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Comparison of endometrial biopsy and postoperative hysterectomy specimen findings in patients with atypical endometrial hyperplasia and endometrial cancer

Filip Kisielewski, Małgorzata Ewa Gajewska, Maja Janina Marczewska, Grzegorz Panek, Mirosław Wielgoś, Paweł Kamiński

Medical University of Warsaw, Poland

ABSTRACT

Objectives: The aim of the study was to assess the concordance between the preoperative endometrial sampling and microscopic examination of the hysterectomy specimens in patients surgically treated for atypical endometrial hyperplasia and endometrial carcinoma.

Material and methods: We analysed a group of 204 patients, of whom 160 (78.43%) underwent surgical treatment for cancer of the corpus uteri and 44 (21.57%) for atypical endometrial hyperplasia. The preoperative diagnosis was based on the histological examination of endocervical and endometrial samples obtained by fractional curettage and it was compared to the histological findings at hysterectomy. The comparison was made for the basic diagnosis, the histological type of the cancer and the grade of tumour differentiation.

Results: When the histological types of cancer diagnosed in endometrial curettage and hysterectomy specimens were compared, the concordance was observed in 134/160 patients (83.75%). The highest concordance was found for endometrioid carcinoma (127/148 patients, 85.81%). The grade of tumour differentiation was accurate in 69.31% of patients. The highest concordance was for moderately differentiated carcinomas. Of 44 patients who underwent surgical treatment for atypical endometrial hyperplasia, the preoperative diagnosis was confirmed by the postoperative histopathological examination in 21 patients (47.73%). In 15 patients (34.09%) endometrial cancer was diagnosed at hysterectomy.

Conclusions: In endometrial cancer our findings demonstrate a high level of concordance between the histological diagnosis on endometrial curettage and at hysterectomy. Own observations have confirmed that over 30% of patients undergoing surgical treatment for atypical endometrial hyperplasia have concurrent endometrial cancer which is determined by surgery.

Key words: endometrial cancer, atypical endometrial hyperplasia, endometrial curettage, hysterectomy

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INTRODUCTION

Endometrial cancer is the leading cause of female genital cancer in Poland and other developed countries [1]. In Poland, it is the 4th most common cancer among women, after breast, lung and skin cancers. In 2010, there were over 5000 new cases and over 900 endometrial cancer deaths [2]. The exact causes of endometrial cancer are not fully understood, but a significant increase in its incidence has been observed in the last decade, mostly in women with the triad of metabolic disorders manifested as obesity, diabetes and hypertension [3]. In such patients the risk is 2.5 to 3 times higher than in the general population [4].

Most endometrial pathologies present with abnormal uterine bleeding or postmenopausal bleeding per vagina. In approximately 15% of the cases, endometrial hyperplasia or carcinoma is diagnosed [5]. Abnormal bleeding, especially in postmenopausal women, usually makes patients seek medical advice which allows fairly prompt detection and 80% of cases are stage I disease. Five-year survival rates are up to 90% [6, 7]. The diagnosis is based on the histological examination of endometrial samples. However, discrepancy between histological findings before and after surgery is well-documented [8–12]. The clinical implications are serious considering the potential effects on surgical staging

Corresponding author:
Małgorzata Ewa Gajewska
Medical University of Warsaw, pl. Starynkiewicza 1/3, 02–015 Warszawa, Poland
e-mail: ma.gajewska@gmail.com

decisions and disease outcomes. With a preoperative diagnosis of atypical hyperplasia of the endometrium, the scope of planned surgical treatment may be inadequate when endometrial cancer is ultimately diagnosed at hysterectomy [8–10] and that is why accuracy of preoperative histology is very important. In cases of a malignant tumour of the uterine corpus, pathological findings in the hysterectomy specimens usually confirm the preoperative diagnosis. Any discrepancies usually concern the histological type and grade of endometrial cancer [10–15].

AIM OF THE STUDY

The aim of the study was to assess the concordance between the preoperative endometrial sampling and microscopic examination of the hysterectomy specimens in patients surgically treated for atypical endometrial hyperplasia and endometrial cancer of the uterine corpus, concerning both the diagnosis of cancer and its grading.

MATERIAL AND METHODS

We performed a retrospective review of clinical and pathological data from medical records of 204 patients treated for endometrial cancer of the uterine corpus or atypical endometrial hyperplasia at the 1st Department of Obstetrics and Gynaecology, Medical University of Warsaw in the years 2007–2014. The patients' ages ranged from 39 to 87 years (mean age: 63.8 ± 10.9 years) and their characteristics are summarized in Table 1. The preoperative diagnosis was based on the histological examination of endocervical and endometrial samples obtained by fractional curettage and it was compared to the histological findings at hysterectomy.

In patients with a preoperative biopsy finding of atypical endometrial hyperplasia total hysterectomy with or without bilateral salpingo-oophorectomy was performed. In the subgroup with endometrial cancer the surgery was more extensive and included total hysterectomy and bilateral salpingo-oophorectomy with or without complete pelvic and para-aortic lymphadenectomy. In cases of endometrial cancer its histological type was assessed. Grading was based on the morphological and cytological criteria recommend by the WHO, i.e.

- cell pleomorphism;
- cell proliferation and crowding;
- loss of cell cohesiveness;
- ratio of glands to stroma.

Three grades of tumour differentiation were distinguished for endometrioid cancers: well-differentiated or low-grade (G1), moderately differentiated (G2) and poorly differentiated or high-grade (G3). Less common types such as serous carcinoma, clear cell carcinoma, small cell carcinoma and sarcoma were always classified as poorly differentiated (G3).

Statistical analysis employed the chi-square test of independence with a cross tabulation and the correlation coefficient for nominal variables. The contingency coefficient C was calculated which shows strength of the relationship between variables as values from 0 to 1, where 0 means no association and 1 — a very strong association.

Table 1. Characteristics of the study population

Study group		n = 204 (100%)
BMI	(< 18.5)	3 (1.47%)
	(18.5–24.99)	45 (22.06%)
	(25.0–29.99)	61 (29.90%)
	≥ 30.0	95 (46.57%)
Parity	Nulliparous	38 (18.63%)
	P1	61 (29.90%)
	P ≥ 2	105 (51.47%)
Hypertension		141 (69.12%)
Diabetes		37 (18.14%)

BMI — body mass index

RESULTS

Of 204 patients included in the study, 160 (78.43%) underwent surgical treatment for endometrial cancer of the uterine corpus and 44 (21.57%) for atypical endometrial hyperplasia. The comparison of prehysterectomy and hysterectomy findings is presented in Table 2.

Patients with a preoperative diagnosis of endometrioid cancer

Based on the histological examination of endometrial samples obtained by curettage, endometrioid cancer was the most common type of cancer diagnosed preoperatively (148/160 patients, 92.50%), followed by serous carcinoma (10/160 patients, 6.25%) and clear cell carcinoma (2/160 patients, 1.25%).

When the histological types of cancer diagnosed in curettage and hysterectomy specimens were compared, the concordance was observed in 134/160 patients (83.75%). The highest concordance level was found for endometrioid cancer (127/148 patients, 85.81%) while serous carcinoma was confirmed in 6/10 patients (60%) and clear cell carcinoma in 1/2 patients (50%).

Statistical analysis demonstrated the concordance between the initial and final diagnoses for all histological types of endometrial cancer. There was a significant association between the two assessments: Chi^2 (df = 14; n = 160) = 56.11; p = 0.000. The strength of association was moderate (C = 0.509).

Subsequently the concordance between grading at curettage and at hysterectomy was examined. Of 160 patients

Table 2. Comparison of endometrial curettage findings and definitive diagnosis determined by surgery in the study population

			Endometrial curettage sample									
			Endometrioid cancer				Serous carcinoma	Clear cell carcinoma	Atypical hyperplasia	TOTAL		
			G1	G2	G3	No G						
Hysterectomy specimen	Endometrioid cancer	G1	1	3	1	5	0	0	5	15	145	170
		G2	6	47	4	49	2	0	9	117		
		G3	0	4	4	3	1	1	0	13		
	Serous carcinoma		0	4	5	1	6	0	1	17		
	Clear cell carcinoma		0	0	3	0	0	1	0	4		
	Small cell carcinoma		0	1	1	0	0	0	0	2		
	Myosarcoma		0	2	0	0	0	0	0	2		
	Atypical hyperplasia		1	0	0	0	1	0	21	23		
	Hyperplasia without atypia		0	1	0	0	0	0	4	5		
	Endometrium		1	0	0	1	0	0	4	6		
	Total		9	62	18	59	10	2	44	204		
			148									
			160									

with cancer diagnosed in endometrial samples, the histological grade was classified in 101 (63.12%), but not in the remaining 59 patients (36.88%). In this group of patients, G2 (moderately differentiated carcinoma) was the most commonly identified grade (62/ 101 patients, 61.39%) while G1 and G3 disease was found in 9/101 patients (8.9%) and 30/101 patients (29.7%) respectively. Histological grading at hysterectomy was performed for all patients with diagnosed endometrial cancer. Similarly, moderately differentiated cancers were the most commonly identified tumours, in 117/170 patients (68.82%). G1 and G3 disease was found in 15/170 (8.82%) and 38/170 patients (22.36%) respectively.

In 70/101 patients (69.31%) the grade identified in the hysterectomy specimens was the same as diagnosed from sampling. The lowest concordance level was for well-differentiated carcinomas. It was 11.11% which means that in 1/9 cases the initial diagnosis was confirmed by the histological examination of the hysterectomy specimen. In cases of moderately and poorly differentiated cancers the concordance levels were high, 75.81% (47/62) and 73.33% (22/30) for G2 and G3 disease respectively. Statistical analysis demonstrated the concordance of grading between the biopsy specimens and the hysterectomy specimens. There was a significant association between the two assessments: Chi^2 (df = 6; n = 101) = 42.56; p = 0.000; the contingency coefficient C = 0.5445.

The concordance between the preoperative and the hysterectomy findings was analysed in 101 patients with the histological type and grade of the tumour assessed preoperatively and confirmed in 59/101 patients (58.42%). The findings are presented in Table 3.

Table 3. Comparison of endometrial curettage findings and definitive diagnosis determined by surgery in 101 patients with endometrial cancer with the histological grade diagnosed on curettage

Hysterectomy specimen		Endometrial curettage findings					
		Endometrioid carcinoma			Clear cell carcinoma	Serous carcinoma	Total
		G1	G2	G3	G3	G3	
Endometrioid cancer	G1	1	3	1			5
	G2	6	47	4		2	59
	G3	0	4	4	1	1	10
Clear cell carcinoma	G3			3	1		4
Serous carcinoma	G3		4	5		6	15
Other types	NS	2	4	1		1	8
Total		9	62	18	2	10	101

Statistical analysis demonstrated the concordance between the histological types and grades of endometrial cancers diagnosed preoperatively and at hysterectomy. There was a significant association between the two assessments: Chi^2 (df = 20; n = 101) = 42.56; p = 0.000; the contingency coefficient C = 0.6239913.

Of 148 patients who underwent surgical treatment for endometrioid cancer diagnosed by endometrial sampling, this type of cancer was confirmed by the final surgical pathology in 127 patients. The grade was assessed in 70/127 patients (55.1%). In 52/70 patients there was agreement between the endometrial sampling diagnosis and the final surgical pathology. The highest concordance level was found for moderately differentiated cancer (87.03%, 47/54 patients). For poorly differentiated cancer it was 44.4% (4/9 patients) and for well-differentiated cancer it was 14.28% (1/7 patients). Statistical analysis demonstrated the concordance of grading between the curettage samples and the hysterectomy specimens. There was a significant association between the two assessments: Chi^2 (df = 4; n = 70) = 12.77; p = 0.01244; the contingency coefficient C = 0.3928.

Patients with a preoperative diagnosis of atypical hyperplasia of the endometrium

Of 44 patients who underwent surgical treatment for atypical hyperplasia of the endometrium, the preoperative diagnosis was confirmed by the final surgical pathology in 21 patients (47.73%). In 15 patients (34.09%) endometrial cancer was diagnosed at hysterectomy (14 endometrioid cancers and 1 serous carcinoma). In 8 cases the final diagnosis did not confirm atypia or endometrial hyperplasia.

DISCUSSION

Cancer of the uterine corpus is most commonly detected in postmenopausal women [16]. In approximately 80% of patients type 1 cancer is diagnosed, *i.e.* endometrioid, hormone-dependent carcinoma preceded by atypical hyperplasia of the endometrium [6, 7, 16, 17]. Unopposed oestrogen effect is a factor responsible for neoplasia and the risk for cancer increases in obese women, in women experiencing anovulatory cycles or in women with preserved uterus on oestrogen-replacement therapy. The treatment for cancer of the uterine corpus is mainly surgical and preoperative histological examination of endometrial samples is of key importance for the surgical management. The extent of surgery and adjuvant therapy depends on the microscopic examination to assess the histological type and grade of cancer which are important prognostic factors. The other predictors are identified by the final diagnosis according to the recommended surgical-pathological staging [18]. Type II cancer or poorly differentiated endometrioid cancer require more extensive surgery while identification of well-differentiated cancer in endometrial sampling with only superficial invasion of the myometrium allows avoidance of regional lymphadenectomy with its potential serious complications [19, 20]. However, the final surgical pathology does not always confirm the preoperative sampling diagnosis which may lead to either too extensive or too limited surgical treatment. In the case of poorly differentiated cancers identified from the hysterectomy specimens, preservation of pelvic and para-aortic lymph nodes, even when the invasion of the myometrium is superficial, is likely to adversely affect the treatment outcome.

According to the literature, the agreement levels between the endometrial sampling diagnosis and the final surgical pathology range from 30 to 60% [10, 11, 13, 15, 21]. The highest level of discrepancy is observed for histological grading [10, 11, 13, 15, 21].

In our material, in patients undergoing surgical treatment for endometrial cancer, grading was confirmed in 134/160 patients (83.75%), a higher percentage than in the study of Vorgias et al. who confirmed preoperative grading in the final surgical pathology in 67.3% of patients [11].

We performed the analysis of preoperative grading accuracy in 101 out of 160 patients with endometrial cancer diagnosed by endometrial sampling (cancer grade was not established preoperatively in 59 patients). The percentage of results which did not satisfy the pathomorphological criteria for a correct preoperative assessment is high. The concordance between the preoperative diagnosis and the surgical pathology was high for moderately and poorly differentiated cancers, 75.81% for G2 and 73.33% for G3. Although G1 disease was confirmed in only one out of 9 patients (11.11%), the overall concordance in tumour grading was confirmed for all 101 patients.

In the group of patients with endometrioid cancer the highest agreement level for the tumour grading was found for moderately differentiated cancers at 87.03% while for poorly differentiated cancers it was just 44.4%. Many authors are of the opinion that the concordance between the preoperative tumour grading and its confirmation at hysterectomy is inversely proportional to the tumour differentiation. The final surgical pathology confirms the initial diagnosis least frequently in the case of well-differentiated cancers. The concordance level increases with the degree of cancer aggressiveness [10–15].

The final diagnosis of endometrial cancer in patients undergoing surgical treatment for atypical hyperplasia is another concern. Atypical hyperplasia of the endometrium is an important clinical problem, because when the preoperative diagnosis is reliable, the adnexa may be spared which is important in premenopausal women who wish to retain the ovaries or in grossly obese patients for whom vaginal

hysterectomy without salpingo-oophorectomy is the simplest and least invasive procedure. In our material, there was a high percentage of cancers, mostly well-differentiated, diagnosed from the hysterectomy specimens in patients undergoing surgical treatment for atypical hyperplasia of the endometrium (34%). Of 14 patients with endometrioid cancer at hysterectomy, none had G3 disease. In the literature, the rate of initially identified atypical hyperplasia of the endometrium which is ultimately diagnosed as endometrial carcinoma at hysterectomy is up to 59% [8, 10, 22]. In the GOG study, of 115 patients undergoing surgical treatment for atypical hyperplasia, endometrial cancer was diagnosed in 39.1% [9].

Summing up, accurate histological examination of endometrial samples informs the decision about the surgical management. Considering the observed differences between the endometrial sampling diagnosis and the final surgical pathology, in a number of cases the extent of the surgery may be inadequate. Lack of concordance in patients undergoing surgical treatment for atypical endometrial hyperplasia which is diagnosed at hysterectomy as endometrial cancer with different expression of the prognostic factors is often seen in clinical practice. In such situation simple hysterectomy with salpingo-oophorectomy may not meet the current therapeutic standards and surgical staging requirements even in 30% of the cases (own data). Accurate histological grading based on the endometrial sampling is another concern. In a large number of cases (36%), the preoperative assessment did not include tumour grading which is a limitation of this study. Although for the study purposes we could retrospectively reassess the endometrial samples after hysterectomy, such approach would not reflect the actual diagnostic data a clinician was offered at the time of surgery. The differences between the preoperative histology and the surgical pathology may also result from the lack of representative endometrial samples. Histology findings reported in a number of studies indicate underestimation rather than overestimation of the histological grade of the tumour [12–15]. One explanation is that pathologists may be wary of overdiagnosing cancer with the resulting burden of extensive surgery and its potential complications for the patient. In our study, precise analysis of the level of discrepancy between the histological findings before and at hysterectomy was difficult because there was no preoperative grading in a large proportion of the study group. The recognition of tumour grade, i.e. the degree of its differentiation may be difficult and it largely depends on the examiner's experience. Another cause of discrepancy may be inadequate information from the clinician collecting endometrial samples from the uterine cavity which makes accurate diagnosis difficult although the sample amount is sufficient.

CONCLUSIONS

In endometrial cancer, our findings demonstrate a high level of concordance between the histological diagnosis on endometrial curettage and at hysterectomy. Own observations have confirmed that over 30% of patients undergoing surgical treatment for atypical endometrial hyperplasia have concurrent well-differentiated endometrial cancer which is determined by surgery.

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