

THE ROLES OF ENDOSCOPY IN ENDOMETRIAL CANCER

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SUMMARY

Advancements in technology have increased the availability of valuable minimally invasive techniques for gynecologists to use in the management of patients with endometrial cancer. Hysteroscopy has recently been confirmed as an accurate diagnostic method for endometrial carcinoma. Several retrospective studies have found increased positive peritoneal cytology in women who underwent hysteroscopy, but recent studies have indicated that there is currently no evidence to suggest that diagnostic hysteroscopy increases the risk of malignant cells spreading into the peritoneal cavity, or worsens the prognosis in women with endometrial carcinoma. Laparoscopy plays an important role in treating endometrial cancer. Most studies have shown no differences in recurrence rates or survival between patients who underwent laparoscopic or abdominal staging surgery. Laparoscopy offers many advantages, including avoidance of an abdominal incision, a shorter hospital stay, and a probable more rapid recovery time. [*Taiwan J Obstet Gynecol* 2008;47(4):379–383]

Key Words: endometrial cancer, hysteroscopy, laparoscopy, staging surgery

Introduction

Endometrial cancer is one of the most common female malignancies in the United States, and has increased in incidence in Taiwan in recent decades. The annual incidence rates are 23.7 per 100,000 and 5.31 per 100,000, respectively. The standard management of endometrial cancer involves a staging laparotomy with total hysterectomy and bilateral salpingo-oophorectomy, combined with pelvic and/or para-aortic lymph node dissection. The benefits of complete surgical treatment include not only a reduction in mortality and recurrence rate, but also improvements in the patients' qualities of life. With advances in minimally invasive techniques, endoscopy has been increasingly applied for the diagnosis and treatment of endometrial cancer.

Although many studies have shown promising results regarding the use of endoscopy in the management of endometrial cancer, some concerns still exist and merit

further discussion and investigation. These issues include the efficacy of hysteroscopy as a diagnostic tool compared with fractional dilatation and curettage (D&C), the potential risk of retrograde dissemination of cancer cells by the distension media, and the feasibility of laparoscopy for the standard staging operation. This review discusses evidence from the literature regarding these issues in endoscopy used in the management of endometrial cancer.

Hysteroscopy is Superior to Fractional D&C in Revealing Lesions in Endometrial Cancer

Gynecologists usually use ultrasonography and fractional D&C as diagnostic tools to detect endometrial lesions. However, ultrasonographic examination is not reliable, and false-negative results for endometrial cancer are not uncommon. D&C relies on blind sampling of endometrial specimens and has recently been found to be unreliable for detecting early or persistent carcinomas following conservative treatment. Clark et al [1] found that hysteroscopy is highly accurate and useful in diagnosing, rather than excluding, endometrial cancer in women with abnormal uterine bleeding.



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A recent study performed by Bedner et al [2] compared the effectiveness of D&C with hysteroscopy and guided biopsy in perimenopausal women at risk of endometrial hyperplasia or cancer. They found that hysteroscopy with directed biopsy was more sensitive than D&C for detecting all types of uterine lesions. Out of a total of 734 patients, hysteroscopy failed to diagnose just four cases of endometrial pathology, compared with 21 cases undiagnosed by D&C. They also found that curettage performed after hysteroscopy and directed biopsy did not improve the detection rate of endometrial cancer.

The Effect of Retrograde Dissemination of Cancer Cells in Hysteroscopy

In a prospective randomized study, Nagele et al [3] compared normal saline and carbon dioxide as distension media in 30 patients undergoing hysteroscopy and laparoscopy for infertility. Endometrial cells were present in the peritoneal fluid in 6.7% of patients before hysteroscopy and in 25% after hysteroscopy, including 23.3% of patients using normal saline and 26.7% using carbon dioxide. These data suggest that malignant endometrial cells were introduced into the peritoneal cavity during hysteroscopy regardless of the use of normal saline or carbon dioxide as the distension medium. Obermair et al [4] performed a retrospective cohort analysis of 113 patients who underwent staging laparotomy and compared groups who underwent D&C with or without prior diagnostic fluid hysteroscopy. Compared with D&C alone (2.6% [1/39]), patients undergoing D&C with diagnostic fluid hysteroscopy had significantly higher positive or suspicious peritoneal cytology (12.2% [9/74]; $p=0.046$). No differences in myometrial invasion, histologic subtype or grade were noted. Zerbe et al [5] found similar results.

Kadar et al [6], however, found that positive peritoneal cytology was not an adverse factor in endometrial carcinoma, unless there was other evidence of extrauterine disease. They studied 269 clinical stage I and II endometrial cancer patients, 34 (12.6%) of whom had positive peritoneal cytology. The 5-year survival rate in patients with disease confined to the uterus was 73% and that in patients with extrauterine disease was 13% ($p<0.001$). Leveque et al [7] studied 19 patients with stage I endometrial cancer who underwent preoperative hysteroscopy. Seven (36.8%) of these patients had positive peritoneal washings at hysterectomy, but did not experience peritoneal recurrences. These studies showed that retrograde seeding of indolent cancer cells did not adversely influence prognosis.

Prospective Use of Hysteroscopy in the Diagnosis of Endometrial Cancer

Office hysteroscopy is an under-utilized technique. In a recent review, Isaacson [8] pointed out that, in comparison to nearly 100% of urologists who utilized office cystoscopy to evaluate bladder pathology, less than 20% of gynecologists utilized office hysteroscopy to evaluate intrauterine pathology. As a result, many women who could have benefited from the use of this technique were referred for more invasive and less useful procedures involving surgery and general anesthesia.

Gynecologists should, therefore, be encouraged to use hysteroscopy. Patients with suspected endometrial hyperplasia and scheduled for curettage should first undergo a hysteroscopy-directed endometrial biopsy or resection. The current indications for hysteroscopic diagnosis of patients with strongly suspected endometrial cancer include: (1) patients presenting with abnormal uterine bleeding and thickened endometrium; (2) patients needing a target biopsy to differentiate between atypical endometrial hyperplasia and cancer; and (3) for follow-up of patients with endometrial cancer receiving fertility-preserving treatment. Other prospective uses of hysteroscopy in the diagnosis and treatment of uterine cancer include: (1) in the differentiation between endometrial and cervical adenocarcinomas; (2) for verification of cervical extension of endometrial cancer if tumor fragments are seen in endocervical curettages; and (3) during fertility-preserving treatment of endometrial cancer.

Feasibility of Laparoscopic Staging of Endometrial Cancer

The Cancer Committee of the International Federation of Gynecology and Obstetrics have changed their staging classification from clinical- to surgicopathologic-based criteria. Adjuvant treatment recommendations are clearly influenced by information obtained from surgical staging. Traditional abdominal surgical staging is preferable to the vaginal approach, because the gynecologist can thoroughly assess the peritoneal cavity, obtain washings for cytology, guarantee removal of the adnexa, and sample the pelvic and para-aortic lymph nodes.

However, with advances in minimally invasive techniques, the laparoscopic-vaginal approach becomes more effective than the conventional transabdominal approach. There are some limitations associated with laparoscopic surgery, such as patient obesity, difficulty

of exposure in advanced cases, the inability to palpate tissues, and the possibility of rupture of cysts or lymph node capsules. However, laparoscopy has many advantages, including less tissue reaction, complete removal of blood clots and debris, and meticulous hemostasis, all of which lead to reduced postoperative pain following laparoscopy. Potential surgical complications, such as infection, hemorrhage and postoperative adhesions, may also be reduced with laparoscopy.

In a prospective randomized study comparing a laparoscopic-vaginal approach and the conventional abdominal approach for the treatment of patients with endometrial cancer, the yield of pelvic and para-aortic lymph nodes, duration of surgery, and incidence of postoperative complications were similar in both groups [9]. Another similar prospective study found that the majority of patients could be treated by laparoscopy with excellent surgical outcomes, shorter hospitalization, earlier recovery and improved quality of life, but at a higher financial cost. They concluded that laparoscopy was a suitable primary modality for the treatment of endometrial cancer [10]. Another recent study confirmed that fewer complications and shorter hospital stays were observed in the laparoscopy group, compared with the conventional treatment group [11].

Cancer cell dissemination caused by the uterine manipulator during laparoscopic hysterectomy is an issue of concern. A prospective study collected two sets of peritoneal washings, i.e. one before and one after the insertion of the Pelosi uterine manipulator. They found no difference between the two sets of washings in all patients (100%; $p < 0.001$); no patients with negative washings before insertion of the manipulator had positive washings after the insertion [12]. However, one recent study noted four cases of recurrence in the vaginal stump in laparoscopically-treated patients, and the authors suggested that efforts should be made during laparoscopic procedures to minimize the risk of vaginal recurrence [11]. Wang et al [13] suggested using a 1-0 Vicryl to close the cervix as the first step during laparoscopy, to prevent cancer cell contamination of the vaginal wall. They also suggested avoiding manipulator use while performing laparoscopic surgery for endometrial cancer, in order to minimize the risk of rapid vaginal cuff recurrence.

Feasibility of Laparoscopy in Obese Patients with Endometrial Cancer

The feasibility and safety of the use of laparoscopy in obese women with endometrial cancer is another issue

of concern. Associated issues, such as the operation costs, hospital stay, patient recall of postoperative pain control, time to return to full activity and to work, may need to be considered. Eltabbakh et al [14] conducted a prospective study of laparoscopic surgery in all women with clinical stage I endometrial cancer and body mass indices between 28.0 and 60.0. Patients with similar characteristics who underwent laparotomy were included as a control. Laparoscopic surgery was successful in 88.1% of obese women, with an open conversion rate at 7.5% of patients. For the proportion of women who underwent lymphadenectomy, the incidence of complications, total cost, patient recall of postoperative pain, and patient satisfaction with management were all similar in both groups. However, laparoscopy was associated with a significantly longer operative time (194.8 vs. 137.7 minutes; $p < 0.001$), more pelvic lymph nodes removed (11.3 vs. 5.3; $p < 0.001$), a smaller drop in postoperative hematocrit (3.9 vs. 5.4; $p = 0.029$), less pain medication (32.3 vs. 124.1 mg; $p < 0.001$), and a shorter hospital stay (2.5 vs. 5.6 days; $p < 0.001$). There was also a trend towards earlier resumption of full activity (23.2 vs. 45.0 days; $p = 0.073$) and return to work (35.3 vs. 67.0 days; $p = 0.055$) among women who underwent laparoscopy. They concluded that laparoscopy was safe and feasible in most obese women with early stage endometrial cancer, and produced better outcomes than laparotomy. Operative endoscopy may, therefore, play an important role in treating patients with endometrial cancer.

Survival Following Laparoscopic Staging Surgery for Endometrial Cancer

Many studies have found similar recurrence and survival rates in patients treated by laparoscopy and laparotomy [9,11,15–22]. These studies reported some disadvantages of the laparoscopic approach, including prolonged operating time, increased blood loss, and increased cost during the learning period. However, trends suggest that laparoscopy will play an important role in the management of endometrial cancer in the near future [23].

Cho et al [11] reported on 10 years' experience of laparoscopic management of early uterine cancer in Korea, compared with patients treated by laparotomy. They found no significant differences between the two groups in terms of progression-free or overall survival, and they, therefore, concluded that laparoscopy was a valid alternative to conventional laparotomy, and does not worsen the prognosis of patients with early

endometrial carcinoma. Another retrospective review of women presenting with clinical stage I endometrial carcinomas found that women who underwent laparoscopy and those who underwent laparotomy had similar 2-year and 5-year estimated recurrence-free survival rates (93% vs. 94% and 90% vs. 92%, respectively), as well as similar 2-year and 5-year overall survival rates (98% vs. 96% and 92% vs. 92%, respectively). There was no apparent difference with regard to the sites of recurrence between the groups [18].

Kalogiannidis et al [22], in a prospective cohort study of 169 consecutive patients, reported that the recurrence rate in the laparoscopically assisted vaginal hysterectomy (LAVH) group was 8.7%, compared with 16% in the laparotomy group (not significant). The actuarial overall and disease-free survival rates in the LAVH group were 93% and 91%, respectively, compared with 86% and 84% in the total abdominal hysterectomy group (not significant).

Some studies further analyzed the risk factors for recurrence using univariate and multivariate analyses. One study found that surgical stage, tumor grade and histology (but not the surgical approach) had significant effects on survival [18], while another study found that histologic subtype was the only independent prognostic factor for disease-free survival, and that surgical technique again had no effect [22].

Conclusion

Advancements in technology have increased the availability of valuable minimally invasive techniques for gynecologists to use in the management of patients with endometrial cancer. Hysteroscopy is indispensable for the initial diagnosis and early detection of occult tumors or tumor recurrence. Although hysteroscopy could facilitate tumor cell dissemination into the pelvic cavity, retrograde seeding of indolent cancer cells does not appear to adversely influence prognosis. Laparoscopy plays an important role in treating endometrial cancer. It offers many advantages, including avoidance of an abdominal incision, a shorter hospital stay, and probably a more rapid recovery time. Moreover, metastatic disease can be detected laparoscopically. Most studies failed to show any difference in recurrence rates or survival between patients treated by laparoscopic or abdominal staging surgery. Laparoscopy could be performed in obese patients and resulted in better operation outcomes than laparotomy. A laparoscopic approach is, therefore, a feasible alternative to the conventional treatment of endometrial cancer.

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