Taiwanese Journal of Obstetrics & Gynecology 54 (2015) 757–760

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Accuracy of hysteroscopic biopsy, compared to dilation and curettage, as a predictor of final pathology in patients with endometrial cancer

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ARTICLE INFO

Article history:
Accepted 15 August 2015

Keywords:
dilation and curettage
endometrial biopsy
endometrial cancer
hysteroscopic biopsy
resectoscopy

ABSTRACT

Objective: To compare the methods of transcervical resectoscopy versus dilation and curettage (D&C) for endometrial biopsy and to compare these methods for the percentage of histological upgrades at the final posthysterectomy pathology findings in endometrial cancer.
Materials and methods: We retrospectively reviewed 253 cases of uterine cancer diagnosed from May 1995 to January 2014. Included in the study were patients who received transcervical resectoscopy (TCR) or D&C biopsy as the diagnostic method and underwent laparoscopic staging at our institution. The International Federation of Gynecologists and Obstetricians (FIGO) grade in the pathological report of the biopsy and final hysterectomy were recorded. The extrauterine risk was stratified using the initial FIGO grade and depth of myometrium invasion. It was compared to the actual risk using final pathological findings.
Results: We identified 203 cases of endometrial cancer; 18 (8.9%) patients had a higher histological grade at the final hysterectomy. Among the 203 patients, 76 patients underwent TCR biopsy and 127 underwent D&C biopsy. The histological grade was upgraded in two (2.6%) patients in the TCR group. Three (3.9%) patients had positive peritoneal washings. In the D&C group, 16 (12.6%) patients with three (2.4%) positive peritoneal washings were upgraded.
Conclusion: Transcervical resectoscopy could provide more precise grading information, compared to D&C (2.6% vs. 12.6%). Doctors could therefore make a more accurate staging plan, based on the preoperative risk evaluation.

Introduction

Endometrial cancer is the most common gynecological malignancy in Western countries. In the United States alone, the incidence of endometrial cancers increased from approximately 40,320 new cases in 2004 to an estimated 49,560 new cases in 2013 [1,2]. In the past, multiple attempts to evaluate the histological grade preoperatively were without significant success [4,7]. Dilation and curettage (D&C) was once the gold standard for endometrial sampling and routinely used with an upgrade rate of 17–26%, compared to the final pathology [8–10]. In an attempt to develop a less invasive diagnostic method, office endometrial sampling became progressively popular. However, studies aimed at investigating office biopsies revealed an apparent inaccuracy in histological grading with an upgrade rate of nearly 30%, compared to hysterectomy pathology [11]. Cutillo et al [12] investigated the accuracy of transcervical resectoscopy (TCR) and revealed a rather optimistic finding of 97.1% correlation with the final pathology. This could be a solution to overcome the hurdle of inevitable upgrades. This method allows direct visualization, a targeted biopsy, and theoretically a more accurate evaluation of preoperative tumor grading. The purpose of this study was to compare the accuracy of TCR biopsy versus D&C biopsy performed before hysterectomy in patients with endometrial cancer to establish a more accurate

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http://dx.doi.org/10.1016/j.tjog.2015.10.013

diagnostic method to try to eliminate the need to over- or under-treat patients with endometrial cancer.

Materials and methods

After we gained approval from our Chang Gung Medical Foundation Institutional Review Board, we retrospectively reviewed 253 cases of uterine cancer that were treated at our institution from May 1995 to January 2014. We reviewed the patients' information from the time of diagnosis until the date of the most recent follow up. All patients underwent TCR or D&C biopsy at our institution or underwent a D&C biopsy as the diagnostic procedure at a local medical department, and received laparoscopic hysterectomy or staging as the treatment by our minimally invasive surgical team. All patients who received a diagnosis outside of our institution were asked to provide the original slides, which were reviewed by our own pathologist.

Patients were also excluded if they had a biopsy during the office hysteroscopy. We excluded women whose endometrial cancer was an incidental finding during hysterectomies performed for other indications. Women with uterine sarcomas detected during the preoperative biopsy were excluded. Patients were included if their preoperative histological grade, based on D&C or TCR examination, was described in the pathology report.

We abstracted data from electronic medical records. When electronic medical records were unavailable, we abstracted data from the patients' original records. Patients whose charts and information were incomplete or missing were excluded. Pathological and surgical records were reviewed for histiotype, final pathological grade, number of resected lymph nodes, lymphovascular space invasion, cervical invasion, adnexa invasion, and washing cytology.

After analyzing preoperative patient risk, we categorized the patients into the TCR group or the D&C group. For each group, we compared the biopsy histological grade with the final hysterectomy grade of patients who were upgraded in the final pathology. We analyzed the end results. All data were calculated and descriptive statistics were performed using SPSS for Windows (version 17.0.0; IBM SPSS, Inc., Chicago, IL, USA).

Results

Using the aforementioned criteria, we included 203 patients. Seventy-six patients underwent a TCR biopsy and 127 patients underwent a D&C biopsy. The mean age of the TCR group patients was 49.7 years, and 48.7% patients had a preoperative diagnosis of Grade 1; 26.3% of patients, Grade 2; and 25.0% of patients, Grade 3. The mean age of women in the D&C group was 54.1 years, and 62.2% of patients had a preoperative diagnosis of Grade 1; 21.3% of patients, Grade 2; and 16.5% of patients, Grade 3. Table 1 summarizes other findings of our patients. All parameters between the two groups were statistically insignificant.

Among 76 patients who underwent TCR biopsy, only two patients were upgraded in the final pathology, which gives an upgrade rate of 2.6% (Table 2). Both patients had mixed type endometrioid adenocarcinoma: the first patient had mucinous papillary carcinoma, and the second patient had serous papillary carcinoma.

As Table 3 shows, in the D&C group of 127 patients, 16 (12.6%) patients were upgraded. These included type I histiotype (i.e., low grade) and type II histiotype (i.e., high grade, serous papillary, clear cell). Of the upgraded cases, eight (6.3%) patients initially diagnosed with Grade 1 were upgraded to Grade 2, and two (1.6%) patients initially diagnosed with Grade 1 were upgraded to Grade 3 at the final pathology. The diagnosis of six (4.7%) patients was upgraded from Grade 2 to Grade 3.

Only three patients had positive peritoneal cytology washings at the time of surgery. Of these three patients, two patients had disseminated Stage III disease with a high histological grade (Stage IIIA, Grade 3 and Stage IIIC1, Grade 3), and one patient had early Stage IA, Grade 2, and <5% myometrium invasion (see Table 4).

Discussion

The primary endpoint of our study was to compare TCR versus D&C for endometrial biopsy and to compare the percentage of histological upgrades at the final posthysterectomy pathology in endometrial cancer. Preoperative tumor evaluation in endometrial cancer is crucial in risk stratification and intraoperative management. Determination of the tumor grade combined with the depth of myometrium invasion can alter a surgeon's decision in completing surgical staging of patients at high risk for extrauterine disease, whereas it may be unnecessary in low-risk patients. In the past, multiple studies aimed to stratify the risk for extrauterine disease to determine the management and treatment of patients with endometrial cancer [3,14,15,17]. Preoperative evaluation of the extrauterine risk facilitates a surgeon's decision to perform comprehensive lymph node dissection. According to an earlier study by the Gynecology Oncology Group [3] in 1987, assessing the extrauterine risk is accomplished by evaluating the depth of myometrium invasion and histological grade. A low risk is typically described as any grade without myometrial invasion or as Grade 1 with minimal myometrial invasion. [3,5,13,16]. However, based on these criteria, it is difficult to accurately evaluate because of multiple limitations. Histological grades are often upgraded when compared to the final pathology after a hysterectomy. In endometrial sampling, upgrade rates up to 27% have been reported [8,28–31]. Our study obtained an upgrade rate of 13% between the D&C biopsy and the final hysterectomy grade, which is compatible with a previous series showing a 15% upgrade rate [8], and reports showing an upgrade rate of up to 26% for Grades 1 and 2 [10]. A previous prospective study showed that TCR has a 97.1% correlation with the final hysterectomy histopathological grade [12]. We obtained similar results with 97.3% correlation and only a 2.6% upgrade. This correlation is much higher than that for D&C.

In the past, studies have attempted to resolve the issue of upgrades at the final hysterectomy pathology. Investigators concluded that D&C blindly scrapes less than 50% of the uterine wall in 60% of patients [18] and misses 11% of endometrial cancers [19]. Endometrial sampling was once believed to be a better alternative because it can be performed in an office setting without anesthesia. After extensive studies, it proved to be less accurate than traditional D&C [8,9,13,20]. The apparent advantage that TCR has over D&C is that direct visualization of the lesion make targeted biopsies highly feasible. In a systematic review, Clark et al [21] reported that hysteroscopic diagnosis has a positive predictive value of 78.5% in diagnosing endometrial cancer and a negative predictive value of 0.6%, which further aids achieving a well-targeted biopsy.

Discrepancies between the initial and final pathology can change the risk of advanced disease and subsequently undertreating patients. In the past, because of a significant number of upgrades, some surgeons may elect to overtreat and perform staging surgery for low-risk patients [5,6]. However, complete lymph node dissection for low-risk disease has not been proven to improve survival [5,6]; therefore, it is possible that women with an initial Grade 1 or 2 diagnosis with minimal myometrium invasion but final Grade 3 disease would not receive a complete lymph node dissection. Therefore, the extrauterine status cannot be determined and may result in inappropriate treatment planning. Undertreatment could lead to rapid progression, a poorer outcome, and increased use of adjuvant therapy [12], whereas overtreating could

Table 1
Patient characteristics.

Variable	TCR	D&C	*p*
No. of patients	76	127	
Age (y)	49.7 (25–77)	54.2 (31–83)	0.378
Preoperative histology grade			0.309
1	37 (48.7)	79 (62.2)	
2	20(26.3)	27 (21.3)	
3	19 (25.0)	21 (16.5)	
Histiotype			0.358
Endometrioid	71 (93.4)	119 (93.7)	
Mixed (papillary serous)	1 (1.3)	4 (3.1)	
Mixed (clear cell)	3 (3.9)	4 (3.1)	
Mixed (mucinous)	1 (1.3)	0 (0)	
Final histology			0.200
1	35 (46.1)	70 (55.1)	
2	21 (27.6)	29 (22.8)	
3	20 (26.3)	28 (22.0)	
Pelvic lymph nodes resected (average)	18.5	16.6	
Para-aortic lymph nodes resected (average)	4.1	2.7	
Myometrial invasion			0.066
Limited to endometrium	36 (47.7)	47 (37.0)	
≤50%	29 (38.2)	55 (43.3)	
>50%	11 (14.5)	25 (19.6)	
Lymphovascular space invasion			0.416
Positive	12 (15.8)	18 (14.2)	
Negative	64 (84.2)	109 (85.8)	
Cervical invasion			0.400
Positive	2 (0.26)	9 (7.1)	
Negative	74 (97.4)	118 (92.9)	
Adnexa invasion			0.411
Preserved ovaries/ovaries absent	3 (3.9)	3 (2.4)	
Positive	6 (7.9)	7 (5.5)	
Negative	67 (88.1)	117 (92.1)	
Washing cytology			0.327
No sample taken	4 (5.2)	12 (9.4)	
Positive	3 (3.9)	3 (2.3)	
Negative	69 (90.8)	112 (88.2)	
Radiotherapy			0.416
Yes	17(22.4)	23 (18.1)	
No	59 (77.6)	104 (81.9)	

Data are presented as *n* (%) or Mean (range), unless otherwise indicated.
D&C = dilation and curettage; TCR = transcervical resectoscopy.

increase morbidity [22]. Preoperative evaluation is consequently imperative to the surgeon's intraoperative behavior, and warrants further investigation for a more accurate diagnostic method.

A prominent concern of using TCR as a diagnostic tool is that it does not have a statistically increased risk of transtubal dissemination; however, this retrospective study was not powered to adequately assess this parameter [23,24]. However, further studies, which include a meta-analysis, have revealed that the spread is clinically insignificant and that there is no evidence to support an association between preoperative hysteroscopic examination and a worse prognosis [25,26]. Furthermore, TCR has a similar risk of intraperitoneal spread as D&C [27]. Our experience and results are concurrent with these findings and revealed only three positive intraperitoneal washings in the TCR group, of which two patients had Stage III disease. Our D&C group had a similar number of positive peritoneal washings with only one patient with Stage III and two patients with Stage IA diagnoses.

A possible explanation for the inconsistency with our series and other studies could be in the technique and operator during TCR. At our institution, the same minimally invasive surgical team performed all TCR procedures, which decreased the incidence of any change in technique and unequivocal expertise. When there was a suspicion of endometrial cancer, our surgeons took extra care to ensure that the cervix was overdilated and high flow and low pressure (<80 mmHg) were maintained in the uterus at all times. On retrospectively examining these cases, we nevertheless question the hypothesis that the distension media during hysteroscopy causes peritoneal spread. To our knowledge, there is insufficient evidence to reject other mechanisms of inducing intraperitoneal spread such as uterine contractions during the endometrial biopsy procedure.

From our study's findings, we can conclude that TCR has a significantly lower percentage of upgraded histological findings, compared to D&C, and it does not have a higher risk of transtubal peritoneal spread of cancer cells into the peritoneal cavity, despite conflicting evidence of earlier studies [23,24]. Given the aforementioned benefits of TCR, we believe that, compared to D&C, TCR may provide a precise and accurate staging plan in the preoperative risk evaluation of patients with endometrial cancer. However, because of the small number of patients in our study, the results should be evaluated carefully. A larger randomized control trial should be performed for further evaluation and confirmation of these preliminary results.

Table 2
The transcervical resectoscopy histological grade, compared to the hysterectomy histological grade.[a,b]

		Final pathology, *n* (%)		
TCR	Grade	1	2	3
	1	35 (46.0)	1 (1.3)	1 (1.3)
	2	—	20 (26.3)	—
	3	—	—	19 (25.0)

TCR = transcervical resectoscopy.
[a] The number of positive washing cytology results: 3 (Stage IA, Grade 2; Stage IIIA, Grade 3; Stage IIIC1, grade 3).
[b] The two-sample test proportions compare TCR1 versus hysterectomy1, $p = 0.183$; TCR123 versus hysterectomy123; $p = 0.181$; kappa = 0.9587.

Table 3
The dilation and curettage histological grade, compared to the hysterectomy histological grade.[a,b]

		Final pathology		
D&C	Grade	1	2	3
	1	70 (55.1)	8 (6.3)	2 (1.6)
	2	—	20 (15.7)	6 (4.7)
	3	—	—	21 (16.5)

Data are presented as *n* (%).
D&C = dilation and curettage.
[a] The number of positive washing cytology results: 3 (Stage IA, Grade 1; Stage IIIC2, Grade 3; and Stage IA, Grade 3).
[b] The two-sample test proportions compared D&C1 versus hysterectomy1, $p = 0.002$; D&C2 versus hysterectomy 2, $p = 0.011$; and D&C123 versus hysterectomy 123, $p = < 0.001$; *kappa* = 0.7789.

Table 4
Para-aortic lymph node dissection for patients with Grade 3 tumors.[a,*]

	Low preoperative risk => high postoperative risk	High preoperative risk => high postoperative risk
Without PALND	6 (66.7)	3 (12.5)
With PALND	3 (33.3)	21 (87.5)
Total	9	24

Data are presented as *n* (%).
* Fisher's exact test, $p = 0.005$.
PALND = para-aortic lymph node dissection.
[a] Patients whose preoperative imaging could not assess depth of myometrial invasion are not included.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

Acknowledgements

We thank Dr. Hsiao-Jung Tseng and her assistance from Chang Gung Memorial Hospital Statistics Center (Taoyuan City, Taiwan) for clinical research and statistical data analysis.

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