GYNECOLOGY

Nomogram to predict recurrence in patients with early- and advanced-stage mucinous and serous borderline ovarian tumors

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OBJECTIVE: Recurrence prediction is a cornerstone of patient management for borderline ovarian tumors. This study aimed to develop a nomogram predicting the recurrence probability in individual patients who had received primary surgical treatment.

STUDY DESIGN: This retrospective multicenter study included 186 patients with borderline ovarian tumor diagnosed from January 1980 through December 2008. A multivariate logistic regression analysis of selected prognostic features was performed and a nomogram to predict recurrence was constructed. The nomogram was internally validated.

RESULTS: The overall recurrence rate was 34.4% (64/186), with noninvasive and invasive forms in 29% (54/186) and 5.4% (10/186) of cases, respectively. International Federation of Gynecology and Obstetrics stage, age at diagnosis, histologic subtype, completeness of surgery, and type of surgery (radical vs fertility sparing) were associated with an increased risk of recurrence and were included in the nomogram. The predictive model had a concordance index of 0.78 (95% confidence interval, 0.76—0.80) and 0.77 (95% confidence interval, 0.75—0.79) before and after the 200 repetitions of bootstrap sample corrections, respectively, and showed good calibration.

CONCLUSION: Our results support the use of the present nomogram based on 5 clinical and pathological characteristics to predict recurrence probability with a high concordance, hence to inform patients on surgical management. External validation is required to recommend this nomogram in routine practice.

Key words: borderline ovarian tumors, conservative treatment, nomogram, recurrence, surgery

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Borderline ovarian tumors (BOTs) are defined by the presence of cellular proliferation and nuclear atypia without stromal invasion and represent 10-15% of epithelial ovarian tumors.[1] Five- and 10-year survival for stage I, II, and III disease are 99% and 97%, 98% and 90%, and 96% and 88%, respectively.[2] Despite this favorable prognosis, up to 25% of patients experience a recurrence.[3] Several epidemiological and histological factors have been correlated with the risk of recurrence after surgical treatment of BOTs[3-5] but none of them are sufficiently accurate in routine practice to identify patients at risk of recurrence.

The past decade has been marked by important advances in therapeutic options such as the advent of fertility-sparing surgery.[6,7] The increased demand for clinicians to help patients make informed decisions regarding the options, benefits, and risks of treatment involves careful insertion of risk factors into the overall treatment recommendations. Predictive models have been developed across most cancer types.[8-10] One of these predictive models is the nomogram that allows a simple graphical representation of a statistical predictive model that generates a numerical probability of a clinical event. As nomograms can generate individualized predictions, they can be used to stratify patients not only for planning treatment but also for providing better information to the patient about their therapeutic options. This can help clinicians to involve patients in the therapeutic decision-making process and may consequently improve their compliance.[8-10] Recently, Obermair et al[11] proposed a nomogram to predict the risk of recurrence in patients with BOTs. However, external validation revealed that it had low relevance which was probably linked to differences in the epidemiological, surgical, and histological characteristics of the 2 populations.[12] Therefore, the objective of the current study was to develop a nomogram to predict the

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probability of recurrence for women with early and advanced stages of BOT.

Materials and Methods

Patients

We conducted a retrospective study using data from patients with BOT who had received primary surgical treatment from January 1980 through December 2008. For each patient, the following parameters were recorded: age, preoperative serum CA 125, type of surgery, completeness of surgery, fertility-sparing surgery, surgical route (laparoscopy or laparotomy), performance of lymphadenectomy, final histological subtype (serous or mucinous), International Federation of Gynecology and Obstetrics (FIGO) staging and occurrence of a recurrence, overall survival, and duration of follow-up.

Fertility-sparing surgery (conservative treatment) was defined as a procedure in which the uterus and at least part of 1 ovary were preserved (ie, unilateral salpingo-oophorectomy [USO] and cystectomy). Surgical treatment was considered nonconservative when bilateral salpingo-oophorectomy (BSO) was performed with or without associated hysterectomy. In line with current French guidelines,[13] initial surgical staging was considered complete once all peritoneal surfaces had been carefully inspected and peritoneal washing, random or oriented multiple biopsies, and infracolonic omentectomy performed. Systematic appendectomy was also a criterion for complete staging of mucinous BOT. Initial surgical staging was considered incomplete in all other cases, independently of the radical or conservative nature. Pelvic and paraaortic lymphadenectomy was not systematically performed. Histological typing was performed according to the World Health Organization's system.[14] Follow-up included a combination of clinical examination, ultrasonography, and measurement of serum tumor markers. For the first 2 years, follow-up evaluation was performed every 6 months and then patients were evaluated annually.

TABLE 1
Baseline characteristics

Parameters	Baseline characteristics		
	Overall cohort, n (%), n = 186	No recurrence, n (%), n = 122	Recurrence, n (%), n = 64
Mean age at diagnosis, mo (median)	34.42 (31)	35.9 (33.5)	31.5 (29)
FIGO staging			
Ia	69 (37.09)	54 (44.26)	15 (23.43)
Ib	7 (3.76)	2 (1.63)	5 (7.81)
Ic	13 (6.98)	8 (6.55)	5 (7.81)
II	24 (12.90)	14 (11.47)	10 (15.62)
III	73 (39.24)	44 (36.06)	29 (45.31)
Histologic subtype			
Serous	123 (66.12)	70 (57.37)	53 (82.81)
Mucinous (intestinal + müllerian)	63 (33.87)	52 (42.62)	11 (17.18)
Completeness of surgical staging			
Complete	81 (43.54)	64 (52.45)	17 (26.56)
Incomplete	105 (56.45)	58 (47.54)	47 (73.43)
Surgical route			
Laparoscopy	41 (22.1)	28 (22.95)	13 (20.31)
Laparotomy	42 (22.5)	27 (22.13)	15 (23.43)
NA	103 (55.4)	67 (54.91)	36 (56.25)
Surgery procedure			
BSO ± TH	75 (40.32)	59 (48.36)	16 (25.00)
USO	43 (23.11)	39 (31.96)	29 (45.31)
Cystectomy	68 (36.55)	24 (19.67)	19 (29.68)
Lymphadenectomy			
No	141 (75.8)	97 (79.50)	44 (68.75)
Pelvic ± paraaortic	33 (17.8)	21 (17.21)	12 (18.75)
NA	12 (6.4)	4 (3.27)	8 (12.50)
CA 125 >35 IU/mL			
No	9 (4.83)	4 (3.27)	5 (7.81)
Yes	177 (95.16)	118 (96.72)	59 (92.18)

BSO, bilateral salpingo-oophorectomy; *FIGO*, International Federation of Gynecology and Obstetrics; *NA*, not available; *TH*, total hysterectomy; *USO*, unilateral salpingo-oophorectomy.

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Development and predictive accuracy of the model

A nomogram was developed to predict the risk of recurrence at 5 years with or without invasive component. A multivariate analysis was performed using the logistic regression model and including all the factors that were significant at univariate analysis. The complexity of the model was controlled using the Akaike information criteria. $P < .05$ was considered significant. The final model equation was then organized as a nomogram designed to