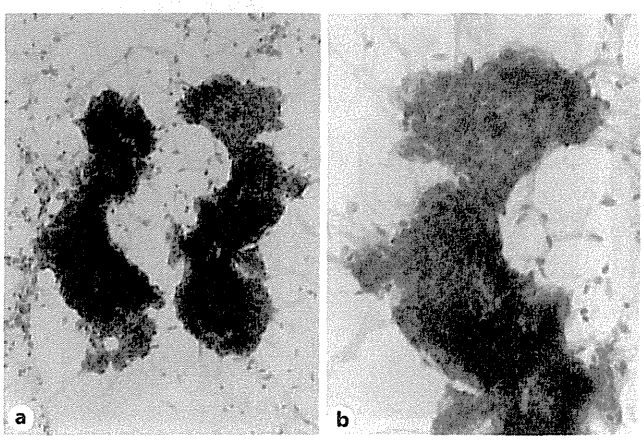

Fig. 5. Atypical endometrial hyperplasia samples. Cell clumps with irregular protrusions. The margins of the cell clumps are composed of irregular lines. However, isolated cells are hardly observed. In these cell clumps, cells and cellular arrangement show an irregular pattern. **a** ×200. **b** ×400.

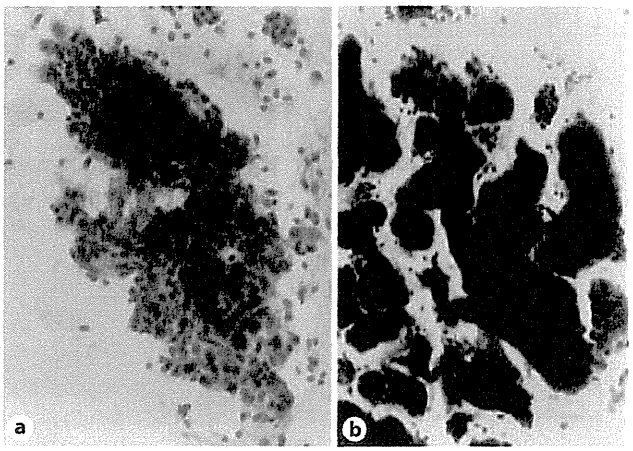

Fig. 6. Malignant tumor samples. Cell clumps with irregular protrusions (**a**) and papillotubular patterns (**b**) obtained from endometrium diagnosed as endometrioid adenocarcinoma, grade 1. In papillotubular clumps, unlike with dilated or branched patterns, cohesion of the endometrial stromal cells was not observed in the margins. In cell clumps with irregular protrusions, isolated malignant cells were observed accompanied with a necrotic background. **a** ×200. **b** ×400.

assessment after 2 or 3 months was required for ATEC-US, whereas histological estimation was necessary in cases of ATEC-A. When the cytological result is other than 'negative for malignancy' or ATEC-US, endometrial biopsy or curettage is required to confirm the endometrial diagnosis.

All the endometrial cytologies were performed for clinical usage or as cancer diagnostic tests. Because transvaginal ultrasonography is usually performed with endometrial cytology in Japan, data on the endometrial appearance were also registered as either normal, irregularly shaped or thickened. Endometrial biopsy is sometimes performed together with endometrial cytology because of an irregularly shaped endometrium recognized with transvaginal ultrasonography, or because of abnormal uterine bleeding. Histological examination was considered to be necessary when the cytological report was 'endometrial hyperplasia', 'atypical endometrial hyperplasia', 'malignant tumor' or ATEC-A. When there was a history of abnormal uterine bleeding and/or irregularly shaped endometrial mucosa was recognized on ultrasound examination, a histological examination was also performed. For these reasons, in this study, the gold standard for endometrial cytological results was the histological diagnosis, which was performed simultaneously or within 3 months of endometrial cytology; however, when the cytological result was 'negative for malignancy' and there was no subsequent histological examination, the case was considered a true negative when the endometrium was assessed as normal on transvaginal ultrasonography and there was no abnormal uterine bleeding. In order to calculate the diagnostic accuracy, histological lesions comprising atypical endometrial hyperplasia, endometrial adenocarcinoma in situ (EIC) and atypical polypoid adenomyoma (APA) were considered in the same group with endometrial adenocarcinomas for the purposes of this study. So, all the cases with a cytological result of 'atypical endometrial hyperplasia', 'malignant tumor' or ATEC-A, and with histological lesions in the spectrum incorporating atypical endometrial hyperplasia, EIC, APA and malignant tumors were considered true positive. All cases with a cytological report of 'negative for malignancy' and normal ultrasound findings of the endometrium without bleeding, with or without histological lesions in the spectrum ranging from benign endometrium to complex endometrial hyperplasia, or with a cytological report of 'endometrial hyperplasia' and with histological lesions in the same spectrum, were considered true negatives. Consequently, all the cases with cytological results of 'atypical endometrial hyperplasia', 'malignant tumor' or ATEC-A, and with histological diagnosis in the range from benign endometrium to com-

Table 2. Cell samplers used

Cell samplers	Total
Uterobrush or Honest Uterine Brush N	3,742
Endocyte	2,074
Endosearch	2,718
Soft Cyto	429
Tube	1,189
Cotton swab	10
Total	10,152

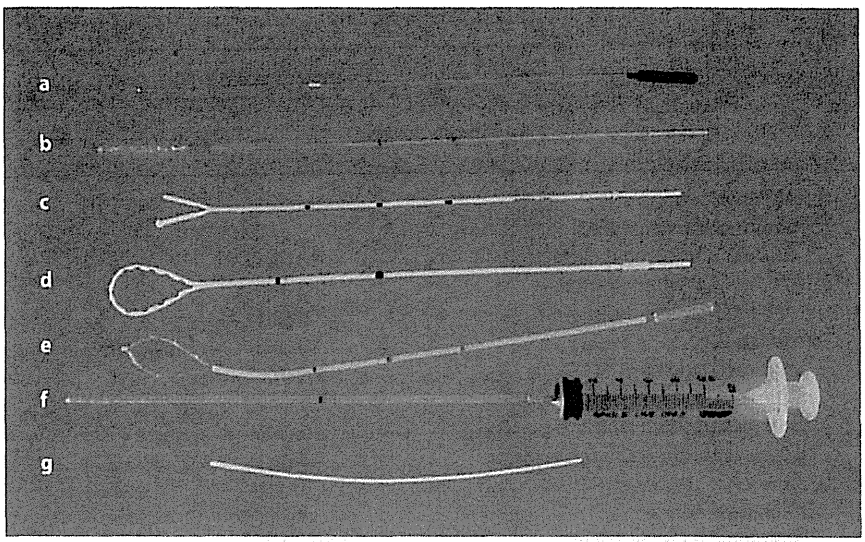

Fig. 7. Uterine endometrial cell samplers. **a** Uterobrush (Cooper Surgical, Trumbull, Conn., USA; ASKA Pharmaceutical Co. Ltd., Tokyo, Japan). **b** Honest Uterine Brush N (Honest Medical Co. Ltd., Tokyo, Japan). **c** Endocyte (Laboratoire CCD, Paris, France). **d** Endosearch (Matsunami Glass Ind. Ltd., Osaka, Japan). **e** Soft Cyto (Soft Medical Co. Ltd., Tokyo, Japan). **f** Tube (Matsuda Ika Co. Ltd., Tokyo, Japan). **g** Cotton swab (JCB Industry Ltd., Tokyo, Japan).

plex hyperplasia were considered false positive. All cases with cytological results of 'negative for malignancy' or 'endometrial hyperplasia' and with histological diagnosis in the spectrum incorporating atypical endometrial hyperplasia, EIC, APA and malignant tumors were considered false negative.

In this study, six types of cell samplers (fig. 7) were used for endometrial cytology (table 2), all of which are commonly used in Japan. All specimens were prepared with a conventional method and no liquid-based cytology preparation method was used.

Results

Five hundred and fifty-seven cases (5.5%) were judged as 'unsatisfactory specimen' (table 3). The most frequent reason for this was 'scant cellularity' (61.8%), followed by 'lack or insufficient clinical information' (27.1%). Although subsequent histological evaluation should have been performed, 1,083 cases (10.7%) were lacking histology and were excluded. Cases evaluated as ATEC-US are not immediately sent for histological evaluation and so these 76 cases (0.7%) were also excluded, after which 8,436 cases were made available for this study. The cytological results and the corresponding pathological diagnoses are shown in tables 4–6. This study included 465 cases with normal endometrium, 70 with benign reactive changes, 45 with endometrial polyp, 20 with simple endometrial hyperplasia, 30 with complex endometrial hyperplasia, 44 with atypical endometrial hyperplasia, 11 with APA and 360 with a malignant tumor. In addition, 7,391 cases did not undergo histological examination and were considered benign endometrium because of the clinical features mentioned previously. The overall performance of endometrial cytology in Japan is shown in table 7. For detecting atypical endometrial hyperplasia or malignant tumors, since ATEC-A was considered cytologically positive, the overall sensitivity and specificity were 79.0 and 99.7%, respectively. The overall sensitivity

Table 3. Unsatisfactory specimens

Reasons for unsatisfactory specimens	n (%)
Specimen rejected, not processed	
Not labeled	–
Slide broken	–
Specimen processed and examined, but unsatisfactory for evaluation of cellular abnormality	
Poor fixation	–
Poor preservation	–
Dry specimen	6 (1.1)
Obscured by inflammation	4 (0.7)
Obscured by blood	8 (1.4)
Distortion of cells or cell clumps at the time of cell preparation	1 (0.2)
Lack or insufficient clinical information	151 (27.1)
Scant cellularity	344 (61.8)
Estimated as unsatisfactory for any two reasons	39 (7.0)
Estimated as unsatisfactory for any three reasons	3 (0.5)
Estimated as unsatisfactory for any four reasons	1 (0.2)
Total	557 (100)

Table 4. Comparisons of histological diagnosis and cytological results (n = 8,436)

Histological diagnosis	Cytological result, n (%)				
	negative for malignancy	ATEC-A	complex hyperplasia	atypical endometrial hyperplasia	malignant tumor
Normal endometrium	433 (5.4)	6 (17.1)	15 (19.5)	2 (7.7)	9 (3.1)
Benign reactive changes					
Due to hormonal dysfunctions	33 (0.4)	1 (2.9)	6 (7.8)	–	–
Due to iatrogenic effects	1 (0.01)	–	–	–	–
Due to inflammatory effects	9 (0.1)	–	–	–	–
Unclassified	13 (0.2)	1 (2.9)	4 (5.2)	–	2 (0.7)
Endometrial polyp	44 (0.6)	–	1 (1.3)	–	–
Simple endometrial hyperplasia	13 (0.2)	1 (2.9)	6 (7.89	–	–
Complex endometrial hyperplasia	15 (0.2)	2 (5.7)	12 (15.6)	–	1 (0.3)
Atypical endometrial hyperplasia	17 (0.2)	2 (5.7)	14 (18.2)	8 (30.8)	3 (1)
APA	4 (0.1)	1 (2.9)	5 (6.5)	–	1 (0.3)
Malignant tumors	33 (0.4)	21 (60)	14 (18.2)	16 (61.5)	276 (94.5)
Histological test not done	7,391 (92.3)	–	–	–	–
Total	8,006	35	77	26	292

Normal endometrium = proliferative, secretory, menstrual and atrophic endometrium.

Table 5. Comparisons of histological diagnosis and cytological results (atypical endometrial hyperplasia; n = 26)

Histological diagnosis	Cytological result, n (%)			
	NOS	atypical endometrial hyperplasia	EIC	APA
Normal endometrium	–	2 (8.3)	–	–
Benign reactive changes				
Due to hormonal dysfunctions	–	–	–	–
Due to iatrogenic effects	–	–	–	–
Due to inflammatory effects	–	–	–	–
Unclassified	–	–	–	–
Endometrial polyp	–	–	–	–
Simple endometrial hyperplasia	–	–	–	–
Complex endometrial hyperplasia	–	–	–	–
Atypical endometrial hyperplasia	–	8 (33.3)	–	–
APA	–	–	–	–
Malignant tumors	2 (100)	14 (58.3)	–	–
Histological test not done	–	–	–	–
Total	2	24	–	–

Normal endometrium = proliferative, secretory, menstrual and atrophic endometrium. NOS = Cytological result was 'atypical endometrial hyperplasia', but could not be further subdivided.

and specificity of the cytological examination versus one condition of the spectrum of complex hyperplasia, ATEC-A, atypical endometrial hyperplasia and malignant tumors, were 84.5 and 99.3%, respectively. The positive predictive value (PPV) and negative predictive value (NPV) of endometrial cytology are also shown in table 7. When the reports of 'malignant tumor', 'atypical endometrial hyperplasia' and 'ATEC-A' interpretations were considered cytologically positive, the PPV and NPV were 92.9 and 98.9%, respectively. When 'malignant tumor', 'atypical endometrial hyperplasia', ATEC-A and 'complex hyperplasia' interpretations were considered cytologically positive, the PPV and NPV were 87.4 and 99.1%, respectively.

Table 6. Comparisons of histological diagnosis and cytological results (ATEC-US)

Histological diagnosis	ATEC-US, n (%)
Normal endometrium	14 (18.4)
Benign reactive changes	
Due to hormonal dysfunctions	–
Due to iatrogenic effects	3 (3.9)
Due to inflammatory effects	1 (81.3)
Unclassified	–
Endometrial polyp	2 (2.6)
Simple endometrial hyperplasia	1 (1.3)
Complex endometrial hyperplasia	2 (2.6)
Atypical endometrial hyperplasia	6 (7.9)
Malignant tumors	15 (19.7)
Histological test not done	32 (42.1)
Total	76

Normal endometrium = proliferative, secretory, menstrual and atrophic endometrium.

Discussion

In this study we devised a new and original reporting format for endometrial cytology which enables the calculation of the specificity and sensitivity of a study group. This format is an experimental one and only for study group usage. The reporting scheme is not authorized by the government nor any society. However, because numerous meetings aimed at the improvement of endometrial cytology have been held without producing a consensus document, it is our opinion that the reporting format used in this study group seems to be a useful tool.

The most common reason for unsatisfactory specimens proved to be scant cellularity and a lack of or insufficient clinical information. The features of uterine endometrial glands and stromal cells usually change markedly according to the menstrual period. Several drugs, including estrogen, progesterone, gonadotropin-releasing hormone antagonists and tamoxifen, are well recognized as being related to endometrial gland and stromal cellular changes. For these reasons, in uterine endometrial cytology, clinical information plays a more important role than it does in uterine cervical cytology. In this study group, common criteria for specimen adequacy were not set and were decided by individual hospitals and facilities. In a previous paper, we proposed criteria for specimen adequacy [1, 2]; however, at present, though each hospital and facility has made an effort to improve the diagnostic accuracy of endometrial cytology with several preparation devices, no consensus on universal criteria for specimen adequacy has been established, meaning the problem of criteria for specimen adequacy therefore remains. In the future, when acceptable criteria for assessing endometrial cytology are established, it will be necessary to decide on rigid criteria for specimen adequacy.

Table 7. Performance characteristics of endometrial cytology, n (%)

	Sensitivity	Specificity	PPV	NPV
Endometrial cytology[a]	328/415 (79.0)	7,996/8,021 (99.7)	328/353 (92.9)	7,996/8,083 (98.9)
Endometrial cytology[b]	376/445 (84.5)	7,937/7,991 (99.3)	376/430 (87.4)	7,937/8,006 (99.1)

[a] 'Malignant tumor', 'atypical endometrial hyperplasia' and 'ATEC-A' interpretations were considered positive as evidence of malignancy.

[b] 'Malignant tumor', 'atypical endometrial hyperplasia', 'ATEC-A' and 'complex hyperplasia' interpretations were considered positive as evidence of neoplastic disease.

For evaluating sensitivity and specificity, the cytological diagnosis was usually compared with the histological diagnosis as a gold standard. In this study, when the cytological finding was 'negative for malignancy' and there was no histological examination, cases in which the endometrium was assessed as normal on transvaginal ultrasonography and did not show any abnormal uterine bleeding were also defined as true negatives. In Japan, endometrial cytology is routinely performed as an endometrial cancer screening test accompanied with endocervical cytology. As a result, a large number of endometrial cytology tests in our study were included in the 'negative for malignancy' group, with normal transvaginal ultrasonography findings and without endometrial histological assessments. Large prospective studies have shown that an endometrial thickness ≤4 mm on transvaginal ultrasound in postmenopausal women with bleeding has a risk of malignancy of 1 in 917 [3]. For women of childbearing age, there are no definite criteria regarding endometrial thickness for detecting abnormality. Whether or not our definition is appropriate for these women is open to discussion.

As for uterine cervical cytology, Pitman et al. [4] reported that reducing or eliminating the diagnosis of atypical squamous cells of undetermined significance appears to decrease the sensitivity of the Pap smear significantly and to be no better than chance at predicting a diagnosis of squamous intraepithelial lesion on biopsy, including high-grade squamous intraepithelial lesion. Because it is speculated that the problem for cytological diagnosis also exists in endometrial cytology, the ATEC category, which does not represent a single biologic entity, has recently been adopted as a descriptive reporting format for endometrial cytology. This terminology is parallel to 'atypical squamous cells' (ASC) or 'atypical glandular cells' (AGC) in the Bethesda System, 2001 [5]. In the Bethesda System, the usage of the term 'atypical cells' is limited to those cases in which the cytologic findings are of undetermined significance. 'Atypia' is not permitted as a diagnosis for otherwise defined inflammatory, preneoplastic or neoplastic cellular changes in the Bethesda System. In the endometrium, inflammatory change, iatrogenic effects or the dysfunctional effects of hormones may cause some kind of cellular changes which makes it difficult to distinguish neoplastic change from nonneoplastic change. For this reason, ATEC is allowed when the significance of the cytological picture is not determined for some reason, possibly due to inflammatory changes, metaplastic changes, iatrogenic effects or any other changes with some cytomorphological impact. ATEC includes two categories, namely, ATEC-US and ATEC-A. While rigid triage methods for ASC or AGC exist, there is no evidence of triage methods for ATEC. As for ATEC-A, endometrial biopsy or curettage is considered to be necessary because with this cytological result an atypical endometrial hyperplasia or adenocarcinoma cannot be excluded. Because the clinical importance of ATEC-US is unclear, we cannot propose an appropriate triage method. At present, repeated endometrial cytology after 2 or 3 months or endometrial biopsy is recommended.

In this study, all cases of ATEC-A were assessed histologically, and 24 of these (68.6%) were diagnosed as atypical endometrial hyperplasia, APA or malignant tumor following simultaneous or subsequent histological tests. In contrast, in 32 (42.1%) of the ATEC-US cases, histological evaluations were not done. As for the remaining 44 cases, the histological diagnosis varied from benign to malignant (table 6). Thus far, ATEC-US does not play an important role in cytological diagnosis. Hereafter, evidence for ATEC should be established and the necessity for ATEC-US and ATEC-A discussed.

To date, there has been no clinical data from a study group concerning the sensitivity or specificity of endometrial cytology. Such data have only previously been reported by a single facility. Tsuda et al. [6] compared transvaginal ultrasonography (TVS) and endometrial cytology for endometrial cancer by screening 600 postmenopausal women. Their reported sensitivity and specificity were 78.9 and 95.4%, respectively. Because the sensitivity and specificity of TVS were 97.4 and 75.7%, respectively, they concluded that TVS was more useful in identifying patients who required further diagnostic investigation, including endometrial histology. Buccoliero et al. [7] studied 917 patients who were scheduled for hysterectomy with the liquid-based cytology method. All the women proceeded sequentially through hysteroscopy, endometrial cytology and endometrial biopsy. According to their study, cytology provided more sufficient information than biopsy; sensitivity and specificity were 96 and 98%, respectively, PPV was 86% and NPV was 99%. In addition, several studies have mentioned the sensitivity and specificity of endometrial cytology [7–9]. In these studies, cytologically 'positive' was also determined for the first time. Comparing these data, the specificity of our data seems to be sufficient, while sensitivity is insufficient for clinical usage. There is no consensus on the criteria for endometrial cytological evaluation. In particular, benign reactive changes, such as endometrial gland and stromal breakdown, and endometrial hyperplasia are thought to be difficult for cytological assessment; there-

fore, some cases tend to be overestimated. This seems to be a most important reason for the low sensitivity and high specificity in this study. The importance of recognizing the architecture of the cell cluster as well as cellular features of endometrial cytology has been emphasized [10–13]. When using cytoarchitectural criteria practically, sufficient diagnostic accuracy has been achieved [1, 14, 15]. In the future, further attempts must be made to improve sensitivity without decreasing specificity.

Disclosure Statement

There are no financial disclosures, nor conflicts of interest.

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動画で学ぶエキスパートのテクニック

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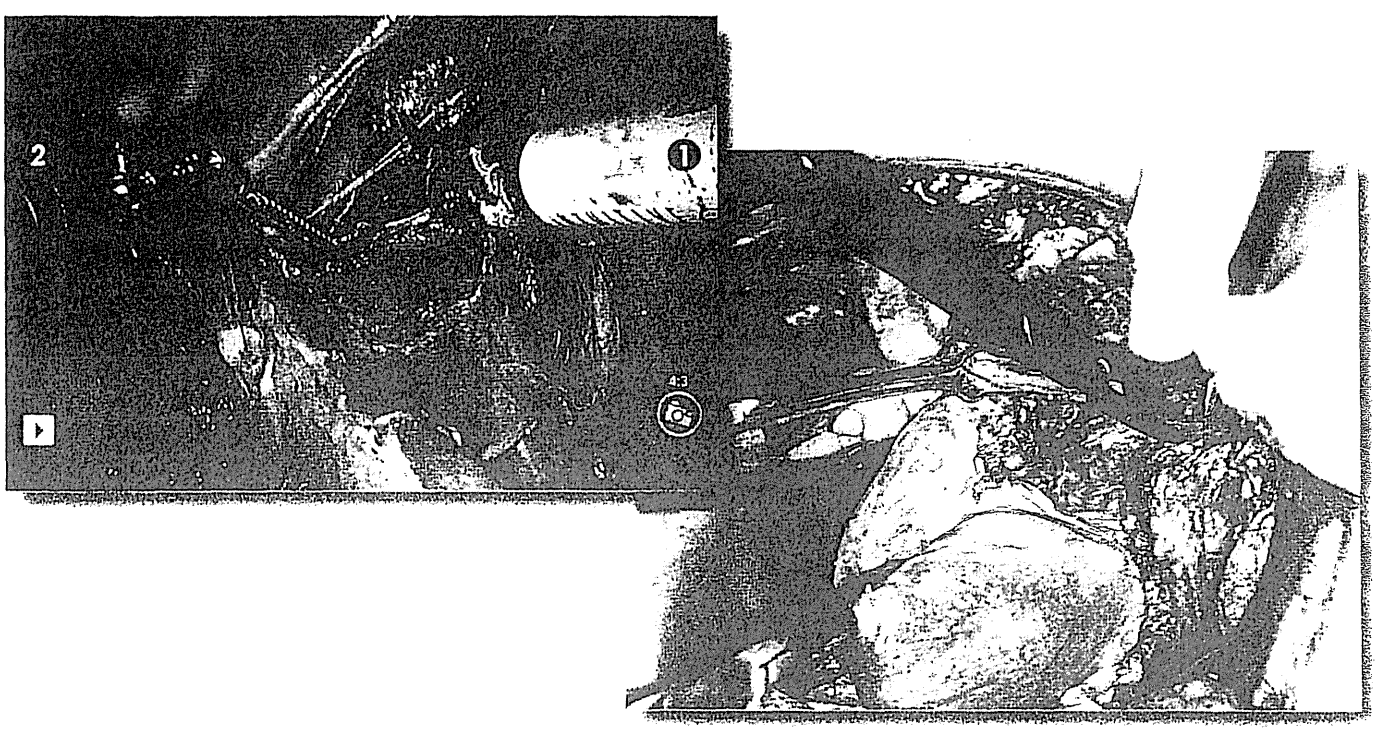

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動画で学ぶエキスパートのテクニック

婦人科がん 低侵襲手術

CONTENTS

広汎子宮全摘術（神経温存）

術式の流れ（右尿管剥離を含む）▶▶動画つき

1．円靭帯ならびに付属器の処理

右円靭帯を切断．右尿管剥離し，ペンローズ6号で吊り上げた状態．右卵巣を残しつつ子宮から切断縫合写真1．

2．骨盤内リンパ節郭清

右側骨盤内リンパ節郭清は，はじめに右側腸腰筋と右側外腸骨動静脈を剥離し，腸腰筋への栄養枝動静脈を切断結紮する．外腸骨動静脈を露出させるようにリンパ節を郭清する．さらに，内腸骨動脈，骨盤底静脈を損傷しないように露出させ，閉鎖神経を分離しつつ郭清する写真2．

3．子宮動脈と尿管の局在確認

右子宮動脈の分離切断，結紮を行う．浅子宮静脈が基靭帯血管へ交通する部分を分離し，切断結紮する写真3．この時の分離は尿管外側に沿って中枢側から末梢側へ剥離操作を行う．右側尿管と子宮との間にある，いわゆる尿管トンネルの入口部（右側膀胱子宮靭帯前層，後層の間隙）を露出する写真4．

4．子宮後方の処理にて下腹神経の確認

ダグラス窩の後腹膜を切開し，直腸を子宮と腟壁より剥離する写真5．右仙骨子宮靭帯切断．直腸と下腹神経を剥離する写真6．

5．骨盤内臓神経の分離と右基靭帯血管部分の切断

右基靭帯の血管部分を骨盤内臓神経と分離し写真7，右基靭帯の血管部分を切断する写真8．右膀胱側腔の腟壁に沿って横走する傍腟血管を確認する（矢印部分）．

6．下腹神経子宮枝と腟枝の分離・切断結紮

右下腹神経子宮枝の分離・切断結紮写真9を行い（クーパーで行い電気メスは使用しない），さらに右下腹神経の腟枝の分離切断写真10を行う．

7．膀胱子宮靭帯前層の処理

膀胱腹膜の切断と子宮・腟壁からの膀胱の剥離写真11．右子宮動脈を子宮側に牽引しつつ尿管トンネルを拡張し，右尿管を膀胱方向に圧排しつつ，膀胱子宮靭帯を分離し，前層鉗子で把握する写真12．右尿管をさらに膀胱側に圧排し，鉗子から遠ざける写真13．膀胱子宮靭帯の前層切断縫合写真14．同靭帯前層の外側上部を分離し切断結紮する．これにより尿管が膀胱方向へ移動する写真15．同靭帯の前層の残りを分離切断縫合（子宮頸部側）する写真16．

8．膀胱子宮靭帯後層の処理

膀胱子宮靭帯後層の一部を分離切断縫合する写真17．尿管を末梢方向にさらに剥離するため，膀胱筋層の一部を切断写真18．クーパーで尿管を末梢側に下げ，傍腟血管と膀胱子宮靭帯の後層との間隙を露出させる写真19．この高さは，基靭帯切断端の下端より下方まで分離．この時，傍腟血管を損傷しないように行う．膀胱子宮靭帯後層の切断縫合写真20．膀胱子宮靭帯の後層の切断縫合後，膀胱への神経が温存されている写真21．

9．後腹膜の処理

右卵巣を後腹膜を通して，骨盤外の右側腹壁に縫合し，クリッピングし目印とする．後腹膜は正中のみ縫合し，両側とも開放してセプラフィルム®を貼る．ドレーンを両側の後腹膜腔に入れ，腹壁から低圧吸引する．

10．膀胱神経温存広汎子宮全摘術，左卵巣卵管切除術の摘出物写真22

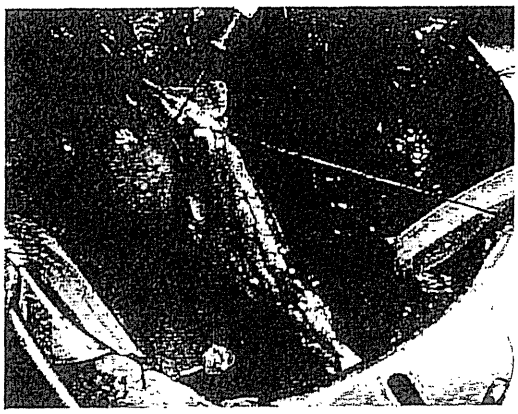

写真1 右卵巣固有靭帯の切断

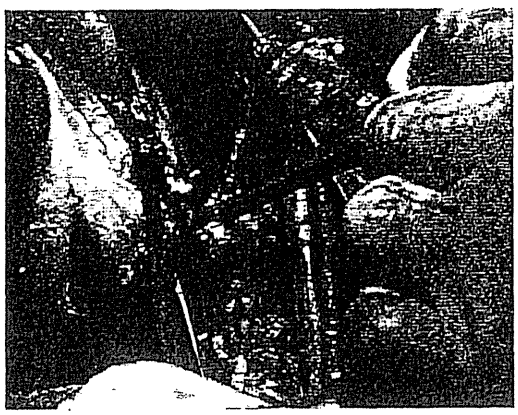

写真2 骨盤リンパ節郭清

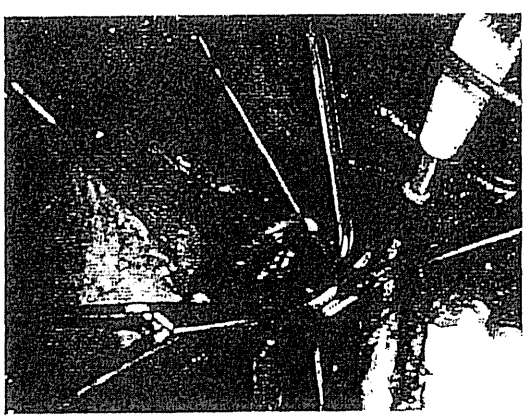

写真3 右子宮動脈と浅子宮静脈の切断結紮

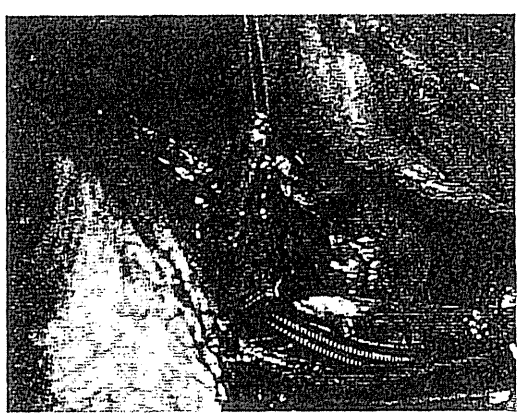

写真4 尿管トンネルの入口部の露出

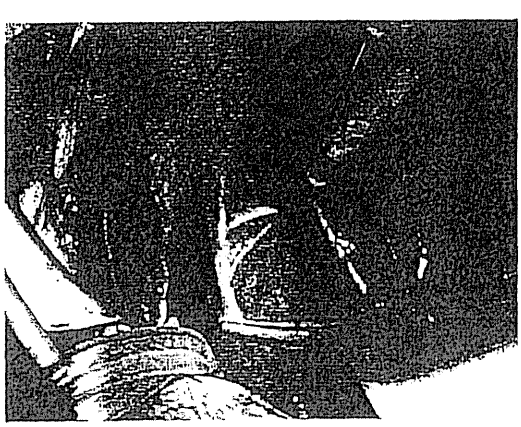

写真5 ダグラス窩腹膜の切開

写真6 下腹神経の確認と剥離

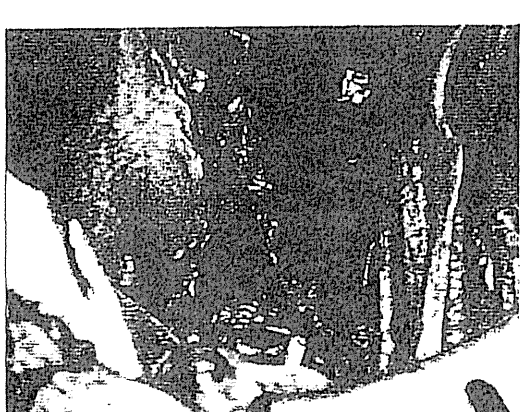

写真7 基靭帯血管部分と骨盤内臓神経の分離

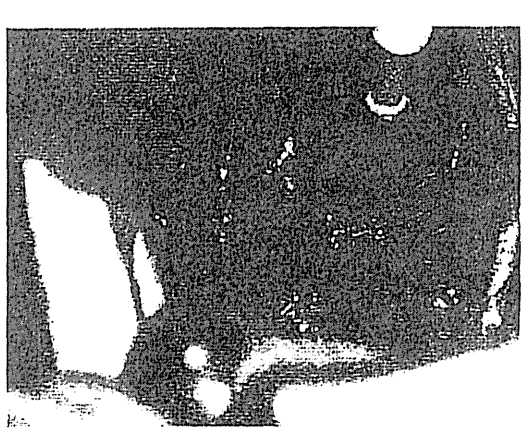

写真8 基靭帯血管部分の切断

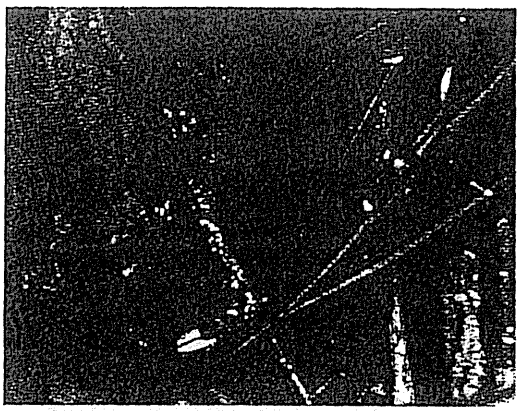

写真9 右下腹神経子宮枝の切断結紮

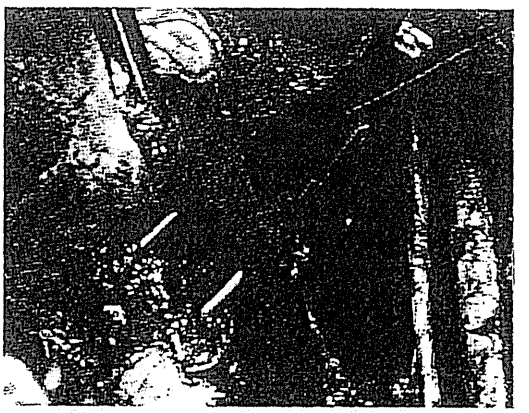

写真10 右下腹神経膣枝の分離切断

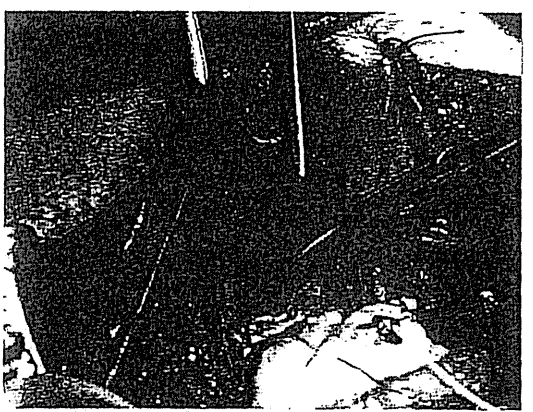

写真11 膀胱剥離

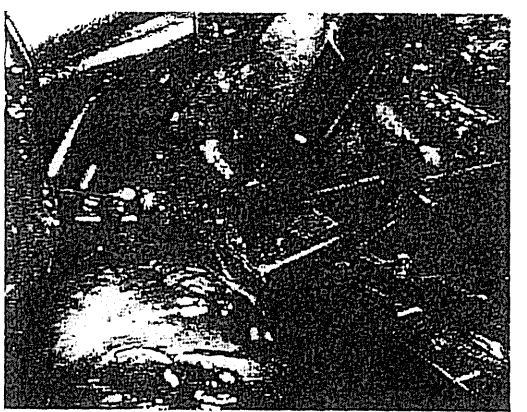

写真12 膀胱子宮靭帯の前層を鉗子で把握

写真13 右尿管の膀胱側への圧排

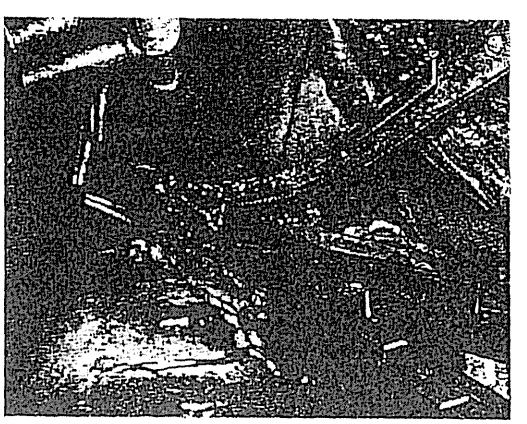

写真14 膀胱子宮靱帯前層切断縫合

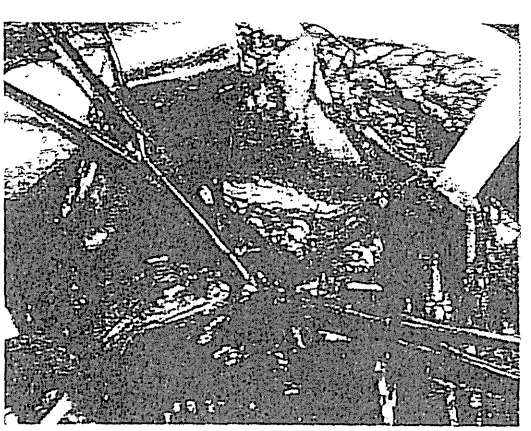

写真15 膀胱子宮靱帯前層外側上部の分離切断

写真16 膀胱子宮靭帯前層の残存部の分離切断

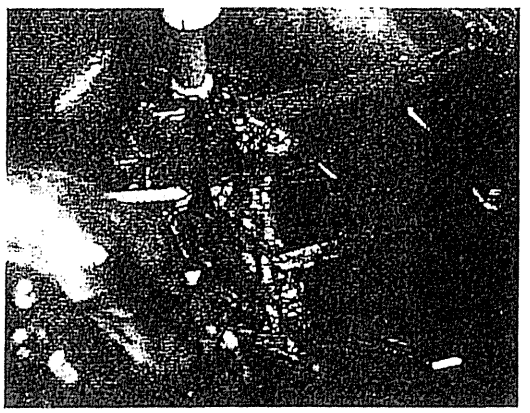

写真17 膀胱子宮靭帯後層の一部を分離切断ならびに縫合

写真18 膀胱筋層の一部の切断

写真19 クーパーにて尿管を末梢側に下げる

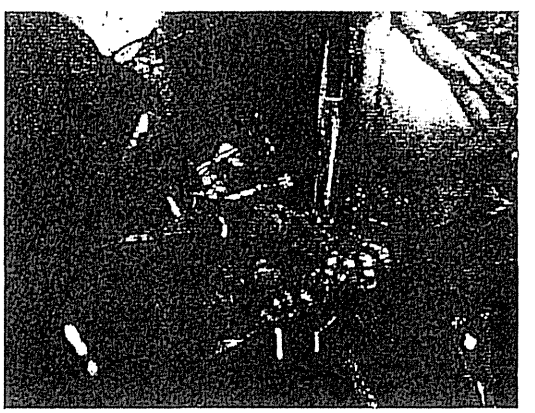

写真20 膀胱子宮靭帯後層の分離切断ならびに縫合の完了

写真21 膀胱への神経が温存されている状況を確認

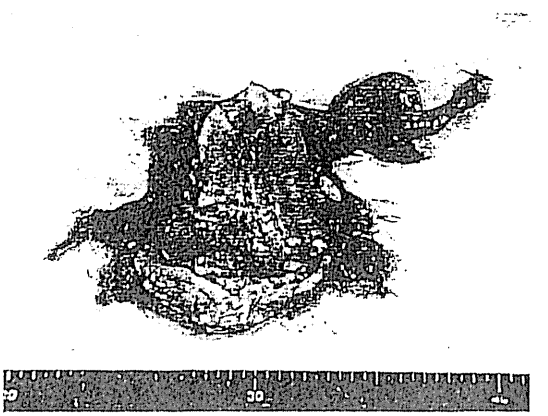

写真22 本術式における摘出物（広汎全摘後の子宮と左付属器）

準広汎子宮全摘術
(子宮動脈からの尿管枝を温存する術式)

術式の流れ(患者左側尿管枝の温存) 動画つき

1. 子宮頸部の後方処理

ダグラス窩腹膜を切開し，直腸を子宮，膣より剥離する写真1．両側尿管を後腹膜より剥離後，ペンロースで吊り上げる．次いで，両側仙骨子宮靭帯の結紮切断縫合を行う写真2 写真3．

2. 子宮動脈周辺処理(右側尿管枝は切断，左側尿管枝は温存)

右子宮動脈の分離，切断，結紮写真4，右浅子宮静脈の分離，切断，結紮写真5，右子宮動脈からの尿管枝を分離し写真6，(右側での術式を表示)尿管枝を切断結紮する写真7．

3. 子宮頸部前方処理

膀胱腹膜を切開し，膀胱を子宮頸部より正中部で剥離する写真8．

①患者右側で尿管枝を切断する術式

まず右側の処理を以下のごとく進める．

右側膀胱脚を分離，切断，結紮する．右側尿管トンネルの入口を確認する．右子宮動脈の尿管枝を切断し，尿管トンネルを拡開する．右膀胱子宮靭帯前層を把握し尿管の遊離を確認する．右膀胱子宮靭帯前層を尿管枝を切断結紮する写真9．右膀胱子宮靭帯後層の一部切断結紮し，尿管を膀胱側に分離する．傍膣血管，右膀胱子宮靭帯後層，基靭帯を露出する．傍膣血管，膀胱子宮靭帯後層，基靭帯の一部を一括し切断縫合する．右直腸膣中隔の一部を切断結紮する写真10．

②患者左側で尿管枝を温存する術式

次いで左側膀胱脚の分離，切断，結紮写真11を行い，左側の尿管を圧迫しつつ，尿管トンネルの入口の確認写真12を行う．左子宮動脈の尿管枝を残しつつ，強湾の曲り鉗子で尿管を膀胱側に圧排しつつ尿管トンネルを拡開写真13し，左膀胱子宮靭帯前層を縦曲り鉗子で把握する．尿管が遊離しているか確認写真14の後，左膀胱子宮靭帯前層を尿管枝を残しつつ切断結紮する写真15．左膀胱子宮靭帯後層の一部を切断結紮し，尿管を膀胱側に分離する写真16．左膀胱子宮靭帯の後層の表面を電気メスにて切開し，尿管をさらに膀胱側に下げる．

4. 直腸膣中隔と傍膣血管・基靭帯の処理

傍膣血管，左膀胱子宮靭帯後層，基靭帯を露出写真17し，左尿管を膀胱側に圧排しつつ，傍膣血管，膀胱子宮靭帯後層，基靭帯の一部を一括で，万能鉗子で把握し切断し8字縫合する．万能鉗子は膣壁が10mm切除できる高さで把握する写真18．

5. 子宮の摘出と膣壁の縫合

膣壁を正中部で切開し，輪状切開して子宮を膣管から切断し摘出する写真19．その後，膣壁を連続縫合し止血する写真20．

6. 骨盤内リンパ節郭清

子宮を準広汎子宮全摘術後，両側骨盤内リンパ節郭清を施行する．

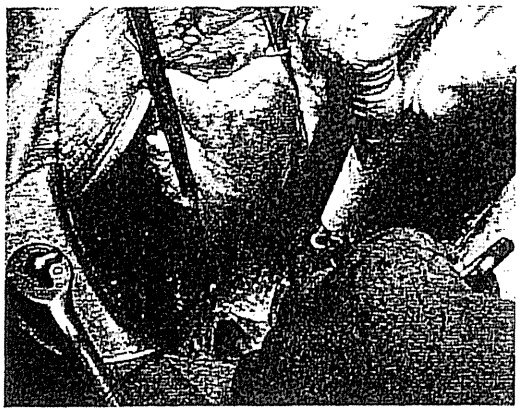

写真1 ダグラス窩腹膜を切開し，直腸を子宮，腟より剥離

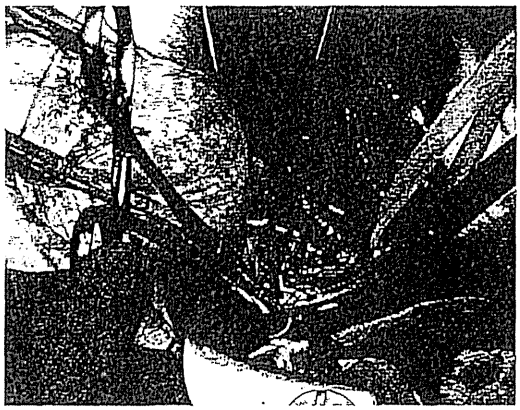

写真2 右側仙骨子宮靭帯の結紮切断縫合

写真3 左側仙骨子宮靭帯の結紮切断縫合

写真4 右子宮動脈の分離，切断，結紮

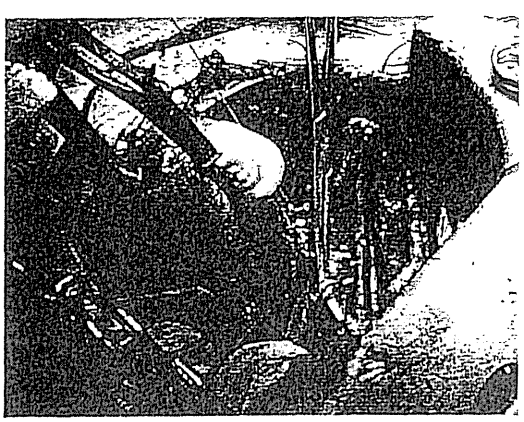

写真5 右浅子宮静脈の分離，切断，結紮

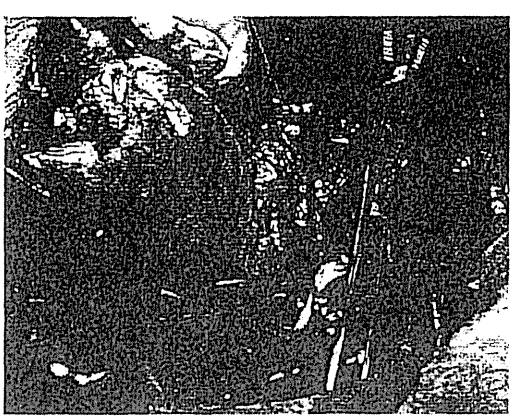

写真6 右子宮動脈からの尿管枝を分離

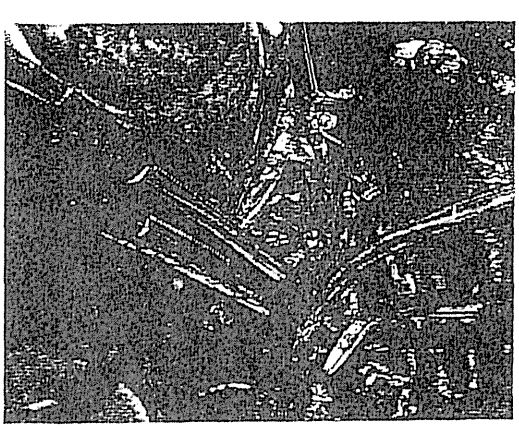

写真7 尿管枝の切断，結紮（患者右側）

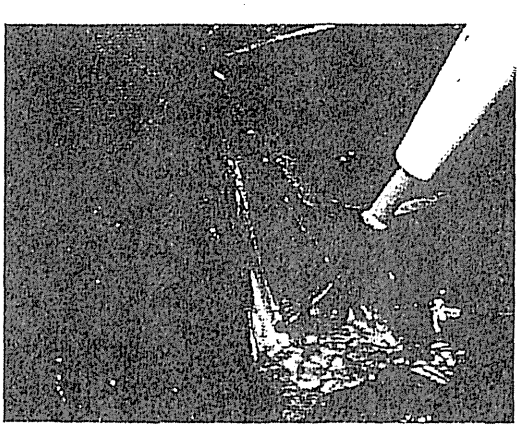

写真8 膀胱を子宮頸部より正中部で剥離

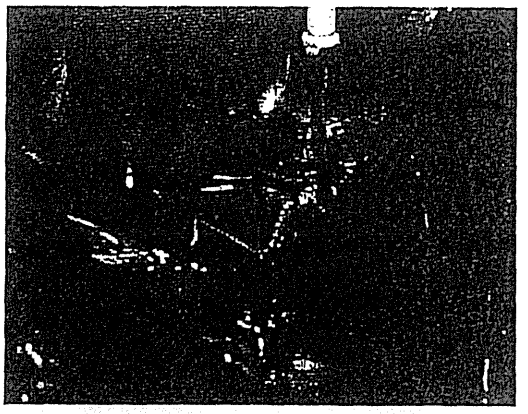

写真9 右膀胱子宮靭帯の切断，縫合

写真10 右直腸膣中隔の一部切断，結紮

写真11 左側膀胱脚の分離，切断，結紮

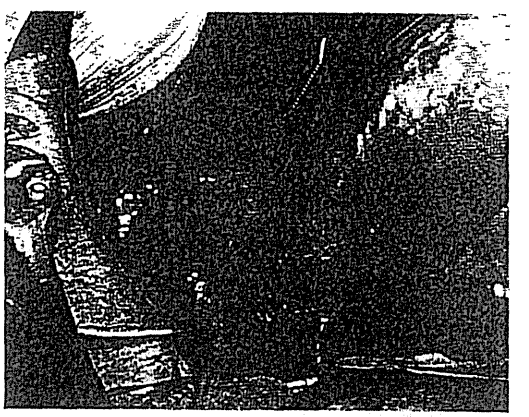

写真12 左側尿管トンネルの入口の確認

写真13 左子宮動脈の尿管枝を残しつつ，尿管トンネルを拡開

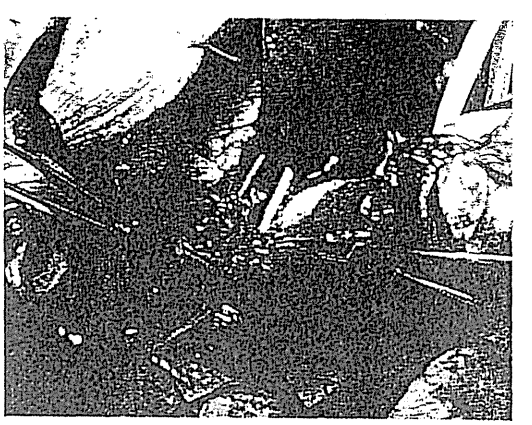

写真14 左膀胱子宮靭帯前層を把握し尿管の遊離を確認

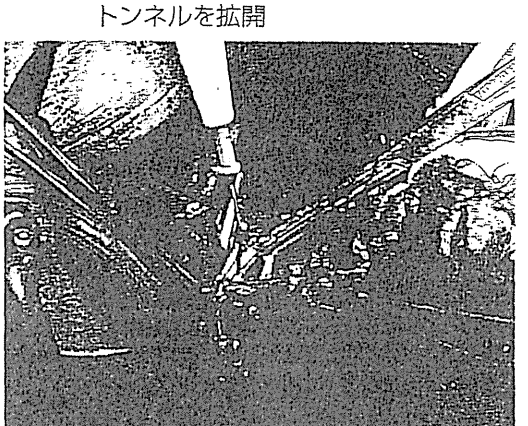

写真15 左膀胱子宮靭帯前層を尿管枝を残しつつ切断，結紮

写真16 左膀胱子宮靭帯後層の一部を切断結紮し，尿管を膀胱側に分離

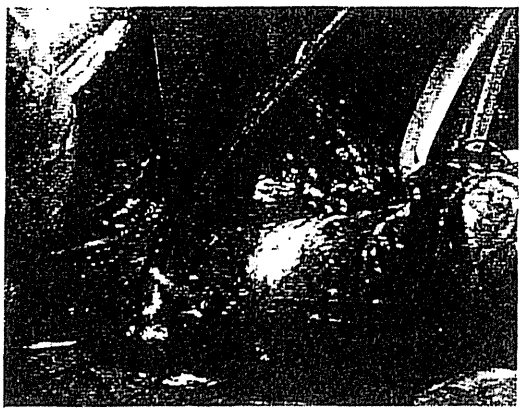

写真17 傍腟血管，左膀胱子宮靭帯後層，基靭帯を露出

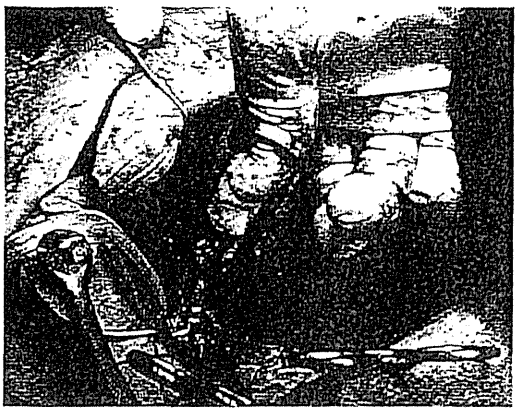

写真18 傍腟血管，膀胱子宮靭帯後層，基靭帯の一部を一括し切断縫合

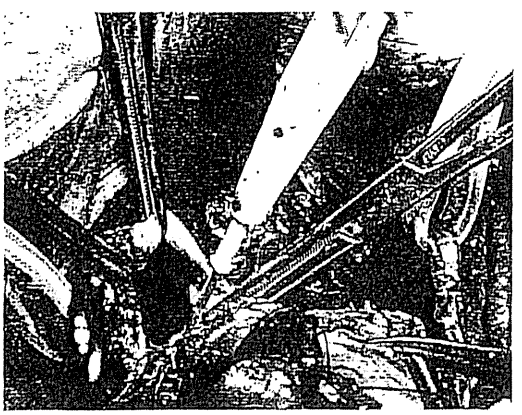

写真19 腟壁を正中部より輪状切開し子宮を摘出

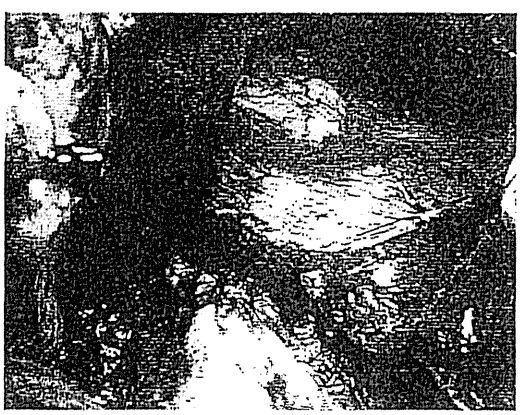

写真20 腟壁の連続縫合

コラム

子宮動脈から尿管枝の扱い

本術式では，子宮動脈からの尿管への栄養枝を切断する方法とその栄養枝を残して行う準広汎子宮全摘術がある．前者の尿管の栄養枝を切断する方法の方が子宮頸部の傍結合織をより多く取ることができるが，膀胱神経の損傷が強くなる欠点がある．子宮動脈の尿管枝を分離切断し，子宮動脈を子宮体部方向に吊り上げるために基靭帯に向かう浅子宮静脈および深子宮静脈を分離切断しないと思わぬ出血をする．この分離切断の要点は尿管に沿って頭側から足側の方向にライトアングル鉗子で静脈をすくい，分離切断することである．決して膀胱方向から腎方向に向かって静脈を分離してはならない．これをすると基靭帯血管を損傷しやすく出血しやすい．これが最も大事なコツである．一方，子宮動脈の栄養枝を残す術式では，尿管と仙骨子宮靭帯周囲の組織を十分剥離して，尿管が膀胱子宮靭帯の前層・後層の間に入る，いわゆる「尿管トンネルの入口」を展開することがコツのひとつである．またこの術式では前層と一緒に子宮動脈が切断されるので，追加で子宮動脈を二重に結紮する必要がある．両術式とも膀胱子宮靭帯の前層処理は，万能鉗子の曲がりもしくは基靭帯鉗子を用いて行う．これはクーパーを用いて行うよりも簡単にできる．

Key Words：lymphedema, lymphaticovenular anastomosis

＜特集：リンパ浮腫の予防と治療＞

婦人科癌術後の下肢リンパ浮腫の危険因子と後腹膜大腿鼠径部でのリンパ管静脈吻合術の有効性

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Risk Factor for Lymphemema of Extremities after Surgery for Gynecological Carcinoma and Effectiveness of Primary Intrapelvic Lymphaticovenular Anastomosis

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Lymphedema of the lower extremities may develop following surgical resection of malignant tumors and intrapelvic lymph node dissection. We performed primary intrapelvic lymphaticovenular anastomosis (PILA) to prevent postoperative lymphedema in the lower extremities. The procedures were conducted in patients with cancer of the uterine body, who underwent total hystero-oophoretomy, together with intrapelvic and para-aortic lymph node dissection. The afferent lymphatics entering suprainguinal lymph nodes were end-to-end anastomosed with branches of the deep inferior epigastric veins. The procedure was performed in 8 patients aged between 35 and 61 years. We performed complete PILA procedures in 7 patients. However, there was one case of right PILA only and one case of left PILA only. The time required to construct PILA ranged from 100 to 200 minutes. There has not been any patient developing postoperative lymphangitis in this series. The follow-up period ranged from 66 to 52 months after surgery. Three patients showed mild lymphedema, two patients just after surgery, and one patient 50 months after surgery. None of the other patients has shown any signs of lymphedema on follow-up to date. PILA following lymph node dissection may be useful for the prevention of lymphedema in the lower extremities.

序　文

リンパ浮腫とはリンパ管やリンパ節の先天的の発育不全，または二次的な圧迫，狭窄，閉塞などによってリンパ流の阻害と減少のために生じた浮腫である。主として四肢にみられ，原因不明の原

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発性と原因が明らかな続発性に分けられる。リンパ浮腫の80％以上は続発性であり，続発性下肢リンパ浮腫のおもな原因は婦人科手術におけるリンパ節郭清である。婦人科癌におけるリンパ節郭清の範囲は子宮頸癌では骨盤内，子宮体癌および卵巣癌では骨盤内から傍大動脈に及ぶ。婦人科癌におけるリンパ節郭清の基本概念は血管を剥き出しながらリンパ節をすべて切除することである。そのため下肢リンパ浮腫が避けられない合併症の1つとして従来から存在している。リンパ浮腫は重症化すれば発赤，疼痛や蜂窩織炎などにより歩行障害を引き起こして日常生活を著しく妨げる。患者さんはQOLが低下し，またボディーイメージを損ねることにより，精神的な苦痛を受ける。癌治療の成績が向上する一方，このような術後の合併症を回避しQOLを向上させることは急務と言える。従来，下肢リンパ浮腫について術後治療は行われてきたが，効果の期待できる予防的な術式は確立されていないのが現状である。今回われわれは厚生労働省助成第3次癌克服10ヵ年戦略事業（QOL改善を目指した外科療法の開発），下肢リンパ浮腫の予防手術（子宮体癌における大腿鼠径部リンパ管・静脈吻合による術後リンパ浮腫予防手術）を行い，その成果の一部について報告する。

方　法

まず子宮頸癌，子宮体癌，卵巣癌にてリンパ節郭清を受けた患者の下肢リンパ浮腫の発現状況および日常生活への影響を調査し，関与する高危険因子を分析し改善策を後方視的に検討した。対象は1997年1月1日から1998年12月31日の2年間で日本の10施設（東京慈恵会医科大学，札幌医科大学，新潟がんセンター，兵庫県立成人病センター，愛知県立がんセンター，富山県立中央病院，独立行政法人国立呉病院，国立四国がんセンター，長崎大学，信州大学）で治療し，かつ組織学的に証明された子宮頸癌，子宮体癌，卵巣癌例で後腹膜リンパ節郭清施行例かつ手術時に他の活動性悪性腫瘍がない例とした。術後3年間の経過後までの下肢リンパ浮腫発現の有無を検討した。10施設で登録症例は717例，除外症例は23例（除外症例の内訳は対象癌腫以外7例，重複癌9例，リンパ節郭清なし7例），解析症例は694例（子宮頸癌258例，子宮体癌301例，卵巣癌135例）であった。本研究は参加各施設の倫理委員会の承認を得て行った。調査項目は，年齢，FIGO臨床進行期，転移の有無，妊娠回数，分娩回数，術後病理組織診断，骨盤内残存腫瘍の有無，手術口，手術式（傍大動脈リンパ節郭清と骨盤内リンパ節郭清の有無，大網切除の有無，子宮の切除法すなわち単純，準広汎，広汎子宮全摘，後腹膜の閉鎖か開放か），術前や術後の化学療法や放射線療法の有無，について解析を行った。下肢リンパ浮腫は主治医の判断で一時的か永続的リンパ浮腫の有無を診断した。

図1　右外側大腿鼠径部における下肢より上行したリンパ管と下腹壁静脈の枝の吻合途中

統計はFisher's exact test, Logistic regressionを用いて，SAS ver. 8.2（SAS Institute, Cary, NC, USA）を使用して解析した。

リンパ管・静脈吻合術の対象症例は，東京慈恵会医科大学で治療した子宮体癌の患者で子宮摘出術とともに骨盤内リンパ節郭清かつ傍大動脈リンパ節郭清を施行する必要がある患者で，かつ本人より文書による同意が得られた患者とした。子宮体癌で単純子宮全摘出術，両側付属器摘出術，傍大動脈リンパ節および骨盤内リンパ節郭清後，傍大動脈リンパ節領域の後腹膜を閉鎖する。骨盤内の後腹膜は開放とし，マイクロサージャリー用顕微鏡下で大腿鼠径上節部腹壁の下腹壁静脈の分岐で直径1.5 mm程度の静脈を1 cmの長さで遊離，大腿鼠径上リンパ節のリンパ管で最も太くリンパ流の良好のリンパ管を選び，これと遊離した静脈の吻合を1または2本行った（**図1**）。リンパ管と静脈の口径が近い場合は端々吻合を行い，リンパ管が細い場合は端側吻合を行った（**図2**）。他のリンパ管は結紮した[1, 2]（**図1, 2**）。全症例の経過観察期間は52～66ヵ月（平均59.75ヵ月）であった。

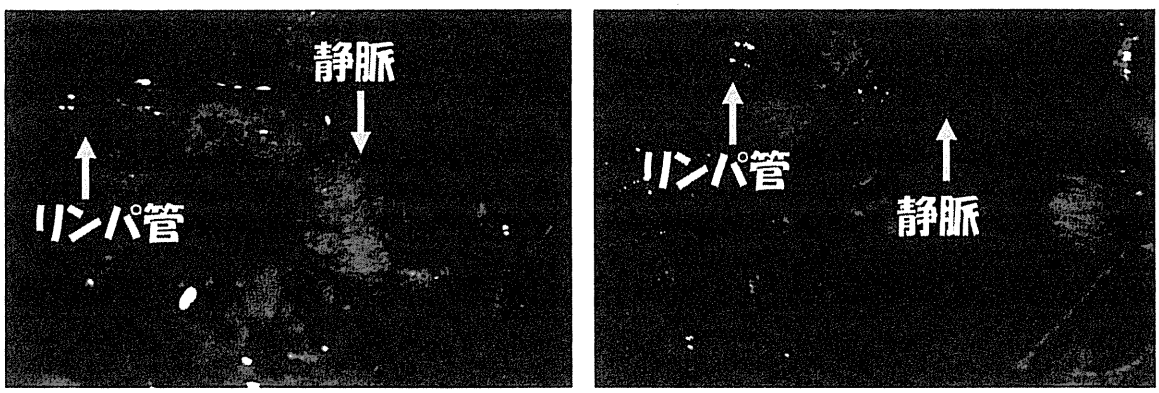

図2　左図　リンパ管・静脈端々吻合
右図　リンパ管・静脈端側吻合

結　果

表1に患者背景を示す。卵巣癌や子宮体癌では術後化学療法が主で，一方子宮頸癌では術後放射線療法が主であった。手術方法では，子宮頸癌，体癌で後腹膜閉鎖術が主であったが，卵巣癌については閉鎮が59.3%，開放が23.7%，不明が17%であった。大網切除は子宮頸癌，体癌ではほとんど施行されていないが，卵巣癌のみで64.4%が施行されていた。子宮の摘出法では卵巣癌は単純子宮全摘出術が主であり，一方子宮頸癌では，広汎子宮全摘出術が主であった。子宮体癌は，準広汎と単純子宮全摘が主体であった。リンパ節郭清の範囲では，卵巣癌の約半分が傍大動脈および骨盤内リンパ節郭清術が施行されていた。しかし，傍大動脈リンパ節まで郭清された率は子宮体癌で21.9%，子宮頸癌では10.9%と少なかった。

リンパ浮腫の発現頻度は27.2%（189/694例）であった（**表2**）。リンパ浮腫の発現時期は，一時的なリンパ浮腫の発現が平均2.6ヵ月で出現し永続的なリンパ浮腫の発現は平均9.7ヵ月であり，両者間に統計的有意差を認めた。また，リンパ浮腫が両下肢に出現する時期が片側性に比し，有意に早く出現した（**表3**）。リンパ浮腫発現に関与する危険因子をLogistic regressionモデルによる単変量および多変量によって解析した結果では，危険因子は卵巣癌では傍大動脈リンパ節郭清（**表3**），子宮頸癌および子宮体癌では術後の放射線治療であった（**表4，5**）。高危険群は子宮頸癌および子宮体癌で傍大動脈リンパ節郭清あるいは／および術後放射線療法を受けた例であった（**表5，6**）。傍大動脈リンパ節郭清と術後放射線治療との比較では，後者のほうがリンパ浮腫の頻度高い。

大腿鼠径部リンパ管・細静脈吻合術を8例に対して実施した（**表7**）。患者の年齢は35～61歳（中央値48歳），Performance statusはいずれも0であった。臨床病期はⅠ期5例，Ⅲ期3例，組織型は癌肉腫1例，類内膜腺癌7例であった。術後に化学療法を施行した例は4例，ホルモン療法を施行した例は2例であった。8例中7例は上記術式を完遂できたが，他の1例は，左側は上記術式を行うことができたが，右側は骨盤内リンパ節郭清時，鼠径部腹壁静脈の損傷が強く，右側リンパ管2本は外腸骨静脈に直接吻合した。吻合に要した時間は100分間～200分間であった。その術式に伴う出血はなく，血液がリンパ管に逆流することはなかった。リンパ管細静脈吻合ができた8例のうち3例（2例は術後より一過性にGrade Ⅰで出現し消失，その後発現なし。1例は術後50ヵ月Grade Ⅰで一過性）に片側性一過性リンパ浮腫を認めたが，いずれも軽度であった（**表7**）。

考　察

694例の後方視的解析では，明らかに放射線治療が術後下肢リンパ浮腫を引き起す最も危険な因子である。日本人の下肢リンパ浮腫についての従来の報告でも同様な報告がある[4, 5]。今回の解析で新たに下肢リンパ浮腫の危険因子としてリンパ節郭清の範囲が広範になることが示された。リンパ節郭清が骨盤内に加え傍大動脈リンパ節郭清を行うと卵巣癌・子宮頸癌・子宮体癌のすべてで，下肢リンパ浮腫は増加傾向である。しかし，リンパ節郭清の範囲は放射線治療のOdds ratioより低く，やはり最大の危険因子は放射線治療である。

表1　患者背景（694症例・全例女性）

Clinical characteristics	Ovarian cancer		Cervical cancer		Endometrial cancer	
Total no. patients	135		258		301	
Age（years）						
Median	51		49		57	
Range	15～79		23～80		19～80	
FIGO stage（N; %）						
I	64	(47.4)	171	(66.3)	196	(65.1)
II	11	(8.2)	76	(29.5)	27	(9.0)
III-IV	60	(44.4)	11	(4.3)	75	(24.9)
Unknown	－		－		3	(1.0)
Surgical procedure（N; %）						
Retroperitoneal						
Closing	80	(59.3)	184	(71.3)	205	(68.1)
Opening	32	(23.7)	16	(6.2)	33	(11.0)
－	23	(17.0)	58	(22.5)	63	(20.9)
Omentectomy						
＋	87	(64.4)	0	(0.0)	25	(8.3)
－	48	(35.6)	258	(100.0)	276	(91.7)
Enterectomy						
＋	9	(6.7)	1	(0.4)	0	(0.0)
－	126	(93.3)	257	(99.6)	301	(100.0)
Salpingo-oophorectomy						
Unilateral	18	(13.3)	34	(13.2)	38	(12.6)
Bilateral	108	(80.0)	133	(51.6)	203	(67.4)
－	9	(6.7)	91	(35.3)	60	(19.9)
Pelvic lymph node dissection						
＋	133	(98.5)	252	(97.7)	295	(98.0)
－	2	(1.5)	6	(2.3)	6	(2.0)
Para-aortic lymph node dissection						
＋	71	(52.6)	28	(10.9)	66	(21.9)
－	64	(47.4)	230	(89.1)	235	(78.1)
Hysterectomy						
Total	93	(68.9)	6	(2.3)	112	(37.2)
Modified radical	31	(23.0)	18	(7.0)	150	(49.8)
Radical	3	(2.2)	230	(89.1)	39	(13.0)
－	8	(5.9)	4	(1.6)	0	(0.0)
Chemotherapy（N; %）						
Neo-adjuvant chemotherapy						
＋	9	(6.7)	20	(7.8)	6	(2.0)
－	126	(93.3)	238	(92.2)	295	(98.0)
Adjuvant chemotherapy						
＋	111	(82.2)	62	(24.0)	119	(39.5)
－	24	(17.8)	196	(76.0)	182	(60.5)
Radiotherapy（N; %）						
Pre-operative radiation						
＋	0	(0.0)	6	(2.3)	0	(0.0)
－	135	(100.0)	252	(97.7)	301	(100.0)
Post-operative radiation						
＋	1	(0.7)	107	(41.5)	29	(9.6)
－	134	(99.3)	151	(58.5)	272	(90.4)