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ORIGINAL ARTICLE

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Diagnosis of endometrial cancer by hysteroscopy does not increase the risk for microscopic extrauterine spread in early-stage disease

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Abstract The purpose of this study was to determine whether women with endometrial cancer have a higher incidence of microscopic extrauterine spread in early-stage disease when diagnosed by hysteroscopy compared with being diagnosed by dilatation and curettage (D&C) or endometrial biopsy (Pipelle). We retrospectively reviewed the medical records of 110 patients who had undergone surgical staging for endometrial cancer from January 1997 to December 2003. They all had a preoperative histological diagnosis of endometrial carcinoma without evidence of extrauterine disease. Diagnosis was made by hysteroscopy in 64 patients (58.2%), by D&C in 17 (15.5%), and by endometrial biopsy using a Pipelle device in 29 (26.3%). The groups were compared for known prognostic factors for microscopic extrauterine spread, including age, grade, stage, and vascular space involvement, and did not differ in these parameters. Microscopic intraperitoneal disease and positive peritoneal cytology were considered the primary endpoints of this analysis. Peritoneal cytology was positive in three of 110 (2.7%) patients. The presence of positive peritoneal cytology was not associated with hysteroscopy as the diagnostic procedure. We conclude that diagnosis of endometrial cancer by hysteroscopy does not increase the risk of microscopic intraperitoneal spread compared with diagnosis by D&C or endometrial biopsy (Pipelle).

Introduction

Carcinoma of the endometrium is the most common gynecologic malignancy [1]. It is usually diagnosed as an organ-confined disease, with 5-year disease-free survival rates of 90% and 80% for patients with stages IA and B disease, respectively [2]. Among the clinicopathologic factors that can be evaluated pre- and intraoperatively, myometrial invasion and tumor grade are well-recognized prognostic factors and predictors of extrauterine spread [3, 4]. Although there is some debate on whether a positive peritoneal cytology worsens the prognosis in the absence of further extrauterine disease, patients with organ-confined endometrial carcinoma who present with malignant cells in the peritoneal washing must be classified as stage IIIA according to the current International Federation of Gynecology and Obstetrics (FIGO) staging classification [5].

Diagnostic hysteroscopy is an effective method for evaluating the uterine cavity and visualizing pathologic conditions such as endometrial polyps, submucous fibroids, and focal endometrial abnormalities, including adenocarcinoma and its precursors [6, 7]. Albeit a common procedure, the role of hysteroscopy in diagnosing endometrial carcinoma is not established. The possibility of retrograde transtubaric seeding of malignant endometrial cells, an event related to increasing intrauterine pressure during hysteroscopy, is an issue of concern. Authors of a number of case reports believe, but have not proven, that there is abdominal dissemination of malignant cells during hysteroscopy in patients with endometrial carcinoma [8–12].

The aim of the current study was to evaluate the incidence of positive peritoneal washings in patients with endometrial carcinoma and to evaluate the risk for positive peritoneal cytology depending on the mode of diagnosis.

Materials and methods

We conducted a retrospective chart review on all endometrial cancer patients who had surgical staging procedures in the Department of Gynecology, Tel-Aviv Sourasky Medical Center, Israel, between January

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1997 and December 2003. Inclusion criteria were histologically proven endometrial carcinoma and informative peritoneal cytology. World Health Organization criteria were used for histologic classification. Surgical records and histology findings were used to determine the stage of disease according to the FIGO 1988 criteria [5].

Hysteroscopy and dilatation and curettage (D&C) were carried out under general anesthesia. Pipelle biopsies were taken with no anesthesia. The D&C and Pipelle procedures were performed according to standard criteria. Hysteroscopy was done using a 5-mm hysteroscope (Richard Wolf, Knittlingen, Germany). The uterine cavity was distended by a continuous flow of 0.9% saline solution at a final flow of 150 ml/min. Each procedure took less than 3 min.

After being diagnosed as having endometrial cancer (2–4 weeks after the diagnostic procedure), all 110 patients underwent a standard surgical procedure of total abdominal hysterectomy and bilateral salpingo-oophorectomy; 56 of them (51%) also had pelvic lymph node sampling. Peritoneal cytology was obtained before the hysterectomy by peritoneal washing of the Douglas pouch with 100–200 ml of sterile saline solution. After centrifugation at 3,000 g for 10 min, the pellets were stained with May-Grunwald-Giemsa and Papanicolaou stains.

The choice of diagnostic procedure was determined by technical considerations (including HMO coverage) and physician's preference. Student's *t*-test/analysis of variance (ANOVA) and Fisher's exact tests were used for statistical analysis.

Results

This analysis is based on the data of all the patients ($n = 110$) diagnosed in our department during the 7-year study period as having endometrial carcinoma with no evidence of extrauterine disease except for the results of peritoneal cytology. Seventeen patients (15.5%) were diagnosed by D&C, 29 (26.3%) by endometrial Pipelle biopsy, and 64 (58.2%) by hysteroscopy. The mean age of the patients was 66.5 years (range 30–90 years). Thirteen patients (12%) were stage IA, 64 (58%) were stage IB, 14 (13%) were stage IC, and 16 (15%) were stage II. Peritoneal cytology was positive in three of 110 cases (2.7%). Two of these patients had undergone hysteroscopy, and the third had a D&C procedure. The presence of malignant cells within the peritoneal fluid was not statistically associated with hysteroscopy ($P = 1.0$).

Discussion

Endometrial assessment is done by biopsy, D&C, or hysteroscopy. Dilatation and curettage had for many years been the method of choice for diagnosing endometrial pathology. In 60% of D&C procedures, however, less than half of the uterine cavity is curetted, thereby raising questions about the accuracy of this method [13]. The Pipelle endometrial biopsy procedure is accurate, safe, economical, and acceptable to patients, clinicians, and pathologists. Its reported detection rates were 99.6% and 91% in postmenopausal and premenopausal women, respectively [14]. Diagnostic hysteroscopy combined with histological examination of an endometrial aspiration or biopsy is, though, considered the "gold standard" for diagnosing intrauterine abnormalities [15, 16] and is recommended in women with abnormal uterine bleeding by evidence-based guidelines.

Performance of hysteroscopy involves forcing a flow of saline through the uterus to distend the endometrial cavity and thereby facilitate visualization while increasing the pressure inside the uterine cavity. This has raised the possibility that hysteroscopy may cause peritoneal seeding of malignant cells from the endometrium into the peritoneal cavity, whereupon an organ-confined disease would be converted to a metastatic one, changing the prognosis and the course of treatment. The authors of several case reports suspected that distention and irrigation of the uterine cavity during fluid hysteroscopy might cause tumor cell dissemination into the abdominal cavity in patients with endometrial carcinoma [8–12]. Leveque et al. [17] reported a high incidence of positive peritoneal cytology (37%) in 19 patients with stage IA–C endometrial carcinoma and assumed that hysteroscopy, which had been carried out preoperatively in all 19 cases, might have been the reason for this. Conversely, Selvaggi et al. [18] did not find that fluid hysteroscopy increased the risk of microscopic intraperitoneal spread in 147 patients with endometrial cancer when comparing hysteroscopy to D&C as the diagnostic procedure. In their report on 113 patients with endometrial carcinoma, Obermair et al. [19] found that positive peritoneal cytology was associated with a history of hysteroscopy, but they did not show any significant differences in short-term disease-free survival that could be related to the diagnostic procedure [20]. Finally, Zerbe et al. [21] reported a statistical difference in the frequency of positive peritoneal cytology in 64 endometrial cancer patients who had hysteroscopy versus those who did not. Given these controversial findings, we searched our own endometrial cancer database for the incidence of positive peritoneal cytology and any links to the preoperative diagnostic procedure.

We found no correlation between the diagnostic procedure (hysteroscopy, Pipelle biopsy, or D&C) and microscopic extrauterine dissemination of malignant cells from the endometrium into the peritoneal cavity. We therefore conclude that hysteroscopy is a well-tolerated, accurate, and sensitive tool that allows direct visualization and biopsy of focal or diffuse abnormalities of the endometrium without exposing the patient to the risk of dissemination of malignant cells.

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References

1. Greenlee RT, Murray T, Bolden S, Wingo PA (2000) Cancer statistics, 2000. CA Cancer J Clin 50:7–33
2. Wingo PA, Ries LA, Rosenberg HM, Miller DS, Edwards BK (1998) Cancer incidence and mortality, 1973–1995: a report card for the US. Cancer 82:1197–1207
3. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB (1987) Surgical pathologic spread patterns of endometrial cancer: a Gynecologic Oncology Group study. Cancer 60(suppl):2035–2041
4. Lampe B, Kurzl R, Handschmann P (1994) Prognostic factors that predict pelvic lymph node metastasis from endometrial carcinoma. Cancer 74:2502–2508
5. International Federation of Gynecology and Obstetrics (1989) Corpus cancer staging. Int J Gynecol Obstet 28:190
6. Nagele F, O'Connor H, Davies A, Badawy A, Mohamed H, Magos A (1996) 2500 outpatient diagnostic hysteroscopies. Obstet Gynecol 88:87–92
7. Schwarzler P, Concin H, Bosch H, Berlinger A, Wohlgenannt K, Collins WP, Bourne TH (1998) An evaluation of sonohysterography and diagnostic hysteroscopy for the assessment of intrauterine pathology. Ultrasound Obstet Gynecol 11:337–342
8. Romano S, Shimoni Y, Muralee D, Shalev E (1992) Retrograde seeding of endometrial carcinoma during hysteroscopy. Gynecol Oncol 44:116–118
9. Schmitz MJ, Nahhas WA (1994) Hysteroscopy may transport malignant cells into the peritoneal cavity. Eur J Gynecol Oncol 2:121–124
10. Egarter C, Krestan C, Kurz C (1996) Abdominal dissemination of malignant cells with hysteroscopy. Case report. Gynecol Oncol 63:143–144
11. Bettocchi S, Di Vagno G, Cormio G, Selvaggi L (1997) Intra-abdominal spread of malignant cells following hysteroscopy. Gynecol Oncol 66:165–166
12. Rose PG, Mendelsohn G, Kornbluth I (1998) Hysteroscopic dissemination of endometrial carcinoma. Gynecol Oncol 71:145–146
13. Stock RJ, Kanbour A (1975) Prehysterectomy curettage. Obstet Gynecol 45:537–541
14. Dijkhuizen FP, Mol BW, Brolmann HA, Heintz AP (2000) The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia: a meta-analysis. Cancer 89:1765–1772
15. Gimpelson RJ, Rappold HO (1988) A comparative study between panoramic hysteroscopy with directed biopsies and dilatation and curettage. Am J Obstet Gynecol 158:489–492
16. Sousa R, Silvestre M, Almeida e Sousa L, Falcao F, Dias I, Silva T, De Oliveira C, Oliveira HM (2001) Transvaginal ultrasonography and hysteroscopy in postmenopausal bleeding. A prospective study. Acta Obstet Gynecol Scand 80:856–862
17. Leveque J, Goyat F, Dugast J, Loiellet L, Grall JY, Le Bars S (1998) Value of peritoneal cytology after hysteroscopy in surgical stage I adenocarcinoma of the endometrium. Oncol Rep 5:713–715
18. Selvaggi L, Cormio G, Ceci O, Loverro G, Cazzolla A, Bettocchi S (2003) Hysteroscopy does not increase the risk of microscopic extrauterine spread in endometrial carcinoma. Int J Gynecol Cancer 13:223–227
19. Obermair A, Geramou M, Gucer F, Denison U, Graf AH, Kapshammer E, Neunteufel W, Frech I, Kaider A, Kainz C (2000) Does hysteroscopy facilitate tumor cell dissemination? Incidence of peritoneal cytology from patients with early stage endometrial carcinoma following dilatation and curettage versus hysteroscopy and D&C. Cancer 88:139–143
20. Obermair A, Geramou M, Gucer F, Denison U, Graf AH, Kapshammer E, Medl M, Rosen A, Wierrani F, Neunteufel W, Frech I, Preyer O, Speiser P, Kainz C (2000) Impact of hysteroscopy on disease-free survival in clinically stage I endometrial cancer patients. Int J Gynecol Cancer 10:275–279
21. Zerbe MJ, Zhang J, Bristow RE, Grumbine FC, Abularach S, Montz FJ (2000) Retrograde seeding of malignant cells during hysteroscopy in presumed early endometrial cancer. Gynecol Oncol 79:55–58