal to the ureter (called the dorsal paracervix in the Q-M classification).

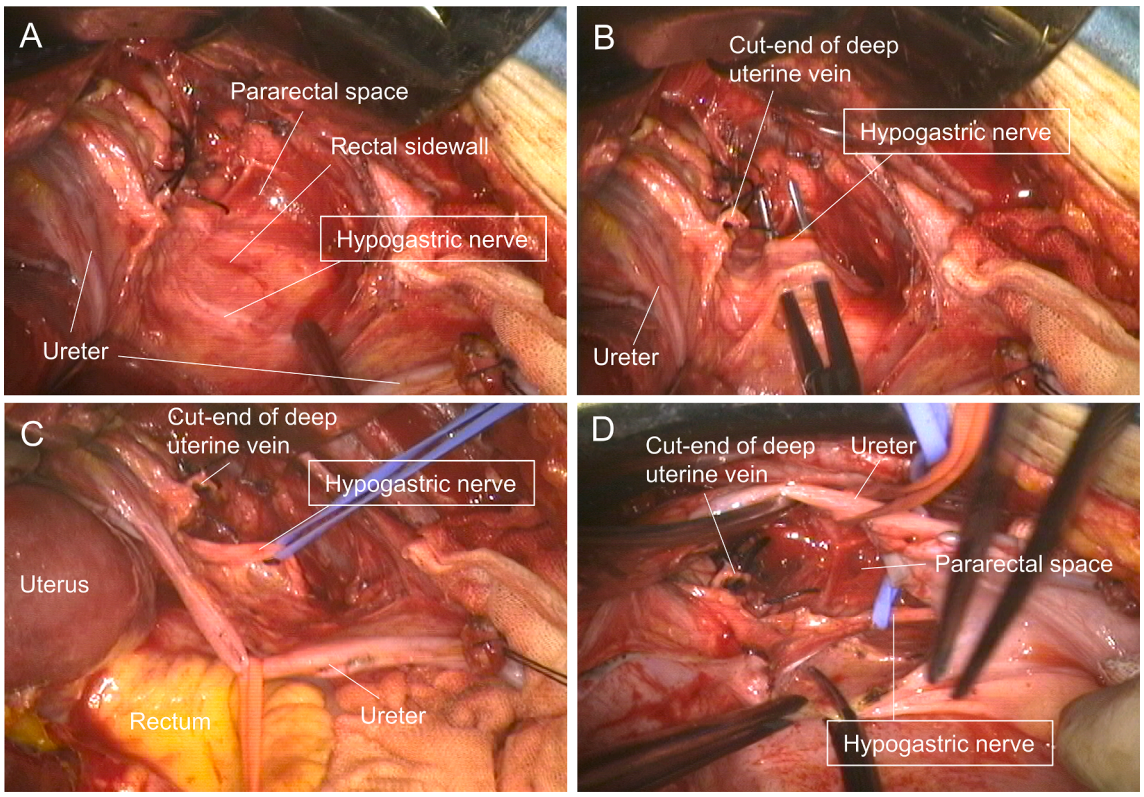

Fig. 2. Surgical photos of definitely identifiable hypogastric nerve on the right side of the pelvis. (A) In the rectal sidewall of the pararectal space 2–3 cm dorsal to the ureter, a white bundle of the hypogastric nerve accompanied by a small blood vessel is visible. (B) The hypogastric nerve is separated from the rectal sidewall. (C) The hypogastric nerve (with vessel tape applied) resides in the same connective tissue layer of the ureter. (D) The ureter is completely separated from the connective tissue layer. The hypogastric nerve is gradually separated from the rectal sidewall to the uterine side of the deep uterine vein.

dorsal to the deep uterine vein is the lateral component of the pelvic splanchnic nerve, while the lateral component of the pelvic splanchnic nerve comprises the lateral part of the uterine and bladder branches.

(3) IHP and bladder branches.

The ureter was unroofed and rolled laterally toward the inguinal side. The paracervical tissue dorsal to the ureter was revealed between the urinary bladder and the cervix/vagina (Fig. 1A–C). During an Okabayashi radical hysterectomy, the paracervical area is separated into two distinct components: the medial vaginal vein attached to the lateral vaginal wall (paracolpium) and the vesical veins laterally from the urinary bladder draining into the deep uterine vein (dorsal layer of the vesicouterine ligament). These two components were separated by Okabayashi's paravaginal space (Fig. 4A). In the dorsal layer of the vesicouterine ligament, 2–3 vesical veins draining into the deep uterine vein were isolated and divided (Fig. 4B–C), but no definitive nerve bundle was observed in this area. The deep uterine vein was separated from the surface of the pelvic splanchnic nerve to the ventral side of the hypogastric nerve (Fig. 5A–B). By the cranial traction of the cut end of the deep uterine vein, the vaginal vein became tense because it drains into the deep uterine vein. This tension created a loose connective tissue space between the vaginal vein and the bladder branch from the IHP. From this space, the uterine branch from the IHP was scooped (Fig. 5A–B) and selectively divided. The caudal extension of the bladder branch ran adjacent to the ventrolateral wall of the rectum on the rectovaginal ligament (Fig. 5C–D, 6A).

With division of the rectovaginal ligament, the bladder branch of the IHP was completely separated from the uterus and the upper vagina. The uterus was connected to the pelvis only by the vaginal wall and vein. With division of the vaginal vein (Fig. 6B), the uterus was removed with the vaginal cuff. In some cases, the vaginal vein is very close to the bladder branch, and a careful surgical technique is required to separate the vaginal vein from the bladder branch.

4. Discussion

The surgically identifiable nerve bundle of the bladder branch of the IHP was located in the medial component of the paracervical tissue and ran parallel and dorsal to the vaginal vein of the paracolpium on the rectovaginal ligament. No identifiable nerve bundle was observed in the lateral component of the paracervical tissue (i.e., dorsal layer of the vesicouterine ligament, lateral part of the bladder pillar, or dorsal paracervix). Careful observation of the branching pattern of the pelvic splanchnic nerve suggests that the lateral part of the pelvic splanchnic nerve extends toward the bladder branch and forms the lateral part of the bladder branch merging with the medial part of the bladder branch from the IHP.

In the pioneering nerve-sparing technique for radical hysterectomy, Kobayashi claimed that separation of the vascular portion (containing the deep uterine vein) from the dorsal hard bundle (containing the pelvic splanchnic nerve) during division of the parametrial tissues is required. He attempted to preserve the bladder branch separating the blood vessels in the paracolpium down to the vagina after dividing the dorsal layer of the vesicouterine ligament. Since then, many doctors have attempted to clarify the detailed surgical neuroanatomy of nerve-sparing radical hysterectomy. Many reports from Western countries have focused on preserving the hypogastric nerve and its caudal extension as a nerve-sparing technique (Höckel et al., 2003). However, preserving the hypogastric nerve itself is not essential for the recovery of postoperative urinary function. In fact, presacral neurectomy as a treatment for intractable pelvic pain sacrifices the hypogastric nerve, while postoperative urinary dysfunction has rarely been reported (Chen and Soong, 1997; Zullo et al., 2003). The superior hypogastric plexus, the origin of the hypogastric nerve, is usually damaged by a *para*-aortic lymphadenectomy; however, the *para*-aortic lymphadenectomy itself does not increase postoperative urinary dysfunction (Harter et al.,

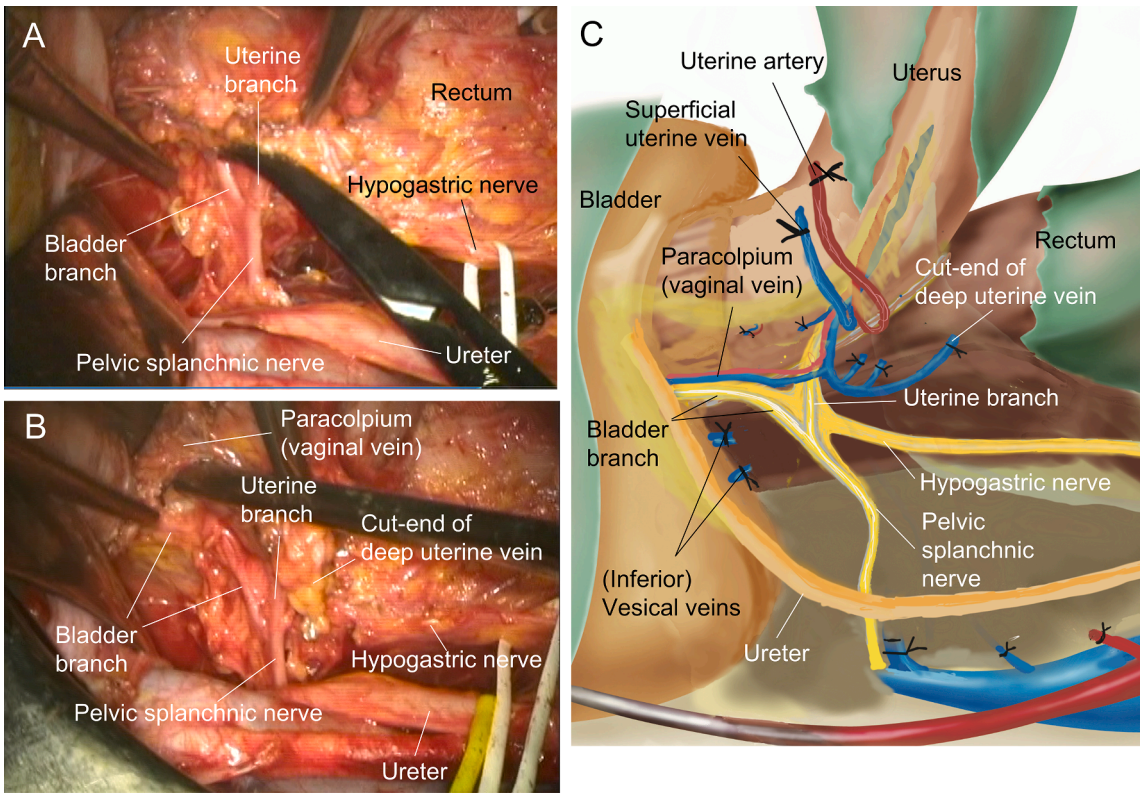

Fig. 3. Surgical photos and an illustration of the definite nerve bundle of the pelvic splanchnic nerve and its branching pattern. (A) The nerve bundle of the pelvic splanchnic nerve, which bifurcates toward the uterus and the lateral wall of the vagina, is visible after division of the deep uterine vein. (B) The nerve bundle toward the lateral wall of the vagina could trace dorsal to the vaginal vein of the paracolpium to the urinary bladder. (C) The branching pattern of the pelvic splanchnic nerve toward the urinary bladder and the uterus is illustrated with the entire inferior hypogastric plexus.

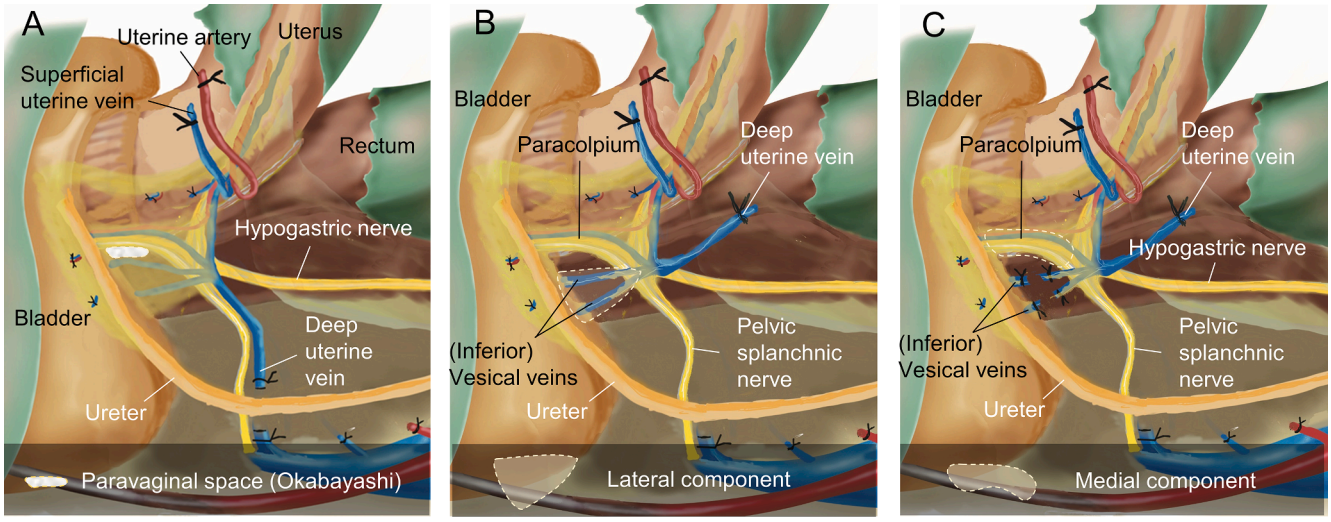

Fig. 4. Illustrations of the separation processes of the paracervical tissue on the dorsal side of the ureter into the medial (paracolpium) and lateral (dorsal layer of the vesicouterine ligament) components. (A) Anatomical location of Okabayashi's paravaginal space, which separates the paracervical tissue into the lateral and medial components. (B) The lateral component (dorsal layer of the vesicouterine ligament) contains several vesical veins that drain into the deep uterine vein. (C) With division of these vesical veins and surrounding connective tissues, the urinary bladder is freed from the uterus and the medial component of the paracolpium with the nerve bundle becomes apparent.

2019). Identification of the hypogastric nerve serves as a landmark of IHP.

The hypogastric T11–L2 nerve fibers and the pelvic splanchnic S2–S4 nerve fibers merge to form the IHP and branch to innervate the uterus and urinary bladder (Aurore et al., 2020). The hypogastric nerve is easily isolated from the rectal sidewall, and the pelvic splanchnic nerve is detectable at the time of division of the deep uterine vein in the parametrial tissue. However, isolation of the bladder and uterine branches may be a little bit difficult if the principal radical hysterectomy does not include an anatomical concept for dividing the paracervical tissue dorsal to the ureter into the medial component (paracolpium) and the lateral component (dorsal layer of the vesicouterine ligament). The

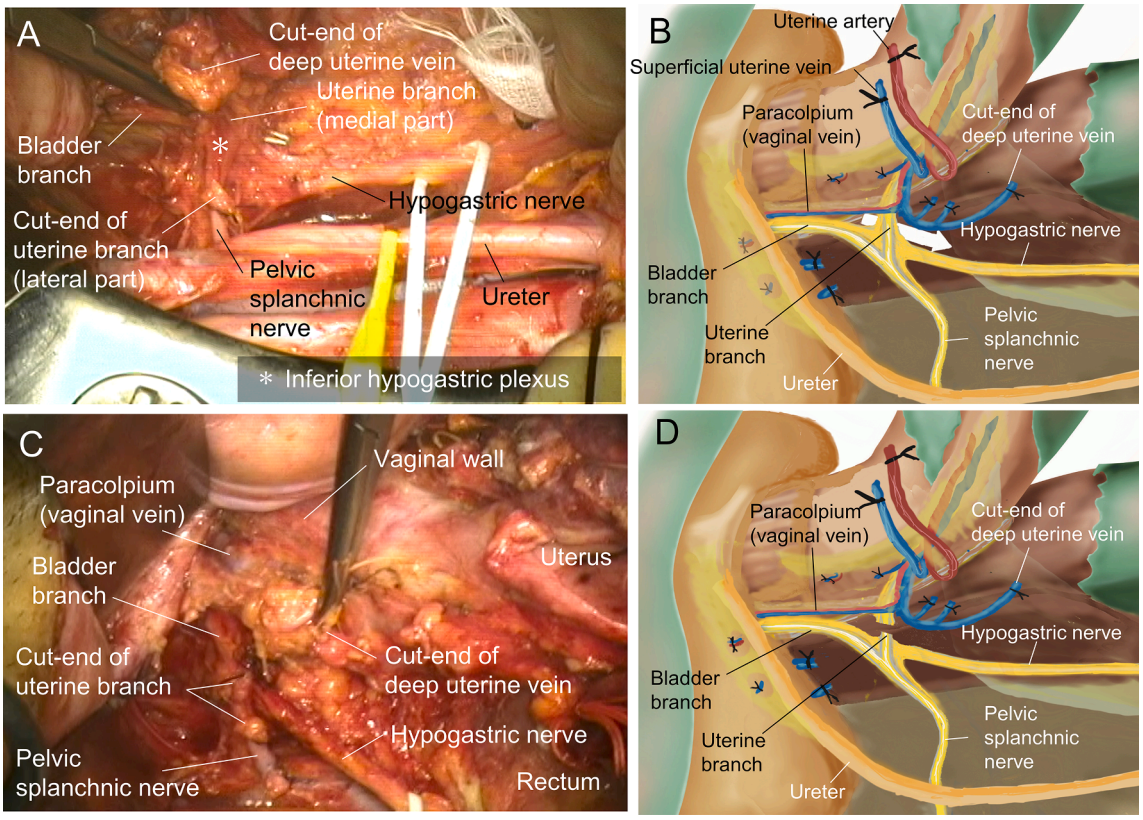

Fig. 5. Separation and division processes of the uterine branch. (A) Surgical photo showing Pean forceps scraping the uterine branch of the inferior hypogastric plexus from the ventral level of the bladder branch to the ventral level of the hypogastric nerve. (B) Illustration of the isolation line (white arrow) of the uterine branch from the inferior hypogastric plexus. (C) Surgical photo after division of the uterine branches showing the caudal extension of the surgically identifiable bladder branch running adjacent to the ventrolateral wall of the rectum. (D) Illustration of the division line of the uterine branch.

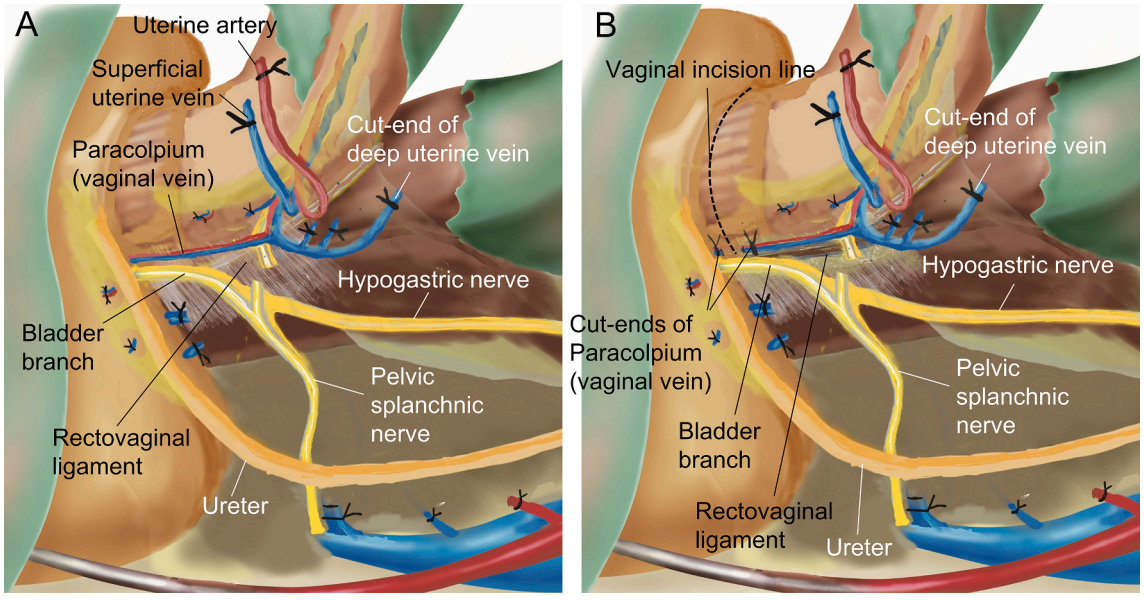

Fig. 6. (A) Illustration of the surgically identifiable bladder branch on the rectovaginal ligament running dorsal to the vaginal veins in the paracolpium. (B) Illustration of the division line of the rectovaginal ligament, divided veins in the paracolpium, and division line of the vaginal wall (dotted line). The division of the rectovaginal ligament and the vaginal veins completely separates the surgically identifiable bladder branch from the vaginal wall and allows division of the vaginal wall at the appropriate level of the disease state without damage to the bladder branch.

type C1 procedure of the Q-M classification, which is based on the Latzko-Meigs technique, is an example of such radical hysterectomy. In such surgeries, it is usually difficult to identify the surgical steps to divide the paracervical tissue dorsal to the ureter into the medial and lateral components. In type C1 surgery, the treatment of the paracervical tissue is described as follows: "The bladder branches of the pelvic plexus

are preserved in the lateral ligament of the bladder (ie, lateral part of bladder pillar). If the caudal part of the paracervix is transected, careful identification of bladder nerves is needed (Querleu and Morrow, 2008)." From this description, it is difficult to understand the exact location of the bladder branch in the paracervical area. Type C1 surgery was revised twice – in 2011 (Cibula et al., 2011) and 2017 (Querleu et al., 2017) – but the paracervical tissue dorsal to the ureter has not been well described. Consequently, the resection line of the paracervical tissues in type C1 became close to that of type B2 in the Q-M classification or Wertheim radical hysterectomy.

Both the vesical veins and the vaginal veins drain into the deep uterine vein. This means that the urinary bladder is connected to the uterus by the vesical veins (Fig. 4B). The paracervical tissue is well removed by division of the vesical veins close to the urinary bladder, and the urinary bladder is freed from the uterus (Fig. 4C). Therefore, division of the vesical veins is an essential step for uterine extirpation. The vaginal vein is then divided at the designed level of the vaginal cuff length (Fig. 6B). If the uterus can be extirpated without these surgical steps, the paracervical tissue dorsal to the ureter must be treated as a mass containing the vesical and vaginal veins (Fig. 1C). In this situation, direct identification of the vaginal vein and the bladder branch in the paracolpium is difficult, and the bladder branch must be estimated blindly from the ventral level at the end of the hypogastric nerve (Höckel et al., 2003). This blind method risks injury to the vesical veins, vaginal vein, and bladder branch of the IHP. Therefore, if surgeons seek to achieve nerve preservation safely and securely, radical hysterectomy with an anatomical concept to divide the paracervical tissue into two components, the paracolpium and the dorsal layer of the vesicouterine ligament, is recommended.

Clinically, the preservation of surgically identifiable nerve bundles can provide satisfactory postoperative voiding function. Although small nerve fibers reportedly intermingle with the vesical veins in the dorsal layer of the vesicouterine ligament (Katahira et al., 2008), we divided these vesical veins in our surgery. However, we did not find any significant adverse effects on urinary function as reported in the literature (Fujii et al., 2007). In addition, during lateral lymph node dissection for rectal surgery, the same vesical veins are often divided, but no apparent disturbance of postoperative voiding function was reported in a recent randomized controlled study (Ito et al., 2018; Mori et al., 1998). Consequently, our nerve-sparing technique that can preserve the surgically identifiable nerve bundles of the IHP is considered to provide satisfactory urinary function after radical hysterectomy.

To accomplish safe and secure nerve-sparing surgery, we emphasize the importance of treating the vascular structures residing close to the surgically identifiable nerve bundles, such as the separation of the deep uterine vein from the dorsally located pelvic splanchnic nerve, separation of the vesical veins in the dorsal layer of the vesicouterine ligament from the paracolpium, and separation of the vaginal vein from the bladder branch in the paracolpium.

Our observations of the branching pattern of the pelvic splanchnic nerve are supported by the embryonic development of autonomic innervation in the female pelvic organs. In the early stage of embryonic development, the primordia of the IHP appear as inferior hypogastric ganglionic cell clusters in the lateral part of the hindgut (rectum) and migrate ventrally as far as the Wolffian ducts in the urogenital sinus (urinary bladder) prior to sexual differentiation (Kruepunga et al., 2020). The pelvic splanchnic nerves that originate from the S2–S4 nerve roots of the sacral plexus reportedly consist of the dorsal (medial) and ventral (lateral) branches. The dorsal branches arise from the S3–S4 and course medially along the ventral aspects of the sacral vertebrae. These medially located nerves supply to the hindgut (rectum) and the posterior part of the IHP, interconnected with the hypogastric nerve. On the other hand, the ventral branches of the pelvic splanchnic nerve arise from the S2–S4 and course laterally around the internal iliac vein. These laterally located nerves enter the anterior part of the IHP surrounding the urinary trigone and the caudal end of the ureter (Kimmel and McCrea, 1958). These embryological findings support our observations of the pelvic splanchnic nerve: (a) the lateral component extended to the bladder neck; and (b) the medial component, which was considered to function primarily to the rectum, was attached to the rectovaginal ligament together with the hypogastric nerve. At around 25 weeks of gestation when sexual differentiation is complete, the greater portion of the IHP reportedly concentrates in the triangularly shaped compartment between the rectum and its ventrally adjacent structures, such as the vagina in females (Fritsch, 1989). This supports our observations that the IHP is located on the rectovaginal ligament and the bladder branch ran parallel and dorsal to the vaginal vein. The uterus and the upper vagina develop between the preexisting rectum (hindgut) and bladder (urogenital sinus). Thus, the innervation to the uterus is considered to develop as extensions from the preexisting innervations to the rectum and bladder. This can explain our observation that the lateral component of the pelvic splanchnic nerve showed dichotomous branching to the uterus and urinary bladder.

If the lateral component of the pelvic splanchnic nerve may primarily innervate the bladder trigone and the bladder neck, we must pay more attention to the preservation of the lateral component of the pelvic splanchnic nerve during nerve-sparing radical hysterectomy. The lateral component of the pelvic splanchnic nerve courses close and dorsal to the deep uterine vein in the cardinal ligament. Furthermore, the bladder branch from the lateral component of the pelvic splanchnic nerve courses close and dorsal to the vesical veins and the vaginal vein, which are draining into the deep uterine vein, in the dorsal paracervix. Therefore, the lateral component of the pelvic splanchnic nerve and the bladder branch are easily damaged during the resection of the cardinal ligament and the dorsal paracervix, unless the veins are separated from the nerves in these areas. The IHP may not be a single nerve plane but could be surgically and functionally divided into lateral and medial portions.

A key strength of this study is that its results are immediately applicable to clinical practice because the uterine branch to be divided and the bladder branch to be preserved are demonstrated based on the actual surgical procedures. A limitation of this study is that further studies are necessary to confirm the importance of the lateral portion of the pelvic splanchnic nerve for urinary function. Another study limitation is that selection bias may have occurred because of its retrospective design and small number of cases. Despite these limitations, this was a carefully confirmed study of the entire structure of the surgically identifiable nerve bundles of the IHP in relation to the blood vessels in the paracervical area, and no exceptions in their anatomical locations suggests that we reported valid general information about the IHP.

5. Conclusions

Our results provide essential information on the surgically identifiable nerve bundles of the IHP for nerve-sparing radical hysterectomy. Preservation of the surgically identifiable nerve bundle of the bladder branch can provide satisfactory postoperative voiding function.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' Contributions.

All authors conceived the study concept and design. Dr. Fujii

performed the surgery assisted by Dr. Sekiyama. Drs. Sekiyama and Fujii reviewed the surgical videos and generated an initial draft of the manuscript. Dr. Fujii provided the original illustrations. All authors critically reviewed and edited the manuscript and approved its final version for publication.

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