Is there a real risk in patients with endometrial carcinoma undergoing diagnostic hysteroscopy (HSC)?

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Summary

Objective: The penetration of distention medium into the peritoneal cavity as well as directly into the bloodstream via injured endometrial vessels occurs in a great proportion of patients at hysteroscopy (HSC). This may cause potential risk of dissemination of the malignant cells of endometrial cancer patients. To evaluate the real risk of a poorer prognosis of these patients a prospective multicentric study was started in 1998.

Material and Methods: Two groups of patients with endometrial carcinoma have been compared. The diagnosis was made in the study group by HSC and targeted biopsy, while in the control group by classical D&C. At the end of the HSC procedure puncture of the cul de sac was performed and the fluid obtained was cytologically examined. In both groups peritoneal lavage was performed at the beginning of the subsequent operation and the collected fluid was again cytologically examined. In the first phase of the study the cytology findings in both groups were compared. In the second phase which is planned for the next five years, the results of follow-up of both groups of patients will be evaluated.

Results: The results were evaluated in 134 patients with HSC and in 61 patients with D&C. In the study group a positive finding of malignant cells from the cul de sac was found in four patients (5.3%), a suspect finding in eight patients (10.7%), and a negative finding in 63 patients (84%). In the remaining 59 patients with HSC no peritoneal fluid was obtained. In the fluid from lavage at the beginning of the operation in the same group of HSC patients, a positive finding of malignant cells was found in 12.1%, a suspect finding in 18.2%, and a negative finding in 69.7%. In the control group (after D&C) the fluid from lavage contained malignant cells in eight patients (13.6%), suspect cells in 12 patients (20.3%), and no malignant cells in 39 patients (66.1%). Both groups were comparable for clinical stages of disease.

Conclusions: Our results suggest that HSC does not increase the risk of penetration of tumour cells into the peritoneal cavity more than estimates in D&C.

Key words: Endometrial cancer; Hysteroscopy; D&C; Malignant cell seeding.

Introduction

The classical D&C is today being more and more often replaced by HSC. The advantage of HSC versus classical D&C is obvious. In cases of endometrial carcinoma HSC makes it possible to estimate the extent of tumourous involvement and, more importantly, to take the bioptic sample from the most suspect site.

It also enables, in typical cases, to differentiate between types I and II of endometrial carcinoma (hyperplastic versus focal). HSC also contributes to more precise staging, which is essential for the proper choice of subsequent therapy.

On the other hand, we have to consider the possible risks. Dissemination of malignant cells can theoretically occur during the HSC procedure. Distention medium usually penetrates through the patent Fallopian tubes and in this way it can cause the penetration of endometrial cells into the abdominal cavity. The malignant cells can also be transferred by intravasation, e.g. the direct penetration of the medium into the circulation via injured endometrial vessels. The mentioned theoretical risks have led some authors even to reject HSC in patients who are evidently suspect for endometrial carcinoma [3, 14]. They accept HSC in such cases only after a previous artificial blockade of the Fallopian tubes.

The aim of our study was therefore to prove to what limit the risk of dissemination of the malignant process during HSC is real and if it objectively deteriorates the prognosis of those patients.

Materials and Methods

The project was launched in 1998 and was designed as a multicentric prospective study. To speed up the recruitment of a sufficient number of patients in a limited time span 12 gynecological departments of district and university hospitals were enrolled in the study. Two groups of patients with endometrial carcinoma were compared. In the study group (134 patients) the diagnosis of malignancy was confirmed by histopathological examination of the endometrial biopsy obtained via HSC. In the control group (69 patients) the endometrial tissue was obtained by the classial D&C. No exact randomisation of patients into respective groups was performed. Nevertheless both groups were comparable for clinical stages (Table 1).

The first group the patients were placed into the anti-Trendelenburg position and puncture of the pouch of Douglas was performed at the end of the HSC procedure. The amount of aspirated fluid was measured and a specimen was sent off immediately for cytological examination. Cytology was performed according to a standard protocol by the cytospin method [18]. The results were classified as positive, negative or suspect.

In the control group the culdocentesis was not performed because no or minimal peritoneal fluid in the cul de sac was expected.

Almost all patients underwent operative treatment in the subsequent period (usually within two to three weeks). In all but four cases hysterectomy plus bilateral salpingo-oophorectomy

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and in most cases also pelvic lymph-node sampling was performed. The remaining four patients were treated by radiotherapy only. The majority of operations were done by the abdominal approach, the rest by laparoscopic lymphadenectomy and vaginal hysterectomy with bilateral salpingo-oophorectomy. At the beginning of the operation lavage of the pelvic cavity was always performed and the fluid obtained was assessed by the same standard cytological protocol.

Results

Table 1 demonstrates the clinical stages of the endometrial carcinoma in the study and control groups.

Both groups are comparable for the clinical stage of the disease. No statistically significant difference between the groups was proved by the χ^2 test for $p<0.05$. Table 2 compares the cytological findings from the fluid obtained from the cul-de-sac puncture and peritoneal lavage in the study group.

There was no fluid obtained at the cul-de-sac puncture in 59 patients after HSC. Only in four patients were malignant cells found in the fluid from the Douglas pouch. At the subsequent peritoneal lavage performed at the beginning of the operation, positive cytology was found in 16 patients. Even if we join the suspect and malignant findings the percentage of these findings is lower in the fluid obtained at HSC than in the subsequent peritoneal lavage (χ^2 test, $p<0.05$).

Table 1. — *Clinical stages of the study and control group*

FIGO	HSC		D&C	
	n	%	n	%
I a	38	28.4	16	26.2
I b	50	37.3	23	37.7
I c	13	9.7	5	8.2
II a	9	6.7	4	6.6
II b	4	3.0	3	4.9
III A	11	8.2	6	9.8
III B	2	1.5	2	3.3
III C	3	2.2	1	1.6
IV A	3	2.2	1	1.6
IV B	1	0.7	0	0
Total	134	100	61	100
Stage I		75.4		72.1
Stage II		9.7		11.4
Stage III		11.9		14.7
Stage IV		3.0		1.8

Table 2. — *Cytological findings from the cul-de-sac puncture and peritoneal lavage in the study group*

	Cytological findings						
	Cul de sac puncture (n=134)				Peritoneal lavage (n=132)		
	no fluid	benign	suspect	malignant	benign	suspect	malignant
n	59	63	8	4	92	24	16
(%)	(44%)	(84%)	(10.7%)	(5.3%)	(69.7%)	(18.2%)	(12.1%)

Table 3. — *Cytological findings of the peritoneal lavage in the study and control groups*

	Cytological findings					
	HSC (n=132)			D&C (n=59)		
	benign	suspect	malignant	benign	suspect	malignant
n	92	24	16	39	12	8
(%)	(69.7%)	(18.2%)	(12.1%)	(66.1%)	(20.3%)	(13.6%)

Table 3 compares the cytological findings of the peritoneal lavage in the study and control groups. There were 13.6% positive findings in the D&C (control) group and 12.1% in the HSC (study) group. Also the percentage of negative findings was higher in the study group than in the control group.

Our results therefore suggest that HSC does not increase the risk of penetration of endometrial tumour cells into the peritoneal cavity more than the estimates in D&C.

Discussion

Diagnostic hysteroscopy combined with a targeted biopsy is more and more often replacing the classical diagnostic curettage, especially in cases of irregular perimenopausal bleeding.

Nevertheless, classial diagnostic curettage belongs to the most frequent gynecological procedures that are still widely used. The principal disadvantage of the currettage results from the fact that it represents the so called "blind procedure", while HSC offers a direct view into the uterine cavity. At the same time, it makes a targeted sampling of the endometrium possible.

An appropriate biopsy sample is essential for an exact histopathological diagnosis. At classical D&C it is therefore necessary to obtain and send off for histological examination all endometrium from the uterine cavity. The incipient and mainly focally restricted malignant tumour can be easily missed either because of incomplete abrasion of the endometrium or because of an improper selection for microscopic processing. The possibility of a false negative diagnosis of malignancy at classical D&C is estimated as 10 to 30%.

Even if the HSC itself can not unambiguously confirm malignancy by direct observation, it enables sampling from the most suspect sites. Otherwise, at least it can stress the necessity of an exhaustive evaluation of the whole bioptic sample. HSC also contributes to the proper staging of the disease which is mandatory to establish optimal subsequent treatment [6].

Today liquid distention media has replaced the gaseous ones even at diagnostic HSC.

During insuflation of the liquid medium into the uterine cavity some medium may escape into the circulation via the injured endometrial vessels. The distention medium also penetrates through the patent Fallopian tubes into the peritoneal cavity. The escape of the distention medium-containing tumor cells into the bloodstream and peritoneal cavity therefore creates a theoretical risk

of development of distant or implantation metastases. The literature reports on this risk have so far been rather sporadic, mostly only within the framework of limited case reports [10-12, 14]. It has also been been observed that D&C itself or other small intrauterine procedures could lead to the penetration of the endometrial cells into the abdominal cavity [13]. The migration of malignant cells into the peritoneal cavity can also occur spontaneously, without any instrumental intervention. This may be confirmed by a positive lavage of the peritoneal cavity performed at the beginning of the operation even in patients without tumor penetration through the uterine wall and previous D&C [13]. The prognosis of the patient with a positive peritoneal lavage is generally believed to be poorer than of those with a negative one [4, 5, 7, 8, 16, 17].

The results of our study give evidence that HSC does not constitute any significant risk of increased penetration of malignant cells into the peritoneal cavity. The cytological findings from peritoneal lavages performed at the beginning of an operation in patients whose diagnosis of endometrial carcinoma was made by HSC are similar to those in patients who were diagnosed by classical D&C. Theoretically, at HSC the malignant cells may also penetrate into the blood circulation. However, the same penetration may happen at D&C, even if to a smaller extent. To answer this question we have to complete Phase II of our study which will compare the follow-up of patients in both groups over a longer time period.

Conclusions

Evaluation of the cytological findings from the peritoneal cavity after HSC and D&C has not shown differences between the study and control group. Both groups were comparable for the clinical stages of the disease.

The conclusion that HSC does not increase the real risk of a poorer prognosis of these patients is therefore plausible.

The theoretical risk that HSC may also cause "seeding" of malignant cells directly into the blood circulation and into the distant organs can not be clearly excluded. The same, however, is true for D&C. Further study comparing the follow-up of patients in both groups is currently in progress.

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