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CLINICAL ARTICLE

Use of risk of malignancy index to indicate frozen section analysis in the surgical care of women with ovarian tumors

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ABSTRACT

Objective: To evaluate the importance of the risk of malignancy index (RMI) in the decision to perform frozen section analysis among women with ovarian tumors. *Methods:* A retrospective study was conducted in 11 centers in the Netherlands. Women who underwent surgical treatment of an ovarian mass with unknown histology between January 2005 and September 2009 were included. The RMI was calculated retrospectively Frozen section analysis and RMI values were assessed for patients with benign, borderline, and malignant ovarian tumors on final histopathology. *Results:* Overall, 670 women were included. Frozen sections were performed in 323 (48.2%) patients, of whom 206 (63.8%) were diagnosed with benign ovarian tumors, 55 (17.0%) with borderline tumors, and 62 (19.2%) with malignant tumors. Overall, 109 (16.3%) women had an RMI below 20, 106 (97.2%) of whom had benign histology results. Among 235 patients with an RMI over 100, 3 (1.3%) postmenopausal women had malignancies that were missed because frozen sections were not performed. *Conclusion:* Women with an RMI below 20 have a low risk of malignancy and therefore do not require frozen section analysis. Postmenopausal women with an RMI greater than 100 should be referred to centers where frozen sections can be performed, and proper facilities and expertise are available to perform staging procedures if necessary.

1. Introduction

The differentiation between benign and malignant histology is crucial in the management of women with ovarian tumors. Along with surgical expertise, accurate histological assessment before surgery, which usually includes ultrasonography, is important in counselling and preoperative planning of the surgical approach. The risk of malignancy index (RMI)—the first simple diagnostic index suitable for use in clinical practice and which defines the optimal combination of diagnostic criteria—was developed by Jacobs et al. [1] to standardize and improve the preoperative evaluation of ovarian tumors. A RMI cutoff value of 200 is generally used to discriminate between benign and malignant ovarian tumors.

Among women with ovarian cancer, surgical staging and optimal cytoreductive surgery are essential and result in improved survival [2,3]. If the ovarian tumor is benign, a more conservative approach—e.g. one-sided salpingo-oophorectomy or cystectomy—will suffice and can contribute to fertility preservation for young women. Nevertheless, despite careful interpretation, current diagnostic procedures do not allow a definitive diagnosis of ovarian cancer to be established preoperatively, merely suggest its presence instead [4,5]. Frozen section analysis could assist in informed decision making to determine the extent of surgery required and prevent undertreatment or overtreatment. Because of its utility and the limited value of preoperative diagnostics, frozen section analysis is frequently used for ovarian tumors. Indeed, the recommended rate of frozen section analysis in general surgical practice is 5%–15% [6,7], whereas for ovarian tumors, rates range from 19% to 66% [8–10].

The accuracy of frozen section analysis is generally good and has been thoroughly assessed in previous studies [11–13]. A systematic review by Geomini et al. [11] showed that frozen section analysis achieves a sensitivity of 71%–100% and a specificity of 98%–100% in malignancy detection. By contrast, frozen section analysis of borderline adnexal masses [13,14] and mucinous histologic tumor types [11,15], seems to be less accurate. In 2012, Cross et al. [16] used frozen section analysis for suspected early ovarian cancer and showed an excellent diagnostic test accuracy, concluding that frozen section analysis assisted gynecologic oncologists to perform the appropriate surgery in 95% of cases. Nevertheless, it should be noted that their study population consisted of women with an RMI of 200 and higher. Further, some retrospective

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studies [17,18] have suggested that the accuracy of frozen section analysis improves when performed by an expert pathologist.

The objective of the present study was to evaluate the importance of the RMI in the decision to perform frozen section analysis among women with ovarian tumors.

2. Materials and methods

A retrospective study was conducted in Radboud University Medical Center (Radboudumc) and 10 cooperating community hospitals in the east of the Netherlands. Women who were admitted for surgical treatment of an ovarian mass with unknown histology between January 1, 2005, and September 30, 2009, were included. Women in whom clear evidence of malignancy was found before or during the surgical procedure (e.g. pleural effusions and evidence of distal organ involvement) were excluded. Part of this study population has been previously described [19–21]. The study was approved by the medical ethics committee of the Radboudumc. Written informed consent was not required because data were abstracted retrospectively from patient files and stored anonymously in a database.

Transvaginal ultrasonography, combined with abdominal ultrasonography when needed, was performed by experienced echoscopists (all medical doctors). Routine preoperative assessment included analysis of serum samples for cancer antigen 125 (CA125), and menopausal status was recorded. Patient RMI parameters were registered by gynecologists as was requested for a previous study [19]. The RMI was calculated as the multiplied value of the ultrasonography score (U), menopausal status (M), and serum CA 125 level (U/mL) as described by Tingulstad et al. [22]: RMI = U × M × CA125. With regard to U, multilocularity, solid areas, bilaterality, ascites, and intra-abdominal metastases were scored as one point each; U = 3 was assigned to a total of 2 or more points and U = 1 to fewer than 2 points. With regard to M, a postmenopausal status was defined as more than 1 year of amenorrhea or age 50 years or older among women who had prior hysterectomies, and was assigned a score of M = 3, whereas premenopausal status scores were assigned as M = 1. Serum CA125 values were entered directly into the equation. Of note, the present study was conducted during a period in which the RMI was not used in routine clinical work-up, and was therefore calculated retrospectively from the registered parameters. This allowed a comparison of the results of clinical practice with a hypothetical situation in which the RMI would have been included in clinical management.

The decision to perform frozen section analysis was made by the surgeon on the basis of the suspicion of ovarian malignancy before or during surgery. The complete ovary or the ovarian cyst was sent fresh to the on-site laboratory of the Department of Pathology, to a centralized pathology department in another hospital, or was analyzed on-site in an adapted setting during surgery by a pathologist from a centralized pathology department. The most suspicious parts of the tumor were selected for frozen section analysis. Final diagnosis of the tumor was based on full histopathologic examination of all surgical specimens removed. The pathologist who examined the paraffin slides was not masked to the frozen section diagnosis. Histology results from both frozen section analysis and paraffin (final) diagnosis were expressed as benign, borderline, or malignant. Borderline malignancies were allocated to the benign group for calculation of diagnostic performance of frozen section analysis. A total of six pathology units covered the pathology activities of the 11 hospitals that participated in this study. One of these units covered four hospitals, two units covered two hospitals, and three units covered one hospital.

To evaluate the significance of the RMI in the decision to perform frozen section analysis, frozen section rates for benign, borderline, and malignant ovarian tumors (i.e. final histopathologic diagnosis) were calculated for various categories of RMI values. Descriptive statistics were performed to describe and present the data quantitatively. SPSS 16.0.1 for Windows (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses.

3. Results

A total of 724 women underwent surgery for an adnexal mass during the study period. One hospital (out of the 11 participating hospitals) only had two registered patients and was therefore excluded from further analyses. For 52 (7.2%) women, frozen section analysis was not performed because of clear evidence of malignancy before or during the surgical procedure, and these women were therefore excluded from the study. Of the remaining 670 women, 531 (79.3%) had benign conditions as the final histopathologic diagnosis, 70 (10.4%) had borderline tumors, and 69 (10.3%) had malignant disease. Median age was 54 years (range 13–93) and 390 (58.2%) were postmenopausal. Median serum CA125 was 20 U/mL (range 2–2914).

Frozen sections were performed in 323 (48.2%) patients, most of whom were diagnosed with benign ovarian tumors (Table 1). Among 169 mucinous tumors, frozen sections were performed for 105 (62.1%). By contrast, among all 501 other histologic types, frozen sections were performed for 218 (43.5%). When frozen sections were performed, 58 (93.5%) of 62 patients with ovarian cancer were properly staged, compared with 6 (85.7%) of 7 for whom no frozen sections were performed.

Table 1
Final histopathologic classification and use of frozen section analysis in ovarian lesions.[a]

Final histopathology	Total (n = 670)	Frozen sections performed (n = 323)	No frozen sections performed (n = 347)
Benign[b]	531/670 (79.3)	206/323 (63.8)	325/347 (93.7)
Mucinous cystadenomas	124/531 (23.4)	69/206 (33.5)	55/325 (16.9)
Serous cystadenomas	92/531 (17.3)	32/206 (15.5)	60/325 (18.5)
Cystadenomas; not otherwise specified	146/531 (27.5)	41/206 (19.9)	105/325 (32.3)
Endometriotic cysts	57/531 (10.7)	16/206 (7.8)	41/325 (12.6)
Dermoid cyst	56/531 (10.5)	14/206 (6.8)	42/325 (12.9)
Fibroma	56/531 (10.5)	34/206 (16.5)	22/325 (6.8)
Borderline	70/670 (10.4)	55/323 (17.0)	15/347 (4.3)
Mucinous	37/70 (52.9)	29/55 (52.7)	8/15 (53.3)
Serous	28/70 (40.0)	21/55 (38.2)	7/15 (46.7)
Borderline; not otherwise specified	5/70 (7.1)	5/55 (9.1)	0
Malignant	69/670 (10.3)	62/323 (19.2)	7/347 (2.0)
Serous adenocarcinomas	29/69 (42.0)	25/62 (40.3)	4/7 (57.1)
Mucinous adenocarcinomas	8/69 (11.6)	7/62 (11.3)	1/7 (14.3)
Endometrioid adenocarcinomas	12/69 (17.4)	12/62 (19.4)	0
Clear cell carcinomas	12/69 (17.4)	11/62 (17.7)	1/7 (14.3)
Other malignancies	8/69 (11.6)	7/62 (11.3)	1/7 (14.3)

[a] Values are given as number/total number (percentage).
[b] Diagnosis is based on the final histopathologic examination of all surgical specimens removed.

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