Chapter 2■ Initial Treatment

Overview

In 1988, the International Federation of Gynecology and Obstetrics (FIGO) adopted a new surgical staging classification system for uterine body cancer, necessitating the selection of surgical procedures that included retroperitoneal lymph node examination for stage determination. Uterine body cancer is known to have lower radiosensitivity than cervical cancer. In addition, the establishment of a standard treatment using anticancer drugs has taken longer for uterine body cancer as compared to ovarian cancer. Therefore, the first choice treatment for uterine body cancer is surgery. Radiotherapy is suitable for inoperable patients, including patients with serious medical conditions and the elderly.

Hysterectomy

In 2005, the Japan Gynecologic Oncology Group (JGOG) conducted a questionnaire survey[1] on uterine body cancer. For the standard surgical procedure for uterine body cancer, one third of institutions replied that they use total hysterectomy, another third replied that they use radical hysterectomy, and the remaining third replied that they modify the procedure according to the stage as estimated preoperatively. Approximately 70% of institutions answered that they do not perform radical hysterectomy for uterine body cancer.

The differences in surgical techniques themselves among institutions are one of the reasons for difficulty in obtaining a consensus on surgical techniques. We can presume that radical hysterectomy is performed using a similar technique throughout Japan. However, differences between institutions are thought to exist in procedures such as extended total hysterectomy and modified radical hysterectomy. Similarly, an Italian report indicated that there were large differences in surgical techniques between institutions.[2] It is also necessary to consider the differences in techniques between Japan and Western countries. In Western countries, hysterectomy is often classified as type I to type IV. Type II corresponds to extended total hysterectomy in Japan, and type III corresponds to radical hysterectomy in Japan.[3] Even if the surgery is nominally the same, techniques used in Japan may differ from those in Western countries. Therefore, it is of dubious value to apply overseas data without modification to Japanese surgical techniques.

In Japan, the rate of vaginal recurrence for stages I and II is 2%, and no significant difference in recurrence rates was reported between total hysterectomy, modified radial hysterectomy, and radical hysterectomy groups.[4] Some institutions advocate the use of modified radical surgery and radical surgery.[5]

Lymphadenectomy

There is no consensus on the best techniques for retroperitoneal lymph node biopsy and lymphadenectomy for uterine body cancer. According to the abovementioned 2005JGOG survey ,[1] almost all institutions stated that they performed pelvic lymphadenectomy for uterine body cancer. A minority of 13% of institutions stated that they performed para-aortic lymph node dissection or biopsy in all cases. The majority of institutions performed lymph node dissection or biopsy only under certain conditions.

According to a U.S. questionnaire survey conducted with gynecological oncologists, pelvic lymphadenectomy was performed by an estimated 69% of surgeons. Among the surgeons who did not perform lymphadenectomy in all cases, 89% incorporated rapid pathological diagnosis using frozen sections in their determination of the surgical technique.[6] In addition, 65% of those surveyed felt that lymph node resection was of clinical significance; 45% considered their technique to be total lymphadenectomy, whereas 31% did not perform para-aortic lymph node biopsy at the time of pelvic lymphadenectomy. In another U.S. survey with 9954 subjects, including general gynecologists, 30% of those surveyed resected lymph nodes for pathological examination.[7] This suggests the possibility that general gynecologists, who generally treat more than half of all patients, are not performing sufficient lymph node evaluations to determine the postoperative stage.

In European reports, in many patients lymph nodes were examined by palpation and visual examination.[8-10] A report from Scotland speculated that one factor associated with a poor prognosis was inadequate evaluation of postoperative stages including lymphadenectomy.[9]

It is difficult to obtain a global consensus on the significance, method, and extent of lymph node dissection and biopsy for uterine body cancer. Readers of these guidelines should be aware that there is ongoing discussion on this matter in Japan as well.

In Western countries, there is a high level of awareness of vaginal recurrence. Therefore, if retroperitoneal lymphadenectomy is not performed, physicians tend to frequently use postoperative radiotherapy. In Japan, more consideration is given to distant metastasis, and radical surgery including retroperitoneal lymphadenectomy is performed. In addition, there is a tendency to perform adjuvant chemotherapy for patients with risk factors for recurrence.

Staging used in our guidelines

When the terms “staging” or “surgical staging” are used, this refers to “surgical staging (Acta Obstetrica et Gynaecologica Japonica 1995, FIGO 1988)” in the General Rules for Clinical and Pathological Management of Uterine Body Cancer of the Japan Society of Obstetrics and Gynecology. For preoperative staging (Acta Obstetrica et Gynaecologica Japonica 1983, FIGO 1982), we use the term “clinical staging”. The clinical staging is used in determining the initial treatment strategy.

Definition and explanation of hysterectomy

In our guidelines, all total hysterectomies are abdominal. Below are various surgical techniques.

(1) **Total hysterectomy**: Uterine support structures and the vaginal canal are severed near the uterine attachment site. This is an extrafascial technique that removes some vaginal wall so that there is no residual cervical area.

Extended simple total hysterectomy: A surgical technique in which 1-2 cm of the vaginal wall is removed in addition to performing a total hysterectomy.

(2) **Modified radical hysterectomy**: The anterior layer of the vesicouterine ligament is separated and resected. The ureters are avoided and displaced laterally, and the uterus is resected by dividing as much as possible the anterior uterine support and vaginal wall from the cervix. However, the posterior layer of the vesicouterine ligament is not separated or severed. An extra 1.5-2 cm of vaginal wall can therefore be removed.

Another characteristic of this technique is that more of the cardinal ligament is resected than in a total hysterectomy.

(3) **Extended total hysterectomy**: This term is used synonymously with modified radical hysterectomy.

(4) **Radical hysterectomy**: The paravesical space and pararectal space are expanded, and each of the anterior, middle, and posterior uterine supports is separated and severed. Portions of the vaginal wall and pelvic connective tissue are widely excised, and a regional pelvic lymph node dissection is performed. That is, the cardinal ligament is severed near the pelvic wall, and the anterior layer of the vesicouterine ligament is separated and severed. The ureters are detached and displaced laterally, and the posterior layer is separated and severed. The rectovaginal ligament and ligament in the rectal space are severed. The paravaginal connective tissue and a portion of the vaginal wall (at least 3 cm) are then excised.

【References】

1. Japanese Gynecologic Oncology Group. Uterine Body Cancer Committee Report. 2005 (Level IV) (in Japanese)
   http://www.jgog.gr.jp/kaiin/kaiin_top.html
2. Maggino T, Romagnolo C, Zola P, Sartori E, Landoni F, Gadducci A. An analysis of approaches to the treatment of endometrial cancer in Western Europe：a CTF study. Eur J Cancer 1995； 31A（12）：1993-7(Level IV）
3. DiSaia PJ, Creasman WT. Chapter 3. Invasive cervical cancer. In：Daia PJ, Creasman WT eds. Clinical Gynecologic Oncology St. louis：Mosby 1997：71-4(Level IV）
4. Nakayama H, Kurose K, Saji H, Tanaka Y, Takeuchi T, Sugiura M, et al. Surgical methods for uterine body cancer: how prognosis is affected by cardinal ligament resection. Journal of the Japan Society of Gynecologic Oncology. 2002; 20:416-20 (Level Ⅲ) (in Japanese)
5. Nagano T, Suzuki A, Ozawa M, Hirano G, Fujita K, Sakakibara A, et al. Surgical methods for uterine body cancer – necessity and the extent of cardinal ligament resection – examination of stage II cases and recurrent cases. Japan Journal of Gynecologic Oncology. 2002; 20:421-7 (Level Ⅲ) (in Japanese)
6. Naumann RW, Higgins RV, Hall JB. The use of adjuvant radiation therapy by members of the society of gynecologic oncologists. Gynecol Oncol 1999；75：4-9(Level IV）
7. Partridge EE, Jessup JM, Donaldson ES, Taylor PT, Randall M, Braley P, et al. 1996 patients care evaluation study（PCF）of cancer of the corpus uteri, National Cancer Database（NCDB）American College of Surgery. Gynecol Oncol 1999；72：445(Level IV）
8. Amadori, A Bucchi L, Gori G, Falcini F, Saragoni L, Amadori D. Frequency and determinants of lymphadenectomy in endometrial carcinoma：A population-based study from Northern Italy. Ann Surg Oncol 2001；8：723-8(Level Ⅲ）
9. Crawford SC, Caestecker LD, Gillis CR, Hole D, Davis JA, Penney G, et al. Staging quality is related to the survival of women with endometrial cancer：a sccottish population based study. Deficient surgical staging and omission of adjuvant radiotherapy is associated with poorer survival of women diagnosed with endometrial cancer in Scotland during 1996 and 1997. Br J Cancer 2002：86：1837-42(Level Ⅲ）
10. Creutzberg CL, Putten WLJ, Koper PCM, Lybeert MLM, Jobsen JJ, Wariam-Rodenhuis CC, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma：multicentre randomized trial. Lancet 2000；355：1404-11(LevelⅡ）

CQ01

Which surgical techniques of hysterectomy are recommended for clinical stage I?

Recommendations

(1) Abdominal total hysterectomy (extrafascial technique) is recommended (Grade C).
(2) Modified radical (extended) hysterectomy is also an option, but its therapeutic benefits have not been confirmed (Grade C).

Background and Objectives

We examined the usefulness of abdominal total hysterectomy for clinical stage I.

Explanations

The focus of papers on surgical techniques for patients at clinical stage I has been on the significance of lymphadenectomy and the significance of concomitant radiotherapy. The standard method has been abdominal total hysterectomy.

Sato et al.[1] conducted a study of patients who underwent radical hysterectomy and modified radical hysterectomy. They found parametrial metastases in 2 of 131 cases (1.5%) at clinical stage I. They stated that parametrial metastasis was a significant prognostic factor. However, they did not recommend any particular surgical technique for clinical stage I patients. Yura et al.[2] reported similar results. Rutledge[3] reviewed the significance of radical hysterectomy in the treatment of uterine body cancer. They concluded that the prognosis after total hysterectomy was good and that radical hysterectomy, with its greater risk, was unnecessary. It has been reported that the 5 year survival rate for clinical stage I after total hysterectomy/bilateral salpingo-oophorectomy exceeded 90%.[4-7] In the GOG study[8] of a large number of cases, clinical stage I and II patients had good survival rates after abdominal total hysterectomy, if there were no risk factors such as cervical stromal invasion, positive peritoneal cytology, or metastases to lymph nodes and adnexae. Cassia et al.[7] reported a recurrence rate of 20% after total hysterectomy in the high risk group (G2 or G3, ≥1/3 myometrial invasion). This recurrence rate was higher than that of 6% in the low risk group. In contrast, Carey et al.[4] reported a 5 year disease-free survival rate of 81% after total hysterectomy in the high risk group (patients with at least one of the following: G3, ≥1/2 myometrial invasion, cervical invasion, or adenosquamous cell carcinoma). Paterson et al.[6] stated that they resected 1 cm of vagina, when possible, even for total hysterectomy, although they did not report its significance.

There have been no studies on surgical techniques according to subclassifications of clinical stage I. However, Cassia et al.[7] found no difference in survival rates between clinical stages Ia and Ib after total hysterectomy. For the subclassifications of surgical stage I, there has been a report examining the significance of postoperative radiotherapy in patients with myometrial invasion of ≥1/2, and another report for patients with myometrial invasion of ≥1/3.[4,5] However, neither discussed modifications in hysterectomy techniques.

As discussed above, we should evaluate concomitant lymphadenectomy according to risk factors, and individualize the postoperative treatment (mainly radiotherapy) for each patient. However, hysterectomy techniques have not been examined in detail, and abdominal total hysterectomy is used most often.

In total hysterectomy, an extrafascial technique is used, and it is necessary to resect some vaginal wall so that there is no residual cervical area. In Japan, there are institutions which perform modified radical hysterectomy for stage I, and radical hysterectomy for stage II or stage I with deep myometrial invasion.[9] Low recurrence rates in the vaginal stump may be associated with the removal of a portion of the paravaginal connective tissue and vaginal wall. Although there are institutions that perform vaginal total hysterectomy, it is not common.

【References】

1. Sato R, Jobo T, Kuramoto H. Parametrial spread is a prognostic factor in endometrial carcinoma. Eur. J. Gynaecol Oncol 2003；24：241-5(Level Ⅲ)
2. Yura Y, Tauchi K, Koshiyama M, Konishi I, Yura S, Mori T, et al. Parametrial involvement in endometrial carcinomas：Its incidence and correlation with other histological parameters. Gynecol Oncol 1996；63：114-9(Level Ⅲ)
3. Rutledge F. The role of radical hysterectomy in adenocarcinoma of the endometrium. Gynecol Oncol 1974；2：331-47(Level Ⅲ)
4. Carey MS, O'Connell GJ, Johanson CR, Goodyear MD, Murphy KJ, Daya DM, et al. Good outcome associated with a standardized treatment protocol using selective postoperative radiation in patients with clinical stage I adenocarcinoma of the endometrium. Gynecol Oncol 1995；57：138-44(Level Ⅲ)
5. Belinson JL, Lee KR, Badger GJ, Pretorius RG, Jarrell MA. Clinical stage I adenocarcinoma of the endometrium-Analysis of recurrences and the potential benefit of staging lymphadenectomy. Gynecol Oncol 1992；44：17-23(Level Ⅲ)
6. Paterson E, Spratt D, Tomkiewicz Z, Lewis C, Rathbun P. Management of stage I carcinoma of the uterus. Obstet Gynecol 1982；59：755-8(Level Ⅲ)
7. Sant Cassia LJ, Weppwlmann B, Shingleton H, Soong SJ, Hatch K, Salter MM. Management of early endometrial carcinoma. Gynecol Oncol 1989；35：362-6(Level Ⅲ)
8. Morrow CP, Bundy BN, Kurman RJ, Creasman WT, Heller P, Homesley HD, et al. Relationship between surgical-pathological risk factors and outcome in clinical stage Ⅰ and Ⅱ carcinoma of the endometrium：A Gynecologic Oncology Group study. Gynecol Oncol 1991；40：55-65(Level Ⅱ)
9. Registration Committee of the Japan Society of Obstetrics and Gynecology. Results of national uterine body cancer survey (4th report): cases in 1989-1990, Japan Society of Obstetrics and Gynecology, Tokyo, 1999; 32 (Level IV) (in Japanese)

CQ02

Which surgical techniques of hysterectomy are recommended for clinical stage II?

Recommendations

If cervical stromal invasion is evident, radical hysterectomy is advised (Grade E).

Background Objectives

We examined the significance of radical hysterectomy and its indications for clinical stage II.

Explanations

The 5 year survival rate for clinical stage II is poor compared to that for stage I.[1-3] However, most results from Western countries involve concomitant radiotherapy in some form. It is therefore difficult to evaluate surgical techniques in isolation. As in stage I, the standard technique is total hysterectomy. However, some studies reported that the use of several techniques ranging from total hysterectomy to radical hysterectomy. They did not indicate the selection criteria for these surgical techniques.

Mannel et al.[4] studied 70 patients with suspected cervical invasion who underwent individualized postoperative treatment based on the pathological findings in the resected specimens. They recommended total hysterectomy for patients with no evidence of cervical stromal invasion and normal macroscopic findings in the cervix. They recommended radical hysterectomy for patients with evidence of stromal invasion in cervical curettage, or with macroscopically obvious cervical invasion. Similarly, a study of 202 patients at clinical stage II showed prognostic improvement with radical hysterectomy in patients with a bulky cervical lesion.[2] In contrast, Leminen et al.[1] performed total hysterectomy or radical hysterectomy for stage II patients after preoperative internal irradiation. They reported no difference in the 10 year survival rate (65% and 77%) between the two surgical methods, and concluded that total hysterectomy is adequate even for stage II disease. In the selection of a surgical technique for clinical stage II, parametrial metastases present a problem. Sato et al.[5] found metastases in 13 of 132 cases (9.8%). However, they concluded that there may not be any great difference in therapeutic outcomes between patients who undergo excision of the parametrium and patients with adjuvant radiotherapy following total hysterectomy.

Studies of surgical stage II patients indicate that radical hysterectomy yields a better prognosis than total hysterectomy.[6-8] In particular, the recurrence rate in the vaginal stump was reported to be lower in patients who underwent radical hysterectomy.[6] Although many reports used concomitant radiotherapy, Mariani et al.[7] and Eltabbakh et al.[9] stated that radical hysterectomy alone was sufficient without adding radiotherapy for surgical stage II without pelvic lymph node metastases. They emphasized the significance of radical hysterectomy. In contrast, despite a poor prognosis regardless of the extent of cervical invasion in surgical stage II, it has been reported that prognostic improvement could not be obtained by radical hysterectomy.[10] In a GOG report,[3] the prognosis was also poor for patients with cervical stromal invasion. However, there have not been any studies of the effect that hysterectomy has on the prognosis of such patients.

In stage II, discrepancies between clinical stages and surgical stages are also a great problem. Creasman et al.[11] reported that only 35 patients were surgical stage II out of 148 patients who were clinical stage II, and 31 patients had extrauterine lesions (total hysterectomy was performed in all patients, and therefore, the rate of parametrial metastases was unknown). Although the prognosis of patients with extrauterine lesions was worse than those with surgical stage II disease, no recommendations regarding surgical techniques were given. When cervical invasion was observed in the excised uterus, there was a higher rate of parametrial metastasis.[5,12,13] However, there is no evidence of prognostic improvement due to radical hysterectomy in patients with parametrial metastases.

In Japan, some institutions perform extended simple total hysterectomy for clinical stage II patients with suspected stromal invasion or without obvious cervical stromal invasion. Extended simple total hysterectomy involves resection of a portion of the vagina in addition to a total hysterectomy or modified radical hysterectomy.

When surgical techniques are considered for clinical stage II patients, first there is the question of the accuracy of the diagnosis. There is little evidence of high quality from studies of surgical techniques. In Japan, each institution tends to favor either total hysterectomy, modified radical hysterectomy, or radical hysterectomy. We can also assume that there is no uniformity among institutions in preoperative methods of diagnosing cervical invasion, or standards for selecting surgical methods. A consensus meeting was held in creating these guidelines. The most heated discussion was on this CQ, and a consensus could not be obtained for recommendations that provided direct answers for this CQ. Further discussion therefore pertained only to “cases with obvious cervical stromal invasion” in which consensus was thought to be relatively easy to obtain. The recommendation given here corresponds to the view of the majority of the participants. In this case, ‘obvious cervical invasion’ indicates invasion evident macroscopically or through diagnostic imaging such as MRI. We cannot say, however, that these recommendations were agreed upon by all participants. At the present time, we can only say that they represent the most commonly accepted opinions. This CQ represents one of the greatest unresolved issues in the treatment of uterine body cancer. More high quality evidence needs to be gathered in both Japan and overseas.

【References】

1. Leminen A, Forss M, Lehtovirta P. Endometrial adenocarcinoma with clinical evidence of cervical involvement：accuracy of diagnostic procedures, clinical course, and prognostic factors. Acta Obstet Gynecol Scand 1995；74：61─6(Level Ⅲ)
2. Bonte MP, Yordan EL, McIntosh DG, Grendys EC, Orandi YA, Davies S, et al. Prognostic factors and long─term survival in endometrial adenocarcinoma with cervical involvement. Gynecol Oncol 1993；51：316─22(Level Ⅲ)
3. Morrow CP, Bundy BN, Kurman RJ, Creasman WT, Hweller P, Homesley HD, et al. Relationship between surgical─pathological risk factors and outcome in clinical stage Ⅰ and Ⅱ carcinoma of the endometrium：A Gynecologic Oncology Group study. Gynecol Oncol 1991；40：55─65(Level Ⅱ)
4. Mannel RS, Berman ML, Walker JL, Manetta A, DiSaia PJ. Management of endometrial cancer with suspected cervical involvement. Obstet Gynecol 1990；75：1016─22(Level Ⅲ)
5. Sato R, Jobo T, Kuramoto H. Parametrial spread is a prognostic factor in endometrial carcinoma. Eur. J. Gynaecol Oncol 2003；24：241─5(Level Ⅲ)
6. Sartori E, Gadducci A, Landoni F, Lissoni A, Maggino T, Zola P, et al. Clinical behavior of 203 stage Ⅱ endometrial cancer cases：The impact of primary surgical approach and of adjuvant radiation therapy. Int J Gynecol Cancer 2001；11：430─7(Level Ⅲ)

7. Mariani A, Webb MJ, Keeney GL, Calori G, Podratz KC. Role of wide／radical hysterectomy and pelvic lymph node dissection in endometrial cancer with cervical involvement. Gynecol Oncol 2001；83：72─80(Level Ⅲ)
8. Cornelison TL, Trimble EL, Kosary CL. SEER data, corpus uteri cancer：Treatment trends versus survival for FIGO stage Ⅱ, 1988─1994. Gynecol Oncol 1999；74：350─5(Level Ⅲ)
9. Eltabbakh GH, Moore AD. Survival of women with surgical stage Ⅱ endometrial cancer. Gynecol Oncol 1999；74：80─5(Level Ⅲ)
10. Homesley HD, Richard F, Boronow C, Lewis JL. Stage Ⅱ endometrial adenocarcinoma─Memorial Hospital of Cancer, 1949─1965. Obstet Gynecol 1977；49：604─8(Level Ⅲ)
11. Creasman WT, DeGeest K, DiSaia PJ, Zaino RJ. Significance of true surgical pathologic staging：A Gynecologic Oncology Group study. Am J Obstet Gynecol 1999；181：31─4(Level Ⅲ)
12. Yura Y, Tauchi K, Koshiyama M, Konishi Ⅰ, Yura S, Mori T, et al. Parametrial involvement in endometrial carcinomas：Its incidence and correlation with other histological parameters. Gynecol Oncol 1996；63：114─9(Level Ⅲ)
13. Tamussino KF, Reich O, Gucer F, Moser F, Zivkovic F, Lang PFJ, et al. Parametrial spread in patients with endometrial carcinoma undergoing radical hysterectomy. Int J Gynecol Cancer 2000；10：313─7(Level Ⅲ)

CQ03

What are the benefits of pelvic lymphadenectomy?

Recommendations

(1) Pelvic lymphadenectomy is significant in enabling determination of accurate staging (Grade A).
(2) No therapeutic benefits have been demonstrated for pelvic lymphadenectomy (Grade C).

Background and Objectives

Pelvic and para-aortic lymph node dissections (or biopsies) are required procedures for determination of FIGO surgical staging. In the NCCN Clinical Practice Guidelines, both pelvic and para-aortic lymphadenectomies were recommended, irrespective of whether myometrial invasion was present. In the PDQ and NCI, pelvic and para-aortic lymph node biopsies were recommended under certain conditions. We examined the use of pelvic lymphadenectomy in terms of diagnostic staging, its therapeutic benefits, and its indications.

Explanations

A number of studies of the therapeutic benefits of pelvic lymphadenectomy have found that good survival rates were obtained through excision of a large number of lymph nodes.[1-5] None of these studies were randomized controlled trials. The GOG examined the benefits of pelvic lymphadenectomy in 9,185 surgical stage I patients and 881 stage II patients. Lymphadenectomy was reported to significantly improve the 5 year survival rate in stage I, G3 patients.[6] This suggests that the decision of whether to perform pelvic lymphadenectomy should be made intraoperatively by the surgeon and pathologist based on pathological examination of the excised uterus. In patients at clinical stage I or with microscopic cervical invasion, survival rates and progression-free survival rates were significantly improved when 12 or more pelvic lymph nodes were excised.[5] In particular, excision of 12 or more pelvic lymph nodes greatly affected the 5 year survival rate and the disease-free survival rate in the high risk group (G3; >1/2 myometrial invasion; serous or clear cell adenocarcinoma). These results emphasize the significance of pelvic lymphadenectomy. On the other hand, there are reports that pelvic lymphadenectomy does not improve the prognosis for stage I[7,8] or stage II cases,[9] failing to demonstrate any therapeutic benefit.

Many reports have indicated that pelvic lymphadenectomy is necessary in the accurate determination of staging and selection of postoperative treatment, but did not state any therapeutic benefits of pelvic lymphadenectomy.[10-12] For instance, one study was conducted in which systematic pelvic lymphadenectomy and para-aortic lymphadenectomy were performed in addition to postoperative chemotherapy and radiotherapy, which were performed if lymph node metastases were detected. Their results indicated improved survival rates for cases with metastatic disease.[13]

There have also been a number of studies with patients in whom pelvic lymphadenectomy was unnecessary.[14-16] Patients not requiring pelvic lymphadenectomy were those with myometrial invasion of ≤1/2, G1 or G2 with ≤2 cm diameter, no obvious extrauterine disease,[14] no clinical findings that raised suspicion of metastases,[15] surgical stage

Ia or Ib, G1 or G2, and diploid DNA index.[16] Even if there were no independent risk factors for pelvic lymph node metastases, metastases were detected in 3.6% of cases. It was therefore suggested that caution should be exercised in omitting pelvic lymphadenectomy.[17] Pelvic lymph node metastases were present in 4% of cases with no myometrial invasion. Some would assert that pelvic lymphadenectomy should be performed in all cases, unless its risks outweigh the possible therapeutic benefits.[3] In actuality, there is no method which unfailingly predicts pelvic lymph node metastases.[17,18] One school of thought holds that it is sufficient to sample only the internal, external and common iliac lymph nodes, which have the highest frequency of metastasis among the pelvic lymph nodes.[8] Presently, pelvic lymphadenectomy can be omitted in cases of G1 endometrioid adenocarcinoma with no macroscopic myometrial invasion and no intraoperative evidence of extrauterine disease.

【References】

1. Kilgore LC, Partridge EE, Alvarez RD, Austin JM, Shingleton HM, Noojin Ⅲ F, et al. Adenocarcinoma of the endometrium：Survival comparison of patients with and without pelvic node sampling. Gynecol Oncol 1995；56：29-33(Level Ⅲ)
2. Fanning J. Long-term survival of intermediate risk endometrial cancer(Stage IG3, IC, Ⅱ) treated with full lymphadenectomy and brachytherapy without teletherapy. Gynecol Oncol 2001；82：371-4(Level Ⅲ)
3. Takeshima N, Hirai Y, Tanaka N, Yamawaki T, Yamauchi K, Hasumi K. Pelvic lymph node metastasis in endometrial cancer with no myometrial invasion. Obstet Gynecol 1996；88：280-2(Level Ⅲ)
4. Larson DM, Broste SK, Krawisz BR. Surgery without radiotherapy for primary treatment of endometrial cancer. Obstet Gynecol 1998；91：355-9(Level Ⅲ
5. Cragun JM, Havellisky LJ, Calingaert B, Syrian I, Secord AA, Soper JT, et al. Retrospective analysis of selective lymphadenectomy in apparent early-stage endometrial cancer. J Clin Oncol 2005；23：3668-75(Level Ⅲ)
6. Trimble EL, Kosary C, Park RC. Lymph node sampling and survival in endometrial cancer. Gynecol Oncol 1998；71：340-3(Level Ⅲ)
7. Candiani GB, Belloni C, Maggi R, Colombo G, Frigoli A, Carinelli SG. Evaluation of different surgical approaches in the treatment of endometrial cancer at FIGO stage I. Gynecol Oncol 1990；37：6-8(Level Ⅲ)
8. Bar-Am A, Ron IG, Kuperminc M, Gal I, Jaffa A, Kovner F, et al. The role of routine pelvic lymph node sampling in patients with stage I endometrial carcinoma：second thoughts. Acta Obstet Gynecol Scand 1998；77：347-50(Level Ⅲ)
9. Sartori E, Gadducci A, Landoni F, Lissoni A, Maggino T, Zola et al. Clinical behaivior of 203 stage Ⅱ endometrial cancer cases：The impact of primary surgical approach and of adjuvant radiation therapy. Int J Gynecol Cancer 2001；11：430-7(Level Ⅲ)
10. Ayhan A, Tuncer R, Tuncer ZS, Yuce K, Kucukali T. Correlation between clinical and histopathologic risk factors and lymph node metastases in early endometrial cancer(a multivariate analysis of 183 cases). Int J Gynecol Cancer 1994；4：306-9(Level Ⅲ)
11. Yenen MC, Dilek S, Dede M, Goktolga U, Deveci MS, Aydogu T. Pelvic-paraaortic lymphadenectomy in clinical stage I endometrial adenocarcinoma：a multicenter study. Eur J Gynaec Oncol 2003；24：327-9(Level Ⅲ)
12. Lo KWK, Cheung TH, Yu MY, Yim SF, Chung TKH. The value of pelvic and para-aortic lymphadenectomy in endometrial cancer to avoid unnecessary radiotherapy. Int J Gynecol Cancer 2003；13：863-9(Level Ⅲ)
13. Onda T, Yoshikawa H, Mizutani K, Mishima M, Yokota H, Nagano H, et al. Treatment of node-positive endometrial cancer with complete node dissection, chemotherapy and radiation therapy. Br J Cancer 1997；75：1836-41(Level Ⅲ)

14. Mariani A, Webb MJ, Keeney GL, Haddock MG, Calori G, Podratz KC. Low-risk corpus cancer：Is lymphadenectomy or radiotherapy necessary？ Am J Obstet Gynecol 2000；182：1506-19(Level Ⅲ)
15. Kim YB, Niloff JM. Endometrial carcinoma：Analysis of recurrence in patients treated with a strategy minimizing lymph node sampling and radiation therapy. Obstet Gynecol 1993；82：175-80(Level Ⅲ)
16. Leijon T, Rosenberg P, Boeryd B. Total abdominal hysterectomy and bilateral salpingo-oophorectomy. A sufficient treatment for patients with low risk endometrial carcinoma. Int J Gynecol Cancer 1997；7：376-80(Level Ⅲ)
17. Todo Y, Sakuragi N, Nishida R, Yamada T, Ebina Y, Yamamoto R, et al. Combined use of magnetic resonance imaging, CA 125 assay, histologic type and histologic grade in the prediction of lymph node metastasis in endometrial carcinoma. Am J Obstet Gynecol 2003；188：1265-72(Level Ⅲ)
18. Watanabe M, Aoki Y, Kase H, Fujita K, Tanaka K. Low risk endometrial cancer：A study of pelvic lymph node metastasis. Int J Gynecol Cancer 2003；13：38-41(Level Ⅲ)

CQ04

What are the benefits of para-aortic lymphadenectomy in addition to pelvic lymphadenectomy?

Recommendations

(1) It aids determination of accurate staging (Grade A).
(2) No therapeutic benefits have been established for para-aortic lymphadenectomy (Grade C).

Background and Objectives

Pelvic and para-aortic lymph node dissections (or biopsies) are required procedures for determination of FIGO surgical staging. In the NCCN Clinical Practice Guidelines, both pelvic and para-aortic lymphadenectomies were recommended, irrespective of whether myometrial invasion was present. In the PDQ and NCI, pelvic and para-aortic lymph node biopsies were recommended under certain conditions. We examined the use of para-aortic lymphadenectomy in terms of diagnostic staging, its therapeutic benefits, and its indications.

Explanations

Para-aortic lymph node metastasis has been reported to be an important prognostic factor.[1,2] There have also been reports of the therapeutic benefits of para-aortic lymphadenectomy.[3-5]

Mariani et al.[5] stated that para-aortic lymphadenectomy was a predictive factor for the 5 year survival rate and the 5 year progression-free rate. However, no evidence has been forthcoming from randomized controlled trials, and the therapeutic benefits of this procedure have not been confirmed. As for pelvic lymphadenectomy, individualization of postoperative treatment is made possible by accurate staging including para-aortic lymphadenectomy. This process has resulted in improved outcomes. Some studies therefore indicate that para-aortic lymphadenectomy should be performed.[1,6,7] Onda et al.[6] reported that good survival rates were obtained in cases with para-aortic lymph node metastases using postoperative chemotherapy followed by radiotherapy. As previously mentioned in CQ03, some reports concluded that pelvic lymphadenectomy was unnecessary. These reports also stated that para-aortic lymphadenectomy was unnecessary. However, another report indicated that if there was no pelvic lymph node metastasis after performing pelvic lymphadenectomy and if peritoneal cytology was negative, para-aortic lymphadenectomy was unnecessary.[8] Presently, para-aortic lymphadenectomy can be omitted if it is endometrioid adenocarcinoma G1 or G2, has myometrial invasion of $\leq$1/2, and has no extrauterine lesion intraoperatively. Cragun et al.[9] stated that excision of 12 or more pelvic lymph nodes improved the prognosis of early uterine body cancer, but they also reported that prognosis was not associated with the performance of para-aortic lymphadenectomy. Many reports stated that the frequency of single metastasis to para-aortic lymph node was a few percent.[2,7,10,11] However, there is still no consensus on the omission of para-aortic lymphadenectomy if there is no pelvic lymph node metastasis in the light of the abovementioned frequency.

For the risk factors of para-aortic lymph node metastasis, the following are considered important: deep myometrial invasion,[1,7,8,12] cervical invasion,[13] positive peritoneal cytology, pelvic lymph node metastasis,[8,12] degree of histological differentiation,[1,7] lymphatic vessel invasion,[12] serum CA 125 level,[9,13] and volume index.[13] Toda et al.[13] indicated that serum CA 125 level and volume index were independent risk factors for pelvic lymph node metastasis and that para-aortic lymphadenectomy was unnecessary in cases without a risk factor. Yokoyama et al.[1] reported that para-aortic lymphadenectomy was necessary for all cases other than stage Ia G1 and stage IV.

【References】

1. Yokoyama Y, Maruyama H, Sato S, Saito Y. Indispensability of pelvic and paraaortic lymphadenectomy in endometrial cancers. Gynecol Oncol 1997；64：411-7(Level Ⅲ)
2. Nishiya M, Sakuragi N, Hareyama H, Ebina Y, Furuya M, Oikawa M, et al. Cox multivariate regression models for estimating prognosis of patients with endometrioid adenocarcinoma of the uterine corpus who underwent through surgical staging. Int J Cancer 1998；79：521-5(Level Ⅲ)
3. Fanning J. Long-term survival of intermediate risk endometrial cancer（Stage IG3, IC, Ⅱ) treated with full lymphadenectomy and brachytherapy without teletherapy. Gynecol Oncol 2001；82：371-4(Level Ⅲ)
4. Larson DM, Broste SK, Krawisz BR. Surgery without radiotherapy for primary treatment of endometrial cancer. Obstet Gynecol 1998；91：355-9(Level Ⅲ)
5. Mariani A, Webb MJ, Galli L, Podratz KC. Potential therapeutic role of para-aortic lymphadenectomy in node-positive endometrial cancer. Gynecol Oncol 2000；76：348-56(Level Ⅲ)
6. Onda T, Yoshikawa H, Mizutani K, Mishima M, Yokota H, Nagano H, et al. Treatment of node-positive endometrial cancer with complete node dissection, chemotherapy and radiation therapy. Br J Cancer 1997；75：1836-41(Level Ⅲ)
7. Ayhan A, Tuncer R, Tuncer ZS, Yuce K, Kucukali T. Correlation between clinical and histopathologic risk factors and lymph node metastases in early endometrial cancer（a multivariate analysis of 183 cases）. Int J Gynecol Cancer 1994；4：306-9(Level Ⅲ)
8. Faught W, Krepart GV, Lotocki R, Heywood M. Should selective paraaortic lymphadenectomy be part of surgical staging for endometrial cancer？Gynecol Oncol 1994；55：51-5(Level Ⅲ
9. Cragun JM, Havellisky LJ, Calingaert B, Syrian I, Secord AA, Soper JT, et al. Retrospective analysis of selective lymphadenectomy in apparent early-stage endometrial cancer. J Clin Oncol 2005；23：3668-75(Level Ⅲ)
10. Lo KWK, Cheung TH, Yu MY, Yim SF, Chung TKH. The value of pelvic and para-aortic lymphadenectomy in endometrial cancer to avoid unnecessary radiotherapy. Int J Gynecol Cancer 2003；13：863-9(Level Ⅲ)
11. Jobo T, Sato R, Arai T, Tamura T, Watanabe J, Kuramoto H. Lymph node pathway in the spread of endometrial carcinoma. Eur J Gynaec Oncol 2005；26：167-9(Level Ⅲ)
12. Hirahatake K, Hareyama H, Sakuragi N, Nishiya M, Makinoda S, Fujimoto S. A clinical and pathologic study on para-aortic lymph node metastasis in endometrial carcinoma. J Surg Oncol 1997；65：82-7(Level Ⅲ)
13. Todo Y, Sakuragi N, Nishida R, Yamada T, Ebina Y, Yamamoto R, et al. Combined use of magnetic resonance imaging, CA 125 assay, histologic type and histologic grade in the prediction of lymph node metastasis in endometrial carcinoma. Am J Obstet Gynecol 2003；188：1265-72(Level Ⅲ)

CQ05

Does partial vaginectomy reduce the rate of vaginal stump recurrence?

Recommendations

Partial vaginectomy has not been shown wall to reduce the vaginal stump recurrence rate (Grade C).

Background and Objectives

We examined whether the vaginal stump recurrence rate can be reduced by partial vaginectomy.

Explanations

Studies have comparing total hysterectomy and radical hysterectomy for surgical stage II disease found that the 5 and 10 year survival rates were significantly better for radical hysterectomy.[1,2] Sartori et al.[1] reported no vaginal stump recurrence in patients who underwent radial hysterectomy, indicating that partial vaginectomy reduces vaginal stump recurrence. Mariani et al.[2] compared patients who underwent total hysterectomy with resection of 2 cm of vaginal wall with those who underwent radical hysterectomy with resection of ≥2 cm of vaginal wall. They reported significantly less vaginal stump recurrence in the latter group, but did not discuss the therapeutic benefits of vaginectomy.

Another study compared total hysterectomy and radical hysterectomy for clinical stage II disease, reporting no difference in survival rates between procedures. They accordingly recommended total hysterectomy.[3]

We found two studies of partial vaginectomy performed for clinical stage I disease,[4,5] neither of which discussed its therapeutic benefits. In Japan, some institutions perform modified radical hysterectomy with partial vaginectomy for stage I, and radical hysterectomy for stage II disease.[6,7] No evidence has been forthcoming, however, concerning the therapeutic benefits of partial vaginectomy. At present, partial vaginectomy is pereformed in conjunction with extended simple total hysterectomy, modified radical hysterectomy, and radical hysterectomy, although there are differences between institutions in Japan. For the high risk group for recurrence, we need to further investigate the benefits of extended simple total hysterectomy with resection of 1-2 cm of the vaginal wall. Vaginal stump recurrence is relatively uncommon in Japan. As indicated in a study (JGOG 2023) conducted by the Japanese Gynecologic Oncology Group, this low recurrence rate may be due to the widespread use of extended surgery in which portions of the parametrium and vaginal wall are resected.

Since the majority of foreign papers deal with the concurrent use of radiotherapy, it is difficult to confirm the benefits of partial vaginectomy and to make comparisons.

【References】

1. Sartori E, Gadducci A, Landoni F, Lissoni A, Maggino T, Zola P, et al. Clinical behavior of 203 stage Ⅱ endometrial cancer cases：The impact of primary surgical approach and of adjuvant radiation therapy. Int J Gynecol Cancer 2001；11：430-7(Level Ⅲ)

2. Mariani A, Webb MJ, Keeney GL, Calori G, Podratz KC. Role of wide/radical hysterectomy and pelvic lymph node dissection in endometrial cancer with cervical involvement. Gynecol Oncol 2001；83：72-80(Level Ⅲ)
3. Leminen A, Forss M, Lehtovirta P. Endometrial adenocarcinoma with clinical evidence of cervical involvement：accuracy of diagnostic procedures, clinical course, and prognostic factors. Acta Obstet Gynecol Scand 1995；74：61-6(Level Ⅲ)
4. Paterson E, Spratt D, Tomkiewicz Z, Lewis C, Rathbun P. Management of stage I carcinoma of the uterus. Obstet Gynecol 1982；59：755-8(Level Ⅲ)
5. Mangioni C, De Palo G, Marubini E, Del Vecchio M. Surgical Pathologic staging in apparent stage I endometrial carcinoma. Int J Gynecol Cancer 1993；3：373-84(Level Ⅲ)
6. Sato R, Jobo T, Kuramoto H. Parametrial spread is a prognostic factor in endometrial carcinoma. Eur. J. Gynaecol Oncol 2003；24：241-5(Level Ⅲ)
7. Yura Y, Tauchi K, Koshiyama M, Konishi I, Yura S, Mori T, et al. Parametrial involvement in endometrial carcinomas：Its incidence and correlation with other histological parameters. Gynecol Oncol 1996；63：114-9(Level Ⅲ)

CQ06

Is ovarian preservation possible in young patients?

Recommendations

Even in young patients, ovarian preservation should only be performed with caution (Grade C).

Background and Objectives

We examined the indications for and problems with ovarian preservation in young patients with uterine body cancer.

Explanations

The problems of ovarian preservation are metastases to the ovaries and of the increased risk of ovarian cancer. Today uterine body cancer is on the increase, even in young people, and ovarian preservation is a major issue in young patients with this condition.

Reported ovarian metastatic rates for clinical stage I and II disease are approximately 5%[1,2] and 10%,[3-7] respectively. The rate of uterine body cancer metastasizing to ovaries is therefore not clinically negligible, so bilateral salpingo-oophorectomy is generally performed regardless of the stage. Our search of the literature failed to yield any prospective studies examining the therapeutic benefits of bilateral salpingo-oophorectomy in the early stages of uterine body cancer. The rate of ovarian metastasis is high for clinical stage II disease, and bilateral salpingo-oophorectomy should be performed. However, there is a dearth of high level evidence regarding this matter. In studies of young patients in whom ovarian preservation becomes an issue, there was no difference in the rate of ovarian metastasis between a group of patients ≤45 years old and a group ≥46 years old.[8,9]

A number of studies have reported that the incidence of synchronous uterine body and ovarian cancers is high in younger patients.[9,10] Gitsch et al.[10] reported that synchronous ovarian cancer was seen in 5 out of 17 body patients with cancer of the uterine body (29.4%) who were ≤45 years old. In Sweden, a largescale study examined almost all cases of uterine body cancer (19,128 patients) and ovarian cancer (19,440 patients) registered between 1961 and 1998.[11] It demonstrated a strong correlation between uterine body cancer and ovarian cancer. In ≤40 year old patients, the frequency of ovarian cancer occurring synchronously with endometrioid adenocarcinoma of the uterine body was very high. In Japan, the reported incidence of body cancer and synchronous ovarian cancer is 2.2-6.6%,[12-14] although these studies did not examine the association with age.

Based on the above results, one cannot avoid the conclusion that the safety of ovarian preservation is low. Evans-Metcalf et al. suggested that ovarian preservation may be feasible for younger patients with well-differentiated stage Ia cancer, but further studies are needed.[9]

No studies have demonstrated any benefits for ovarian wedge resection, sometimes performed to confirm the presence of ovarian metastases.

【References】

1. Takeshima N, Hirai Y, Yano K, Tanaka N, Yamauchi K, Hasumi K. Ovarian metastasis in endometrial carcinoma. Gynecol Oncol 1998；70：183─7(Level Ⅲ)

2. Boronow RC, Morrow CP, Creasman WT, DiSaia PJ, Silverberg SG, Miller A, et al. Surgical staging in endometrial cancer：Clinical-pathologic findings of a prospective study. Obstet Gynecol 1984；63：825-32(Level Ⅲ)
3. Bonte MP, Yordan EL, McIntosh DG, Grendys EC, Orandi YA, Davies S, et al. Prognostic factors and long-term survival in endometrial adenocarcinoma with cervical involvement. Gynecol Oncol 1993；51：316-22(Level Ⅲ)
4. Creasman WT, DeGeest K, DiSaia PJ, Zaino RJ. Significance of true surgical pathologic staging：A Gynecologic Oncology Group study. Am J Obstet Gynecol 1999；181：31-4(Level Ⅲ)
5. Leminen A, Forss M, Lehtovirta P. Endometrial adenocarcinoma with clinical evidence of cervical involvement：accuracy of diagnostic procedures, clinical course, and prognostic factors. Acta Obstet Gynecol Scand 1995；74：61-6(Level Ⅲ)
6. Sato R, Jobo T, Kuramoto H. Parametrial spread is a prognostic factor in endometrial carcinoma. Eur. J. Gynaecol Oncol 2003；24：241-5(Level Ⅲ)
7. Yura Y, Tauchi K, Koshiyama M, Konishi I, Yura S, Mori T, et al. Parametrial involvement in endometrial carcinomas：Its incidence and correlation with other histological parameters. Gynecol Oncol 1996；63：114-9(Level Ⅲ)
8. Yamazawa K, Seki K, Matsui H, Kihara M, Sekiya S. Prognostic factors in young women with endometrial carcinoma：A report of 20 cases and review of literature. Int j Gynecol Cancer 2000；10：212-22(Level Ⅲ)
9. Evans-Metcalf ER, Brooks SE, Peale FR, Baker SP. Profile of women 45 years of age and younger with endometrial cancer. Obstet Gynecol 1998；91：349-54(Level Ⅲ)
10. Gitsch G, Hanzal E, Jensen D, Hacker NF. Endometrial cancer in premenopausal women 45 years and younger. Obstet Gynecol 1995；85：504-8(Level Ⅲ)
11. Hemminki K, Aaltonen L, Li X. Subsequent primary malignancies after endometrial carcinoma and ovarian carcinoma. Cancer 2003；97：2432-9(Level Ⅲ)
12. Sakaguchi I, Nitsuta S, Miyahara Y, Sonoda N, Suenaga Y, Otake H, et al. Clinical examination of 97 cases of synchronous gynecological cancers. Obstetrical and Gynecological Therapy 2002; 85:120-5(Level Ⅲ) (in Japanese)
13. Sasagawa M, Tamura N, Tsukada K, Honma S, Takahashi T. Synchronous cancers including uterine body cancer. Acta Obstetrica et Gynaecologica Japonica 2000; 52:756-60 (Level Ⅲ) (in Japanese)
14. Kamikatahira S, Jobo T, Kuramoto H. Endometrial carcinoma with synchronous ovarian malignancy-Differentiation between independent and metastatic carcinomas. Int J Clin Oncol 1996；1：100-8(Level Ⅲ)

CQ07

In surgical staging, inguinal lymph node metastases are often mentioned. Should inguinal lymph nodes be biopsied?

Recommendations

(1) If inguinal lymphadenopathy is detected in preoperative imaging such as CT scanning, biopsy should be performed to determine the surgical stage (Grade C).
(2) If inguinal lymphadenopathy is not detected, the benefits of biopsy are not yet clear (Grade D).

Background and Objectives

From FIGO staging (1988) and the General Rules for Clinical and Pathological Management of Uterine Body Cancer (1994) of Japan, inguinal lymph nodes (Figure 1b, (9)) are not considered to be regional lymph nodes for uterine body cancer, and inguinal metastases are regarded as distant metastases. We examined the indications and therapeutic benefits of inguinal lymph node biopsy.

Explanations

There are three routes for lymphogenous metastasis from the uterus. The first route travels from the uterine cervix via the cardinal ligament to the pelvic lymph nodes and then to the para-aortic lymph nodes. The second route travels along the infundibulopelvic ligament, via the ovarian vessels, to the para-aortic lymph nodes . The third route travels along the round ligament of the uterus to the inguinal lymph nodes.[1-3] The main routes from the uterine fundus are *via* the infundibulopelvic ligament, round ligament, and cardinal ligament pathways.[4] The main route from the lower portion of the uterine corpus is *via* the cardinal ligament pathway. Takeshima et al.[5] examined the lymph node metastasis predilection sites in 393 cases of clinical stage II uterine body cancer. These were the internal iliac nodes in 5.6%, external iliac nodes in 7.1%, and obturator nodes in 6.9% of cases. The frequency of metastasis to the suprainguinal nodes is 3.1% (unknown for inguinal nodes). The main routes for lymphogenous metastasis are therefore the infundibulopelvic ligament and cardinal ligament pathways. The frequency of metastasis *via* the round ligament pathway is low. Most cases positive for inguinal lymph node metastases also have pelvic lymph node metastases.

A case report presented a case of inguinal lymph node metastases without pelvic lymph node metastasis in a patient with clear cell adenocarcinoma confined to the endometrium.[6] It is therefore important to confirm whether inguinal lymphadenopathy is present.

Several case reports have discussed therapeutic outcomes in cases with inguinal lymph node metastases.[7-10] There have not been any studies with large subject numbers examining the benefits of inguinal lymph node biopsy. If inguinal lymphadenopathy is detected in preoperative imaging such as CT scanning, biopsy should be performed to determine the surgical stage.

【References】

1. Barakat RR, Grigsby PW, Sabbatini P, Zaino RJ. Corpus. Epithelial Tumors. In：Principles and practice of gynecologic oncology（3rd ed, ed by Hoskins WJ, Perez CA, Young RC）. Lippincott Williams＆Wilkins. Philadelphia. 2000, 919-59(Level IV)
2. Japan Society of Obstetrics and Gynecology, Japanese Society of Pathology, and Japan Radiological Society, editors. General rules for clinical and pathological management of uterine body cancer (revised, 2nd ed.) Kanehara & Co., Tokyo, 1996; 15-8 (general rules) (in Japanese)
3. Japan Society of Clinical Oncology, editor. Japan Society of Clinical Oncology: Classification of Regional Lymph Nodes in Japan. Kanehara & Co., Tokyo, 2002; 12-16, 35-6 (general rules) (in Japanese)
4. Sato R, Jobo T, Kuramoto H. Parametrial spread is a prognostic factor in endometrial carcinoma. Eur J Gynaecol Oncol. 2003；24：241-5(Level III)
5. Takeshima N, Umezawa S, Shimizu T, Fujimoto I, Yamauchi K, Hasumi K. Pelvic lymph node metastasis of uterine body cancer. Acta Obstetrica et Gynaecologica Japonica 1994; 46:883-8 (Level III) (in Japanese)
6. Kato K, Horiuchi A, Shiobara S, Shiozawa A, Orii F, Nikaido T, et al. A case of intramucosal uterine body cancer with subepidermal lymph node metastasis of the inguinal area. Journal of the Japan Society of Gynecologic Pathology and Colposcopy 1998; 16:58 (Level IV) (in Japanese)
7. Scholz HS, Lax S, Petru E, Benedicic C, WinterHeinz R. Inguinal lymph node metastasis as the presenting symptom of endometrial cancer：a case report. Anticancer Research 2002；22：2531-2(Level III)
8. Kaneyasu Y, Okawa T, Yajima M, Saito R, Nakabayashi M, Seshimo A, et al. Stage IVB uterine endometrial cancer successfully salvaged by chemoradiotherapy and surgery. Int J Clin Oncol 2003；8：60-4(Level III)
9. Katz LA, Andrews SJ, Fanning J. Survival after multimodality treatment for stage □C endometrial cancer. Am J Obstet Gynecol 2001；184：1071-3(Level III)
10. Alders JG, Abeler V, Kolstad P. Stage IV endometrial carcinoma：a clinical and histopathological study of 83 patients. Gynecol Oncol 1984；17：75-84(Level III)

Table 4 Comparison of Terminologies

Japan Society of Obstetrics and Gynecology	**Japan Society of Clinical Oncology**
(1) Para-aortic lymph nodes (inferior border of the left renal vein to the root of the inferior mesenteric artery) (#326b1)	Para-abdominal aortic lymph nodes (inferior border of the left renal vein to the root of the inferior mesenteric artery)
(1) Para-aortic lymph nodes (root of the inferior mesenteric artery to the aortic bifurcation) (#326b2)	Para-abdominal aortic lymph nodes (root of the inferior mesenteric artery to the aortic bifurcation)
(Not applicable)	Lymph nodes at the aortic bifurcation
(7) Sacral lymph nodes (#412)	Median sacral lymph nodes Lateral sacral lymph nodes
(2) Common iliac lymph nodes (#413)	Common iliac lymph nodes
(3) External iliac lymph nodes (#403)	External iliac lymph nodes
(4) Suprainguinal lymph nodes (#401)	Suprafemoral lymph nodes
(5) Internal iliac lymph nodes (#411)	Internal iliac lymph nodes
(6) Obturator lymph nodes (#410)	Obturator lymph nodes
(8) Parametrial lymph nodes (#405)	Parametrial lymph nodes
(9) Inguinal lymph nodes (#401a)	Inguinal lymph nodes

The names of structures established in the "General Rules for Clinical and Pathological Management of Uterine Body Cancer; revised, 2nd ed." (Japan Society of Obstetrics and Gynecology, Japanese Society of Pathology, and Japan Radiological Society, editors; 1996)[2] are considered the names commonly proposed for various organs and established in the "General Rules and Statements on Cancer: Japan Society of Clinical Oncology" (Japan Society of Clinical Oncology: Joint Committee on Cancer Treatment, editors; 1991). The use of numbers for lymph nodes was eliminated in the "Japan Society of Clinical Oncology: Classification of Regional Lymph Nodes in Japan" (Japan Society Clinical Oncology, editor; 2002).[3]

Figure 1 "General Rules for Clinical and Pathological Management of Uterine Body Cancer; revised, 2nd edition" (1996, Kanehara & Co.)[2]

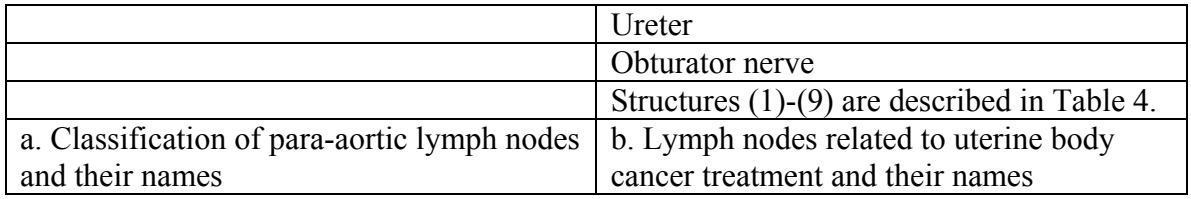

Figure 2 "Japan Society of Clinical Oncology: Classification of Regional Lymph Nodes in Japan" (2002, Kanehara & Co.)[3]

腹部大動脈周囲リンパ節	Para-abdominal aortic lymph nodes	胸管	Thoracic duct
b2 群 大脈前リンパ節	b2 group Precaval lymph nodes	上腸間膜動脈	Superior mesenteric artery
大脈外側リンパ節	Laterocaval lymph nodes	腹部大動脈周囲リンパ節	Para-abdominal aortic lymph nodes
大動脈分岐部リンパ節	Lymph nodes at the aortic bifurcation	a2 群 大動脈後リンパ節	a2 group Retroaortic lymph nodes
正中仙骨リンパ節	Median sacral lymph nodes	大動脈外側リンパ節	Lateroaortic lymph nodes
総腸骨リンパ節	Common iliac lymph nodes	b1 群 大脈後リンパ節	b1 group Retrocaval lymph nodes
外腸骨リンパ節	External iliac lymph nodes	大動脈外側リンパ節	Lateroaortic lymph node
閉鎖神経	Obturator nerve	腹部大動脈周囲リンパ節	Para-abdominal aortic lymph nodes
閉鎖リンパ節	Obturator lymph nodes	大動静脈間リンパ節	Interaorticocaval lymph node
子宮円索	Round ligament of the uterus	大動脈前リンパ節	Preaortic lymph node
基靱帯リンパ節	Parametrial lymph nodes	下腸間膜動脈	Inferior mesenteric artery
		卵巣動脈	Ovarian artery
		閉鎖リンパ節	Obturator lymph nodes
		大腿上リンパ節	Suprafemoral lymph nodes
		鼠径靱帯	Inguinal ligament
		深鼠径リンパ節	Deep inguinal lymph nodes
		浅鼠径リンパ節	Superficial inguinal lymph nodes
		臍動脈索	Medial umbilical ligament

CQ08

Is omentectomy necessary?

Recommendations

If macroscopic intrapelvic or peritoneal dissemination is observed, or if the tissue diagnosis is serous adenocarcinoma or clear cell adenocarcinoma, it is diagnostically preferable to perform omentectomy and examine the resected specimen for dissemination (Grade C)

Background and Objectives

If omental metastases are detected pathologically, the case is surgical stage IVb, and the information obtained by omentectomy is important in determining postoperative treatment. We examined the indications and diagnostic and therapeutic benefits of omentectomy.

Explanations

The omentum contains many blood vessels including capillaries. Omental milky spots, found throughout the omentum, are omentum-specific lymphoid tissues that are involved in the intraperitoneal host defense mechanism. The omentum itself can be considered as a collection of lymph nodes are bordered by a space, the peritoneal cavity. Omentectomy can therefore be regarded as a type of lymphadenectomy.[1]

In the National Comprehensive Cancer Network (NCCN) Guidelines (version 1, 2005),[2] even if the tumor is thought to be confined to the uterus, the following are considered necessary: detailed examination and palpation of the intraperitoneal structures (peritoneal surface, liver, omentum, diaphragm, and intestinal tract). If the CA-125 level is high or extrauterine spread is indicated in MRI/CT scans, omentectomy is a useful part of the search for intraperitoneal dissemination, along with ascitic cytology and peritoneal biopsy (diaphragmatic biopsy).

Studies have examined the correlations between various pathological factors and omental metastases in clinical stage I patients who underwent surgery. Saygili et al.[3] retrospectively examined 97 cases with clinical stage I disease and found omental metastases in 6% of patients (of whom 2/3 had microscopic metastases). Omental metastases were seen in 20% of patients with myometrial invasion of >1/2, 22% of G3 patients, 40% of patients with clear cell adenocarcinoma, 33% of patients with adnexal metastases, 45% of patients with positive ascitic cytology, and 30% of patients with pelvic lymph node metastases. Chen et al.[4] prospectively examined 84 patients with clinical stage I disease. Omental metastases were seen in 8.3% of all patients (of whom 5/7 had microscopic metastases), in 39% of patients with clear cell adenocarcinoma, 38% of patients with lymph node metastases, and 75% of patients with adnexal metastases.

From the above evidence, omental biopsy is possibly useful in staging. In particular for the following cases, omentectomy and histopathological determination of dissemination status are considered to be of diagnostic significance: myometrial invasion of >1/2, histological type of endometrioid adenocarcinoma G3, serous adenocarcinoma or clear cell adenocarcinoma, macroscopic adnexal metastases, and macroscopic pelvic or peritoneal dissemination. If dissemination is not macroscopically evident, and the primary is not

histologically highly malignant, the benefits of omentectomy have not been established. In this text, omentectomy refers to incision biopsy of the omentum (partial resection).

【References】

1. Aoki T, Hirai K. Omentectomy. Atlas of Obstetrics and Gynecology View 16: Ovarian surgery. Kuwabara Y, editor. Medical View, Tokyo, 1995, 88-94 (Level IV) (in Japanese)
2. Teng N, Rustum NA, Bahador A, Bookman MA, Campos S, Cho KR, et al. NCCN Practice Guidelines in Oncology Version1.2005. Uterine cancers. http：//www.nccn.org/professionals/physician(guideline)
3. Saygili U, Kavaz S, Altunyurt S, Uslu T, Koyuncuoglu M, Erten O. Omentectomy, peritoneal biopsy and appendectomy in patients with clinical stage I endometrial carcinoma. Int J Gynecol Cancer 2001；11：471-4(Level III)
4. Sidney SC, Gregory S. Stage I endometrial carcinoma. Role of omental biopsy and omentectomy. Journal of Reproductive Medicine 1991；36：627-9(Level III)

CQ09

Is rapid intraoperative pathological diagnosis useful for the determination of histological type and degree of differentiation?

Recommendations

In cases where it is difficult preoperatively to determine the histological type and degree of differentiation, rapid intraoperative pathological diagnosis can confirm the necessity of pelvic lymphadenectomy, para-aortic lymphadenectomy, or omentectomy (Grade C).

Background and Objectives

Some are questioning the necessity of cytoreductive surgery is becoming the subject of discussion tofrom the viewpoint of avoiding surgical complications, such as lower limb lymphedema following lymphadenectomy. We therefore examined the benefits of rapid intraoperative pathological diagnosis and the indications for surgical techniques, in particular lymphadenectomy.

Explanations

With endometrial biopsy, the histological type and degree of differentiation can be diagnosed to some extent preoperatively. However, since heterogeneity can exist within a tumor, rapid intraoperative pathological diagnosis from the resected uterus can help in obtaining a more accurate diagnosis.

The NCCN Guidelines (version 1, 2005)[1] indicated that 15-20% of tumors graded by preoperative endometrial biopsy were upgraded after examination of fixed specimens of the resected uterus. They stated that lymphadenectomy can be omitted if the patient has G1 disease and is negative for myometrial invasion in preoperative investigations. They also stated that, ideally, rapid pathological diagnosis should be used to determine the degree of differentiation and whether there is myometrial invasion. In addition, they recommend pelvic lymphadenectomy and para-aortic lymphadenectomy for all patients with G2/G3 disease, myometrial invasion of ≥1/3, cervical invasion, or positive lymph node metastasis.

Some studies have examined the diagnostic accuracy for the degree of differentiation with rapid intraoperative pathological diagnosis.[2-5] The overall accuracy was 84-92%: 93-97% for G1, 66-92% for G2, and 40-86% for G3. Lower diagnostic accuracies were achieved with the less differentiated cases. Rapid intraoperative pathological diagnosis was unable to diagnose 71% of histological types with poor prognosis. These studies concluded that preoperative endometrial curettage and biopsy need to be used in conjunction with intraoperative pathological diagnosis to increase the diagnostic accuracy of the histological type.[6]

A number of studies have indicated that the indications for lymphadenectomy are determined by the intraoperative degree of differentiation and extent of myometrial invasion. However, there are no standardized criteria. Cases in which lymphadenectomy could be omitted were reported to be: G1 with <1/3 myometrial invasion,[1,7] G2 with <1/3 myometrial

invasion,[2] G1 with <1/2 myometrial invasion,[4] and G1/G2 with less than inner 1/3 myometrial invasion.[6]

The above discussion includes the use of rapid pathological diagnosis to determine the histological type and degree of differentiation. However, a consensus has yet to be reached on how this method can be used to determine the indications for lymphadenectomy and omentectomy. In addition, there have not been any prospective studies on whether outcomes are improved using rapid pathological diagnosis.

【References】

1. Teng N, Rustum NA, Bahador A, Bookman MA, Campos S, Cho KR, et al. NCCN Practice Guidelines in Oncology Version1.2005. Uterine cancers. http：//www.nccn.org/professionals /physician(guideline)
2. Zorlu CG, Kuscu E, Ergun Y, Aydogdu T, Cobanoglu O, Erdas O. Intraoperative evaluation of prognostic factors in stage I endometrial cancer by frozen section：how reliable？ Acta Obstetracia et Gynecologica Scandinavica 1993, 72：382-5(Level III)
3. Kayikoglu F, Boran N, Meydanli MM, Tulunay G, Kose FM, Bulbul D. Is frozen-section diagnosis a reliable guide in surgical treatment of stage I endometrial carcinoma？ Acta Oncologica 2002；41：444-6(Level III)
4. Kucera E, Kains Ch, Reinthaller A, Sliutz G, Leodolter S, Kucera H, et al. Accuracy of intraoperative frozen-section diagnosis in stage □ endometrial adenocarcinoma Gynecol Obstet Invest. 2000；49：62-6(Level III)
5. Quinlivan JA, Petersen RW, Nicklin JL. Accuracy of frozen section for the operative management of endometrial cancer British journal of obstetrics and gynecology 2001；108：798-803(Level III)
6. Shim JU, Rose PG, Reale FR, Soto H, Tak WK, Hunter RE. Accuracy of frozen-section diagnosis at surgery in clinical stage I and II endometrial carcinoma Am J Obstet Gynecol. 1992；166：1335-8(Level III)
7. Altintas A, Cosar E, Varder MA, Demir C, Tuncer I. Intraoperative assessment of depth of myometrial invasion in endometrial carcinoma Eur. J. Gynec. Oncol. 1999；20：329-31(Level III)

CQ10

How should the degree of myometrial invasion be determined intraoperatively?

Recommendations

An incision is made in the uterine wall at the site of the deepest invasion according to the preoperative MRI findings and the macroscopic findings of the resected uterus. The depth of myometrial invasion should be confirmed by macroscopic examination of the sectioned surface (Grade C).

Background and Objectives

We examined methods of intraoperatively determining the depth of myometrial invasion, including the accuracy of rapid intraoperative pathological diagnosis. We examined the indications for the surgical techniques, in particular lymphadenectomy.

Explanations

The depth of myometrial invasion is determined by making an incision in the uterine wall at the site of the deepest invasion according to the preoperative MRI findings and the macroscopic findings of the resected uterus. The cut surface is then examined macroscopically. The area of lateral (elevated) growth is excluded. The depth of invasion is compared with the uterine wall thickness. If the tumor is extensive, the original wall thickness may be unclear. For G1 disease, the area of deepest myometrial invasion often shows expansive spread, so the greatest depth of invasion is easily determined. In G3 disease, the tumor does not form large cancer nests at the site of deepest invasion, and the greatest depth of invasion is often difficult to determine macroscopically. This leads to reduced accuracy for macroscopic determinations of the depth of myometrial invasion.[1]

The diagnostic accuracy for myometrial invasion (<1/2, >1/2) by macroscopic observation is 88-91%.[2,3] In particular, macroscopic diagnosis of G2/G3 lesions is reported to be difficult.[4] The diagnostic accuracy for myometrial invasion by rapid intraoperative pathological diagnosis was reported to be 87-91% in one study (if classified as confined to the endometrium: inner 1/3, middle 1/3, outer 1/3),[5-7] and 95% in another study (myometrial invasion: <1/2, >1/2).[8] Rates of correct diagnosis have been reported to be higher with greater numbers of sections.[9] When rapid intraoperative pathological diagnosis is combined with macroscopic examination, the diagnostic accuracy rises to 97%.[10] However, the findings in 33% of G3 cases made by rapid intraoperative pathological diagnosis were inconsistent with those determined from fixed specimens.[11] There are still problems that need to be addressed in the determination of myometrial invasion for G3 tumors.[12]

The NCCN Guidelines (version 1, 2005)[1] state that lymphadenectomy can be omitted if the preoperative investigations are negative for myometrial invasion, or for G1 disease with myometrial invasion confined to the inner 1/3 of the uterine wall. They also stated that, ideally, rapid pathological diagnosis should be used to determine the degree of differentiation and whether there is myometrial invasion. A number of studies have attempted to determine

the indications for lymphadenectomy based on the intraoperative degree of differentiation and myometrial invasion, although no standardized criteria have been agreed upon.[2,5,7,9,11]

Omental metastases were detected in 20% of cases with >1/2 myometrial invasion.[13] Omentectomy and histopathological evaluation of the extent of dissemination are indicated if the degree of myometrial invasion is >1/2.

As mentioned above, there is no consensus on the indications for lymphadenectomy and omentectomy based on rapid intraoperative pathological diagnosis. Our search of the literature yielded no prospective studies examining whether outcomes are improved using rapid pathological diagnosis. In addition, rapid pathological diagnosis cannot be performed in all institutions, and it is therefore unreasonable to use such a diagnostic method as a standard.

【References】

1. Teng N, Rustum NA, Bahador A, Bookman MA, Campos S, Cho KR, et al. NCCN Practice Guidelines in Oncology v.1.2005. Uterine cancers. http：//www. nccn.org/professionals/physician(guideline)
2. Doering DL, Barnhill DR, Weiser EB, Burke TW, Woodward JE, Park RC. Intraoperative evaluation of depth of myometrial invasion in stage I endometrial adenocarcinoma. Obstetrics & Gynecology 1989；74：930-3(Level III)
3. Vorgias G, Hintipas E, Katsoulis M, Kalinoglou N, Dertimas B, Akrivos T. Intraoperative gross examination of myometrial invasion and cervical infiltration in patients with endometrial cancer：decision-making accuracy. Gynecol Oncol 2002；85：483-6(Level III)
4. Goff BA, Rice LW. Assessment of depth of myometrial invasion in endometrial adenocarcinoma. Gynecol Oncol 1990；38：46-8(Level III)
5. Zorlu CG, Kuscu E, Ergun Y, Aydogdu T, Cobanoglu O, Erdas O. Intraoperative evaluation of prognostic factors in stage I endometrial cancer by frozen section：how reliable？ Acta Obstetracia et Gynecologica Scandinavica 1993, 72：382-5(Level III)
6. Kayikioglu F, Boran N, Meydanli MM, Tulunay G, Kose FM, Bulbul D. Is frozen-section diagnosis a reliable guide in surgical treatment of stage I endometrial carcinoma？ Acta Oncologica 2002；41：444-6(Level III)
7. Shim JU, Rose PG, Reale FR, Soto H, Tak WK, Hunter RE. Accuracy of frozen-section diagnosis at surgery in clinical stage I and II endometrial carcinoma Am J Obstet Gynecol. 1992；166：1335-8(Level III)
8. Quinlivan JA, Petersen RW, Nicklin JL. Accuracy of frozen section for the operative management of endometrial cancer British journal of obstetrics and gynecology 2001；108：798-803(Level III)
9. Kucera E, Kains Ch, Reinthaller A, Sliutz G, Leodolter S, Kucera H, et al. Accuracy of intraoperative frozen-section diagnosis in stage I endometrial adenocarcinoma Gynecol Obstet Invest. 2000；49：62-6(Level III)
10. Malviya VK, Deppe G, Malone JMJ, Sundareson AS, Lawrence WD. Reliability of frozen section examination in identifying poor prognostic indicators in stage I endometrial adenocarcinoma. Gynecol Oncol 1989；34：299-304(Level III)
11. Altintas A, Cosar E, Varder MA, Demir C, Tuncer I. Intraoperative assessment of depth of myometrial invasion in endometrial carcinoma Eur. J. Gynec. Oncol. 1999；20：329-31(Level III)
12. Sun T, Ho Y, Kuramoto H. Evaluation of intraoperative macroscopic diagnosis of myometrial invasion for uterine body cancer. International Journal of Clinical Oncology. 1994; 29:1942-7 (Level III) (in Japanese)
13. Saygili U, Kavaz S, Altunyurt S, Uslu T, Koyuncuoglu M, Erten O. Omentectomy, peritoneal biopsy and appendectomy in patients with clinical stage I endometrial carcinoma. Int J Gynecol Cancer 2001；11：471-4(Level III)

CQ11

Is rapid intraoperative pathological diagnosis useful for the detection of lymph node metastases?

Recommendations

We examined the status of lymph node metastases as determined by rapid intraoperative pathological diagnosis. The results indicated that there was insufficient evidence to recommend any change in surgical techniques (Grade C).

Background and Objectives

Attempts have been made to reduce intra- and postoperative complications and adverse reactions by the following processes: individualization of uterine body cancer surgery and identification of cases in which pelvic and para-aortic lymphadenectomy can be omitted. In this section, we will review past studies to determine whether accurate diagnosis of lymph node metastases can be made by rapid intraoperative pathology, and whether pelvic and para-aortic lymphadenectomy can be omitted in cases negative for lymph node metastases.

Explanations

Our search of the available literature yielded no studies investigating patients with suspected metastases from uterine body cancer and the omission of lymphadenectomy after submitting specimens for rapid intraoperative pathological diagnosis. We did find a study of cervical cancer, regarding frozen sections and fixed specimens of dissected lymph nodes. The specificity in the frozen specimens was 100%, but sensitivity was low at 68%. These results indicated that the wrong diagnosis might be made using frozen specimens of lymph nodes with very small metastatic lesions.[1] Similar studies have been conducted for prostate and breast cancer, but no consensus has been reached.[2-4] To answer this clinical question, the following issues must be addressed: how can a surgeon accurately detect lymph node metastases intraoperatively,[5] and how to achieve diagnostic accuracy with frozen sections. This will require improvements in the accuracy of visual examination and palpation of lymph nodes, standardized methods of removing lymph nodes, and accurate pathological diagnosis. These issues are presently under evaluation in clinical trials. In addition, the benefits of intraoperative sentinel lymph node biopsy have not been established.

【References】

1. Bjornsson BL, Nelson BE, Reale FR, Rose P. Accuracy of frozen section for lymph node metastasis in patients undergoing radical hysterectomy for carcinoma of the cervix . Gynecol Oncol 1993；51：50-3(Level III)
2. Dixon JM, Mamman U, Thomas J. Accuracy of intraoperative frozen-section analysis of axillary nodes. Br J Surg 1999；86：392-5(Level III)
3. Young MPA , Kirby RS, O'Donoghue EPN, Parkinson MC. Accuracy and cost of intraoperative lymph node frozen sections at radical prostatectomy. J Clin Pathol 1999；52：925-7(Level III)
4. Chao C, Wong SL, Ackerman D, Simpson D, Carter MB, Brown CM, et al. Utility of intraoperative frozen section analysis of sentinel lymph nodes in breast cancer. Am J Surg 2002；182：609-15(Level III)

5. Arango HA , Hoffman MS, Roberts WS, Decesare SL, Fiorica JV, Drake J. Accuracy of lymph node palpation to determine need for lymphadenectomy in gynecologic malignancies Obstet Gynecol 2000；95：553-6(Level III)

CQ12

Is positive peritoneal cytology an independent factor associated with a poor prognosis?

Recommendations

Positive peritoneal cytology is not an independent factor associated with a poor prognosis if surgery is performed to accurately determine the stage, and if there are no other factors associated with a poor prognosis apart from positive peritoneal cytology, or no findings of extrauterine spread (Grade B).

Background and Objectives

In 1988, FIGO adopted a new staging classification system for uterine body cancer. In this system, patients with positive peritoneal cytology are classified as stage IIIa. Positive peritoneal cytology has been established as a factor associated with a poor prognosis by univariate analysis, although the question of whether it is an independent factor has not yet been resolved.

Explanations

The relationship between positive peritoneal cytology and the prognosis is affected by whether the stage is determined as the clinical or surgical stage. A number of studies have reported that positive peritoneal cytology is an independent prognostic factor in clinical staging,[1,2] and other studies have found that it is not an independent prognostic factor.[3,4] Studies with patients in whom the retroperitoneal lymph nodes were thoroughly examined and surgery was performed to determine the surgical stage found that if the tumor was confined to the uterus, positive peritoneal cytology was not a predictor for a poor prognosis.[5,6] Some studies reported that if the tumor had spread to an extrauterine site, positive peritoneal cytology became a factor associated with a poor prognosis.[7,8] In studies where lymph nodes were not examined in all cases, or where evaluation of surgical stages also included patients who also underwent preoperative radiotherapy, some reported that positive peritoneal cytology was a factor associated with a poor prognosis,[9,10] although others stated that it was not a factor associated with a poor prognosis.[11-14] NCCN (version 1, 2005) recommends monitoring for patients with G1 and G2 uterine body cancer with tumor confined to the endometrium and otherwise positive only for peritoneal cytology.[15] Summarizing the above studies, positive peritoneal peritoneal cytology is often accompanied by other factors associated with a poor prognosis (such as deep myometrial invasion, G3 disease, and findings of extrauterine spread). If there are no findings of extrauterine spread and no other factor associated with a poor prognosis , positive peritoneal cytology is not considered to affect recurrence or survival time. If there are findings of extrauterine spread or other factors associated with a poor prognosis, positive peritoneal cytology is associated with distant metastasis and intra-abdominal recurrence, and therefore with reduced survival time.[7] In other words, positive peritoneal lavage cytology can be said to be a factor that amplifies the effect on survival of other factors associated with a poor prognosis.[8]

【References】

1. Kashimura M, Sugihara K, Toki N, Matsuura Y, Kawagae T, Kamura T, et al. The significance of peritoneal cytology in uterine cervix and endometrial cancer. Gynecol Oncol 1997；67：285-90(Level II)
2. Obermair A, Geramou M, Tripcony L, Nicklin JL, Perrin L, Crandon AJ. Peritoneal cytology：impact on disease-free survival in clinical stage I endometrioid adenocarcinoma of the uterus. Cancer lett 2001；164：105-10(Level III)
3. Konski A, Poulter C, Keys H, Rubin P, Beecham J, Doane K. Absence of prognostic significance, peritoneal dissemination and treatment advantage in endometrial cancer patients with positive peritoneal cytology. Int J Radiat oncol Biol Phys 1988；14：49-55(Level III)
4. Hirai Y, Fujimoto I, Yamauchi K, Hasumi K, Masubuchi K, Sano Y. Peritoneal fluid cytology and prognosis in patients with endometrial carcinoma. Obstet Gynecol 1989；73：335-8(Level III)
5. Kasamatsu T, Onda T, Katsumata N, Sawada M, Yamada T, Tsunematsu R, et al. Prognostic significance of positive peritoneal cytology in endometrial carcinoma confined to the uterus. Br J Cancer 2003；88：245-50(Level II)
6. Ebina Y, Hareyama H, Sakuragh N, Yamamoto R, Furuya M, Sogame M, et al. Peritoneal cytology and its prognostic value in endometrial carcinoma. Int Surg 1997；82：244-8(Level II)
7. Kadar N, Homesley HD, Malfetano JH. Positive peritoneal cytology is an adverse factor in endometrial carcinoma only if there is other evidence of extrauterine disease. Gynecol Oncol 1992；46：145-9(Level II)
8. Takeshima N, Nishida H, Tabata T, Hirai Y, Hasumi K. Positive peritoneal cytology in endometrial cancer：enhacement of other prognostic indicators. Gynecol Oncol 2001；82：470-3(Level III)
9. Turner DA, Gershenson DM, Atkinson N, Sneige N, Wharton T. The prognostic significance of peritoneal cytology for stage I endometrial cancer. Obstet Gynecol 1989；74：775-80(Level III)
10. Harouny VR, Sutton GP, Clark SA, Geisler HE, Stehman FB, Ehrlich CE. The importance of peritoneal cytology in endometrial carcinoma. Obstet Gynecol 1988；72：394-8(Level III)
11. Saji F, Kamiura S, Morishige K, Yamamoto T, Ota Y, Ohira H, et al. Is there significance in ascitic cytology (1982-1998) of T1 and T2 uterine body cancer? The World of Obstetrics and Gynecology 2003; 55:83-7 (Level III) (in Japanese)
12. Tebeu PM, Popowski GY, Verkooijen HM, Casals J, Ludicke F, Usel M, et al. Impact of peritoneal cytology on survival of endometrial cancer patients treated with surgery and radiotherapy. Br J Cancer 2003；89：2023-36(Level III)
13. Mazurka JL, Krepart GV, Lotocki RJ. Prognostic significance of positive peritoneal cytology in endometrial carcinoma. Am J Obstet Gynecol 1988；158：303-6(Level III)
14. Yazigi R, Piver MS, Blumenson L. Malignant peritoneal cytology as prognostic indicator in stage I endometrial cancer. Obstet Gynecol 1983；62：359-62(Level III)
15. Teng N, Rustum NA, Bahador A, Bookman MA, Campo S, Cho KR, et al. NCCN practice Guidelines in Oncology Version1.2005. Uterine cancers. http：//www.nccn.org/professionals/physician(guideline)

CQ13

Is rapid intraoperative peritoneal cytology necessary for determination of the surgical technique?

Recommendations

There is insufficient evidence to support deciding the surgical technique based on the results of rapid intraoperative peritoneal cytology (Grade C).

Background and Objectives

In 1988, FIGO adopted a new staging classification system for uterine body cancer. Evaluation by peritoneal cytology became an essential part of staging. In this section, we will review the literature to determine whether the degree of tumor malignancy and metastastic status can be determined by intraoperative evaluation of peritoneal cytology, and whether surgical techniques should be modified according to the results.

Explanations

All available studies of peritoneal cytology in patients with uterine body cancer have involved postoperative evaluation. We were unable to find any clinical studies of the use of rapid intraoperative peritoneal cytology in determining the surgical technique. For uterine cervical cancer, some studies have compared exfoliative cytology and frozen specimens in evaluating lymph node metastases and peritoneal dissemination.[1,2] One study also used imprint cytology with immunostaining of antioncogene p53 to examine the degree of malignancy.[3] These studies are still at the clinical trial level, however. In addition, many studies have concentrated on examination of sentinel lymph nodes to evaluate breast cancer metastasis using imprint cytology. There is insufficient evidence at present to support the use of this method as a standard.[4] Extrauterine spread of cancer is reported to be a factor associated with a poor prognosis in patients with positive peritoneal cytology.[5-8] For patients with positive rapid intraoperative peritoneal cytology, consideration should be given to modification of the surgical technique from the aspect of cytoreductive surgery.[9]

【References】

1. Hasenburg A, Ledet SC, Ardaman T, Levy T, Kieback DG. Evaluation of lymph nodes in squamous cell carcinoma of the cervix：touch imprint cytology versus frozen section histology. Int J Gynecol Cancer 1999；9：337-41(Level III)
2. Anastasiadis P, Sivridis E, Koutlaki N, Tamiolakis D, Galazios G, Tsikouras P. The significance of rapid intraoperative cytology in the evaluation of intraperitoneal and retroperitoneal spread of cervical cancer. Gynecol Oncol 2002；84：102-9(Level III)
3. Athanassiadou P, Petrakakou E, Liossi A, Nakopoulou L, Zerva C, Dimopoulos A, et al. Prognostic significance of p53, bcl-2and EGFR in carcinoma of the endometrium. Acta Cytol 1999；43：1039-44(Level III)
4. Karamlou T, Johnson NM, Chan B, Franzini D, Mahin D. Accuracy of intraoperative touch imprint cytologic analysis of sentinel lymph nodes in breast cancer. Am J Surg 2003；185：425-8(Level III)

5. Kadar N, Homesley HD, Malfetano JH. Positive peritoneal cytology is an adverse factor in endometrial carcinoma only if there is other evidence of extrauterine disease. Gynecol Oncol 1992；46：145-9(Level II)
6. Takeshima N, Nishida H, Tabata T, Hirai Y, Hasumi K. Positive peritoneal cytology in endometrial cancer：enhacement of other prognostic indicators. Gynecol Oncol 2001；82：470-3(Level III)
7. Hirai Y, Fujimoto I, Yamauchi K, Hasumi K, Masubuchi K, Sano Y. Peritoneal fluid cytology and prognosis in Patients with endometrial carcinoma. Obstet Gynecol. 1989；73：335-8(Level III)
8. Yanoh K, Takeshima N, Hirai Y, Minami A, Tsuzuku M, Toyoda N, et al. Identification of a high-risk subgroup in cytology-positive stage III a endometrial cancer. Acta Cytol. 2001；45：691-6(Level III)

Kuramoto H, Jobo T, Arai M. Malignant tumor of the uterine corpus. F treatment method, i surgical method. In: Shin Josei Igakudaikei 35. Nakayama Shoten 2001; 169-86 (Level IV)

CQ14

Will endoscopic surgery become the standard surgical technique?

Recommendations

At present, endoscopic surgery has not been established as the standard surgical technique (Grade D).

Background and Objectives

In gynecological surgery, laparoscopic surgery is often performed for reasons of cosmetics, and reducing the duration of hospitalization, medical expenses and patient burden due to surgery. There is a body of thought that advises caution in applying laparoscopic surgery to malignant tumors. In this section, we will examine whether laparoscopy could become a standard technique as in conventional laparotomy for uterine body cancer.

Explanations

Although the subject numbers were small, a randomized trial was conducted compared laparotomy and laparoscopy-assisted vaginal total hysterectomy for uterine body cancer. The results indicated that laparoscopy-assisted vaginal total hysterectomy produced few complications in the perioperative stage, and there was no difference in patient outcomes compared to laparotomy.[1] Some retrospective studies have also compared laparotomy and laparoscopy, stating that these procedures produce similar results in terms of patient outcomes and the number of resected lymph nodes.[2-8] It has been suggested that laparoscopy could become a standard procedure in the early stages of uterine body cancer.[4] Laparoscopic techniques vary between reports, however, and have yet to be standardized. In addition, in laparoscopy-assisted vaginal total hysterectomy, there have been reports of a significantly higher proportion of cases with positive peritoneal cytology, thought to be due to manipulator operation.[9] For this method, there are have also been reports of vaginal stump recurrence[10] and recurrence at the trocar puncture site.[11] At the present time, there is insufficient evidence to recommend laparoscopy as the standard technique which will replace laparotomy. More clinical studies with large patient numbers are required.

【References】

1. Malur S, Possover M, Michels W, Schneider A. Laparoscopic-assisted vaginal versus abdominal surgery in patients with endometrial cancer- A prospective randomized trial. Gynecol Oncol 2001；80：239-44(Level II)
2. Eltabbakh GH. Analysis of survival after laparoscopy in women with endometrial carcinoma. Cancer 2002；95：1894-901(Level III)
3. Fram KM. Laparoscopiically assisted vaginal hysterectomy versus bdominal hysterectomy in stage I endomtrial cancer. Int J Gynecol Cancer 2002；12：57-61(Level III)
4. Funamoto H, Kojima Y, Hashimoto G, Maida Y, Arai N, Ametani Y, et al. Laparoscopy for uterine body cancer. Obstet and Gynecol 2000; 67:927-32 (Level IV) (in Japanese)
5. Litta P, Fracas M, Pozzan C, Merlin F, Saccardi C, Sacco G, et al. Laparoscopic management of early stage endometrial cancer. Eur J Gynaec Oncol 2003；24：41-4(Level III)

6. Lim BK, Lavie O, Bolger B, Lopes T, Monaghan JM. The role of laparoscopic surgery in the management of endometrial cancer. BJOG 2000；107：24-7(Level III)
7. Langebrekke A, Istre O, Hallqvist AC, Hartgill TW, Onsrud M. Comparison of laparoscopy and laparotomy in patients with endometrial cancer. J Am Assoc Gynecol Laparosc 2002；9：152-7(Level III)
8. Manolitsas TP, McCartney AJ. Total laparoscopic hysterectomy in the management of endometrial carcinoma. J Am Assoc Gynecol Laparosc 2002；9：54-62(Level III)
9. Sonoda Y, Zerbe M, Smith A, Lin O, Barakat RR, Hoskins WJ. High incidence of positive peritoneal cytology in low-risk endometrial cancer treated by laparoscopically assisted vaginal hysterectomy. Gynecol Oncol 2001：80：378-82(Level III)
10. Chu CS, Randall TC, Bandera CA, Rubin SC. Vaginal cuff recurrence of endometrial cancer treated by laparoscopic-assisted vaginal hysterectomy. Gynecol Oncol 2003；88：62-5(Level IV)
11. Muntz HG, Goff BA, Madsen BL, Yon JL. Port-site recurrence after laparoscopic surgery for endometrial carcinoma. Obstet Gynecol 1999；93：807-9(Level IV)

CQ15

Can lymphadenectomy be omitted if sentinel node biopsy is performed?

Recommendations

There is insufficient evidence to support omission of retroperitoneal lymphadenectomy if the sentinel lymph node concept is applied (Grade C).

Background and Objectives

As part of the trend to individualization and minimization of surgery for uterine body cancer, attempts are being made to apply the sentinel lymph node concept to uterine body cancer. In this section, we will examine reports of such attempts, and whether the sentinel lymph node concept can be applied to uterine body cancer treatment.

Explanations

Methods of identifying sentinel lymph nodes are the dye method, RI method, and a combination of the two methods. There are also different types of tracers.[1-2] In addition, the injection site can be the cervical region, the uterine body, or both. A standardized method has not been established.[4] Niikura et al. were able to identify an average of 3.1 sentinel lymph nodes in 23 out of 28 patients by infusion of technetium-99m using a hysteroscope.[5] The lymph nodes most often detected are the para-aortic, external iliac lymph, and obturator lymph nodes. At present, the sentinel lymph node concept has not yet been established as applicable for uterine body cancer. Sentinel lymph nodes should therefore be identified, and compared with the lymphadenectomy findings. Clinical trials are required to clarify this question.

【References】

1. Echt ML, Finan MA, Hoffman MS, Kline R, Robert W, Fiorica JV. Detection of sentinel lymph nodes with lymphazurin in cervical uterine, and vular malignancy. South Med J 1999；92：204-8(Level IV)
2. Gargiulo T, Giusti M, Bottero A, Leo L, Brokaj L, Armellino F, et al. Setinel lymph node（SLN）laparoscopic assessment early stage in endonmetrial cancer. Minerva Ginecol 2003；55：259-62(Level III)
3. Pelosi E, Arena V, Baudino B, Bello M, Giusti M, Gargiulo T, et al. Pre-operative lymphatic mapping and intra-operative sentinel lymph node detection in early stage endometrial cancer. Nucl Med Comm 2003；24：971-5(Level III)
4. Holub Z, Jabor A, Kliment L. Comparison of two procedures for sentinel lymph node detection in patients with endometrial cancerz：A pilot study. Eur J Gynaec Oncol 2002；23：53-7(Level IV)
5. Niikura H, Okamura C, Utsunomiya H, Yoshinaga K, Ito K, Yaegashi N, et al. Sentinel lymph node detection in patients with endometrial cancer. Gynecol Oncol 2004：92；669-74(Level III)

CQ16

Is radiotherapy useful for inoperable patients who are elderly or who have other medical conditions?

Recommendations

Radiotherapy is recommended for these patients (Grade B).

Background and Objectives

Radiotherapy is performed for patients who are unsuitable for surgery for any reason.

Explanations

Surgery is the treatment of first choice for uterine body cancer. However, if patients are unsuitable for surgery because they are elderly or have other medical conditions, then radiotherapy is useful. Generally, the therapeutic outcomes for radiotherapy are inferior to those from surgery. However, since patient backgrounds and methods of staging differ between these treatment modalities, it is difficult to compare their outcomes. According to retrospective studies on mainly clinical stage I patients, the 5 year survival rate for radiotherapy alone was 60-80%.[1-7]

Definitive radiotherapy is generally performed by a combination of whole-pelvis external-beam and intracavitary irradiation. Intrauterine tandem insertion of various applicators is the usual method overseas. In Japan, there are technical difficulties due to the low proportion of large uteri suitable for this method, limiting its popularity. Unlike the standard treatments for cervical cancer, standardized guidelines have not been established for uterine body cancer. Therefore, there are no clear criteria for which patients should concurrently undergo whole-pelvis external-beam irradiation. In inoperable patients who are elderly or have other medical conditions, radiotherapy should be considered after evaluation of their performance status. The quality of intracavitary irradiation can vary between institutions. Radiation source placement, evaluation method of dose, optimum dose, and fractionation regimen have not been standardized as for cervical cancer.

【References】

1. Grigsby PW, Kuske RR, Perez CA, Walz BJ, Camel MH, Kao MS, et al. Medically inoperable stage I adenocarcinoma of the endometrium treated with radiotherapy alone. Int J Radiat Oncol Biol Phys 1987；13：483-8(Level III)
2. Taghian A, Pernot M, Hoffstetter S, Luporsi E, Bey P. Radiation therapy alone for medically inoperable patients with adenocarcinoma of the endometrium. Int J Radiat Oncol Biol Phys 1988；15：1135-40(Level III)
3. Lehoczky O, Bosze P, Ungar L, Tottossy B. Stage I endometrial carcinoma：treatment of nonoperable patients with intracavitary radiation therapy alone. Gynecol Oncol 1991；43：211-6(Level III)
4. Kupelian PA, Eifel PJ, Tornos C, Burke TW, Delclos L, Oswald MJ. Treatment of endometrial carcinoma with radiation therapy alone. Int J Radiat Oncol Biol Phys 1993；27：817-24(Level III)
5. Rouanet P, Dubois JB, Gely S, Pourquier H. Exclusive radiation therapy in endometrial carcinoma. Int J Radiat Oncol Biol Phys 1993；26：223-8(Level III)

6. Chao CK, Grigsby PW, Perez CA, Mutch DG, Herzog T, Camel HM. Medically inoperable stage I endometrial carcinoma: a few dilemmas in radiotherapeutic management. Int J Radiat Oncol Biol Phys 1996; 34: 27-31(Level III)
7. Knocke TH, Kucera H, Weidinger B, Holler W, Potter R. Primary treatment of endometrial carcinoma with high-dose-rate brachytherapy: results of 12 years of experience with 280 patients. Int J Radiat Oncol Biol Phys 1997; 37: 359-65(Level III)