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Predicting poor prognosis recurrence in women with endometrial cancer: a nomogram developed by the FRANCOGYN study group

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Background: The purpose of this study was to develop a nomogram to predict 'poor prognosis recurrence' (PPR) in women treated for endometrial cancer (EC).

Methods: The data of 861 women who received primary surgical treatment between January 2001 and December 2013 were abstracted from a prospective multicenter database. Data were randomly split into two sets: training and validation with a predefined 2/3 ratio. A Cox proportional hazards multivariate model of selected prognostic features was performed in the training cohort ($n = 574$) to develop a nomogram predicting PPRs. The nomogram was validated in the validation cohort of 287 patients.

Results: In the training cohort, 82 (14.3%) developed subsequent PPR. Age, histologic type and grade, lymphovascular space invasion status, FIGO stage, and nodal staging (SLN \pm pelvic and/or para-aortic lymphadenectomy) were independently associated with subsequent PPR. The nomogram showed an area under the receiver operating characteristic curve (AUC) of 0.82 (95% confidence interval (CI), 0.73–0.89) in the training set. The validation set showed a good discrimination with an AUC of 0.75 (95% CI, 0.65–0.83).

Conclusions: We have developed a robust tool that is able to predict subsequent PPRs in women with FIGO I–III EC.

Endometrial cancer (EC) is the most common gynaecological cancer in developed countries. It generally has a favourable prognosis, with a 5-year overall survival reaching 80% mainly because most women are diagnosed at an early stage and managed by surgery alone with a low risk of recurrence (Amant *et al*, 2005). Adjuvant radiotherapy and systemic treatment are options for

women at increased risk of recurrence. In this specific setting, several studies have demonstrated that women's age, histological type and grade, depth of myometrial invasion, cervical involvement, and lymphovascular space involvement (LVSI) status can predict recurrence and survival (Morrow *et al*, 1991). Hence, risk groups for recurrence have been described based on these

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clinicopathological prognostic factors to identify women with poor prognosis who may benefit from adjuvant therapy.

Although relatively few women with EC experience recurrence, it accounts for most EC-related deaths. Moreover, there are several types of recurrence with different impact on survival and for which management may be based on either surgery or systemic treatment, or a combination of both. However, the various types of recurrence in EC have not been clearly defined to date although authors agree that the development of distant metastases (i.e., brain, lung, liver, bone metastases, and supra-diaphragmatic nodal metastases) results in a significant reduction in overall survival (Creasman *et al*, 1987). It would be of particular interest to identify women with a 'poor prognosis recurrence' (PPR) for EC for whom surgical treatment is rarely an option. These women could then benefit from more individualised counselling in terms of prognosis, therapeutic options at initial management, monitoring strategies, and lifestyle modifications.

In this French retrospective multicenter study, we developed a nomogram based on selected clinical and histological variables to predict the likelihood of 3-year PPR in women with early stage EC.

MATERIALS AND METHODS

Study population. From January 2001 to December 2013, the data of all women who had undergone primary surgical treatment for EC were retrospectively abstracted from prospectively maintained databases of eight institutions in France (Tours University hospital, Creteil Hospital, Reims University Hospital, Jeanne de Flandre University Hospital, Dijon Cancer Center, Rennes University Hospital, and Tenon University Hospital), and from the Senti-Endo trial (Ballester *et al*, 2011; Daraï *et al*, 2015). All the women had presumed early stage EC and final 2009 International Federation of Gynecology and Obstetrics (FIGO) (Pecorelli and Sergio, 2009) stages I–III cancer (with primary tumour confined to the corpus uteri). The medical records were reviewed to determine age, body mass index (BMI, calculated as weight in kilograms divided by the square of height in metres), surgical procedure, final pathological analysis (histologic type and grade, depth of myometrial invasion, LVSI status, and final nodal status), and adjuvant treatments. Histologic type 1 included endometrioid tumours (whatever the grade) and histologic type 2 included serous carcinomas, clear cell carcinomas, and carcinosarcomas (Colombo *et al*, 2016a). Lymphovascular space involvement was considered positive if lymphatic, vascular, or angiolymphatic invasion was reported. Patients were included if they had all these data available. The research protocol was approved by the institutional review board of the French College of Obstetricians and Gynecologists (CEROG 2014-GYN-020).

Treatment and follow-up. Women were included if they had undergone primary surgical treatment, including at least total hysterectomy with bilateral salpingo-oophorectomy, with or without nodal staging (sentinel lymph node (SLN) \pm pelvic \pm para-aortic lymphadenectomy). Some aspects of the management of EC changed during the study period. Before 2010, nodal staging was recommended for all women and included pelvic \pm para-aortic lymphadenectomy; after 2010, both pelvic and para-aortic lymphadenectomy were exclusively recommended for women with high-risk EC or metastatic pelvic lymph nodes. Since the publication of French guidelines in 2010, lymphadenectomy was no longer recommended for women with low-/intermediate- risk EC. Women with early stage EC who were enrolled in the Senti-Endo trial from July 2007 to August 2009 underwent a pelvic SLN biopsy with systematic pelvic lymphadenectomy. When the pelvic SLN was found to be metastatic at intraoperative histology or after final histology, a

para-aortic lymphadenectomy was recommended. (Querleu *et al*, 2011; Colombo *et al*, 2013; Colombo *et al*, 2016a). The decision whether to introduce adjuvant therapy was made by a multidisciplinary oncology committee based on international guidelines; it included vaginal brachytherapy and/or external beam radiotherapy and/or chemotherapy (Querleu *et al*, 2011; Colombo *et al*, 2013; Colombo *et al*, 2016a). Clinical follow-up consisted of physical examination and the use of imaging techniques according to the findings and for high-risk group of recurrence.

Statistical analysis

Development of the nomogram. EC recurrence was diagnosed by biopsy or imaging studies and divided into: (i) vaginal vault recurrence; (ii) isolated locoregional lymph nodes recurrence (pelvic and/or infra-diaphragmatic para-aortic lymph nodes); (iii) local central pelvic recurrence; (iv) peritoneal carcinomatosis, and (v) distant metastases including brain, lung, liver, and bone metastases, as well as supra-diaphragmatic nodal metastases. We assumed that PPR included distant metastases and peritoneal carcinomatosis. To develop a well-calibrated and exportable nomogram for PPRs, data were randomly split into a training set and an external validation set with a predefined 2/3 ratio. This split was expected to provide balanced statistical power to identify and assess predictors (Steyerberg, 2009).

In the training cohort (2 out of 3 of the whole population), we first defined PPR by analysing 3-year overall survival according to recurrence site. Demographics and histological factors were then tested individually for association with PPR using log-rank tests. Factors with a *P*-value < 0.1 were then included in a Cox proportional hazards model. The final model equation was then designed to calculate patient-specific probabilities of PPR. Multivariate analyses were performed by using the Cox proportional hazards model. Hazard ratios were calculated from the model coefficients. The model performance for predicting outcome was evaluated by calculating the concordance index (c-index), which is a generalisation of the area under the curve of the receiver operating characteristics (ROC) curve and can be applied to continuous outcome and censored data (Hanley and McNeil, 1982; Harrell *et al*, 1988; Heagerty *et al*, 2000). Complexity of the model was controlled using Akaike information criteria (Akaike, 1985). A *P*-value < 0.05 was considered significant.

For external validation, the nomogram was then applied to the validation cohort (1 out of 3 of the whole population). We performed the calibration (i.e., agreement between observed outcome frequencies and predicted probabilities of subsequent PPR) using graphic representations of the relationship between the observed outcome frequencies and the predicted probabilities. The clinical significance of calibration reflected the accuracy of individual predictions of subsequent PPR. Moreover, we evaluated average and maximal errors between predictions and observations obtained from the calibration curve.

Optimal threshold of the nomogram. The optimal threshold (cutoff points) of the nomogram in terms of clinical utility, sensitivity, specificity, negative predictive values, positive predictive values, and its overall diagnostic accuracy (i.e., probability for a woman to be correctly classified by the nomogram) was evaluated by the ROC curve area and the Youden Index (Schisterman *et al*, 2005).

Poor prognosis recurrence-free survival estimates were based on Kaplan–Meier calculations and recurrence-free survival (RFS) defined as the time from the date of surgery to the date of PPR. The difference in RFS was assessed by a log-rank test.

Other statistical analyses. The categorical and numerical variables were analysed using the χ^2 -test and the Student *t*-test, respectively. *P*-values < 0.05 were considered to denote significant differences.

Data were managed with an Excel database (Microsoft, Redmond, WA, USA) and analysed using R 2.15 software, available online with caTools, rms, presence/absence, and verification libraries (<https://www.r-project.org/>).

RESULTS

During the study period, 1207 women with presumed early stage EC were documented as having received primary surgical treatment. Women with incomplete pathological data or with a follow-up <12 months without recurrence were excluded. About 861 women were included in the analysis according to the following distribution: Tours University Hospital (*n* = 240, 27.9%), Creteil Hospital (*n* = 112; 13.0%), Reims University Hospital (*n* = 101; 11.7%), Dijon Cancer Center (*n* = 97; 11.2%), Jeanne de Flandre University hospital (*n* = 95; 11.0%), Rennes University Hospital (*n* = 56; 6.5%), Tenon University Hospital (*n* = 54; 6.3%), and Senti-Endo trial (*n* = 106; 12.3%). The demographics and clinicopathological characteristics of women in the training cohort (*n* = 574) and the validation cohort (*n* = 287; Figure 1) are reported in Table 1.

Analysis of overall survival from time of EC diagnosis in the training cohort according to recurrence site revealed marked differences (Figure 2). Three-year overall survival was 96.2% for

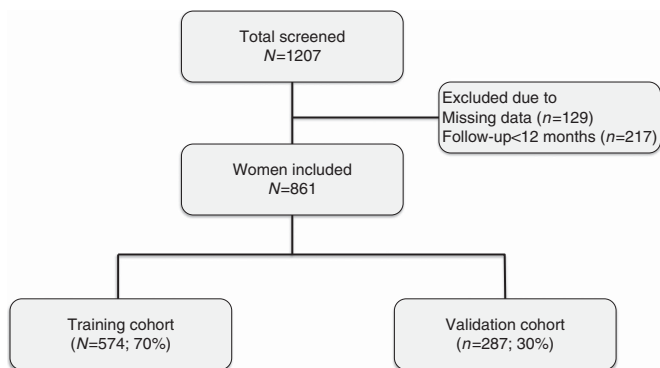


Figure 1. Flow chart of study participants.

Table 1. Women’s characteristics of the training (N = 574) and the validation (N = 287) cohorts

Characteristics	Training cohort N = 574 N of patients	%	Validation cohort N = 287 N of patients	%	P-value
Age median (yrs)	66		67		0.43
Mean	65.5		66.1		
Range	28–98		33–90		
Menopausal status					
Yes	451	78.6	229	79.8	0.67
Hormonal replacement therapy					
Yes	94	20.8	35	15.3	0.08
Histologic type					
Type I	466	81.2	243	84.7	0.20
Type II	108	18.8	44	15.3	
Histologic grade					
1	240	41.8	136	47.4	0.29
2	176	30.7	78	27.2	
3	158	27.5	73	25.4	
Depth of myometrial invasion					
< 50	294	51.2	160	55.7	0.45
≥ 50	257	44.8	116	40.4	
Unknown	23	4	11	3.9	
Lymphovascular space involvement					
Yes	178	31	80	27.9	0.34
No	396	69	207	72.1	
Classification ESMO-ESGO-ESTRO					
Low	185	32.2	111	38.7	0.29
Intermediate	77	13.4	33	11.5	
High intermediate	60	10.5	29	10.1	
High	252	43.9	114	39.7	
Lymphadenectomy					
Yes	437	76.1	223	77.7	0.60
No	137	23.9	64	22.3	
Lymph node involvement					
Yes	80	18.1	37	16.6	0.62
No	362	81.9	186	83.4	
Final FIGO stage					
I	391	68.1	210	73.2	0.31
II	53	9.3	22	7.7	
III	130	22.6	55	19.1	
Adjuvant therapy					
Chemotherapy/radiotherapy	147	25.6	67	23.3	0.19
ERT/brachytherapy	148	25.8	59	20.5	
Brachytherapy	142	24.7	82	28.6	
Surveillance	137	23.9	79	27.6	

Abbreviations: ERT = external radiation therapy; FIGO = International Federation of Gynecology and Obstetrics.

women with no recurrence; 73.4% women with vaginal vault recurrence, locoregional nodal recurrence, local central pelvic recurrence; and 38.1% for women with distant metastases and peritoneal carcinomatosis. Therefore, distant metastases and peritoneal carcinomatosis were confirmed as PPR. In the training set, 137 women did not undergo lymphadenectomy: 52 high-risk EC, 17 high-intermediate-risk EC, 15 intermediate-risk EC and 53 low-risk EC. Of the 52 high-risk women, 49 were older than 75 years, 21 had severe obesity with inherent morbidities (BMI ≥ 40).

Prediction of the probability of PPR in women with EC. Of the 574 women in the training cohort, 82 (14.3%) experienced PPR (Table 2). Treatment characteristics of women with PPR are

reported on Table 3. The median time between initial diagnosis and PPR was 9.0 months (range, 1–114 months). Table 4 summarises univariate and multivariate analyses. In the Cox proportional hazard model, the occurrence of PPR was independently associated with older age, EC histological type (2 vs 1), a higher histological grade (1 or 2 vs 3), FIGO stage, LVSI status (positive vs negative), and the performance of surgical nodal staging.

On the basis of the covariates independently associated with PPR, we constructed a nomogram and probabilities of PPR were reported at 3 years (Figure 3A). The prediction model had a concordance index of 0.82 (95% confidence interval (CI), 0.73–0.89).

External validation of the nomogram. The concordance index of the nomogram in the external validation model was 0.75

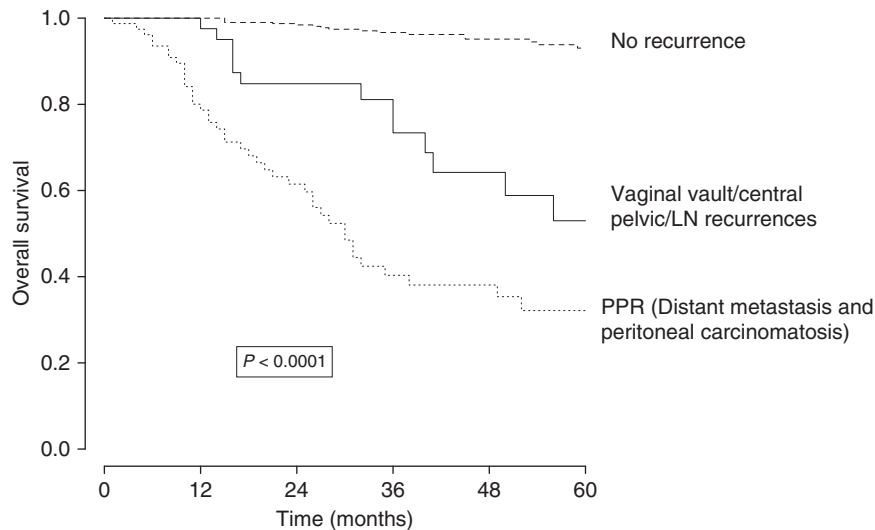


Figure 2. Overall survival according to recurrence site in women of the training cohort.

Table 2. Recurrence characteristics and follow-up					
Characteristic	Training cohort N = 574 N of patients	%	Validation cohort N = 287 N of patients	%	P-value
Sites of the distant metastases					
Bone	9	1.6	1	0.3	0.17
Visceral	17	3	13	4.5	0.23
Brain	3	0.5	3	1	0.40
Sus diaphragmatic LN	2	0.3	1	0.3	1
Distant metastases					
Yes	52	9	23	8	0.60
No	522	91	264	92	
Peritoneal carcinomatosis					
Yes	30	5.2	12	4.2	0.50
No	544	94.8	275	95.8	
Other sites of recurrence					
Vaginal vault	12	2.1	8	2.8	0.52
LN (pelvic/pa)	21	3.6	11	3.8	0.89
Central pelvic	10	1.7	3	1	0.04
Time between diagnosis and PPR (months)					
Median	9		10		0.59
Mean	17.0		15.9		
Range	1–114		2–61		
Follow-up (months)					
Median	34		30.5		0.27
Mean	42.9		41.3		
Range	1–151		1–165		

Abbreviations: LN = lymph node; pa = para-aortic; PPR = poor prognosis recurrence.

Table 3. Treatment characteristics of women with poor prognosis recurrences

	Brachytherapy	Chemotherapy/ radiotherapy	ERT/Brachytherapy	Surveillance
High (n = 61)	3 (4.9%)	23 (37.7%)	29 (47.5%)	6 (9.9%)
HIR (n = 9)	1 (11.1%)	1 (11.1%)	6 (66.7%)	1 (11.1%)
Intermediate (n = 4)	0	0	4 (100%)	0
Low (n = 8)	1 (12.5%)	0	1 (12.5%)	6 (75%)

Abbreviations: HIR = high intermediate risk.

Table 4. Univariate and multivariate analysis of factors predicting poor prognosis recurrence in the training set of women with endometrial cancer (N = 574)

Variables	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	P-value	Hazard ratio	95% CI	P-value
Age ≥60 years	2.55	1.34–4.84	0.004	1.69	0.87–3.30	0.12
Lymphadenectomy (pelvic and/or pa)	0.61	0.37–0.99	0.04	0.45	0.25–0.78	0.0047
Histologic type (II vs I)	6.00	3.79–9.50	<0.001	2.67	1.29–5.50	0.0079
Grade						
I	1.00					
II	2.29	1.05–4.99	0.03	1.71	0.72–4.05	0.22
III	8.21	4.13–16.3	<0.001	2.84	1.13–7.13	0.026
Lymphovascular invasion	5.17	3.03–8.84	<0.001	2.91	1.62–5.21	0.0003
FIGO staging						
I	1.00					
II	2.75	1.34–5.64	0.005	1.89	0.84–4.26	0.12
III	4.21	2.57–6.89	<0.001	2.00	1.11–3.60	0.02

Abbreviations: CI = confidence interval; FIGO = International Federation of Gynecology and Obstetrics.

(95% CI, 0.65–0.83). Of note, the nomogram was well calibrated. The mean absolute error in predicted probabilities was 1.9%, and the maximum error was <0.001%.

Optimal threshold of the nomogram. According to the PPR distribution at each probability of the nomogram, two groups were identified: a low-risk PPR group (PPR probability <0.15, 73.5% of the validation cohort, and PPR rate = 5.1%) and a high-risk PPR group (PPR probability ≥0.15, 26.5% of the validation cohort, and PPR rate = 29.6%). A PPR probability ≥0.15 corresponded to the optimal threshold of the Risk Stratification System (RSS) in terms of clinical utility with an overall diagnostic accuracy of 77.6%. At this threshold, sensitivity and specificity of the nomogram were 67.7% and 78.9%, respectively.

RFS and overall survival according to the optimal threshold of the nomogram. The median follow-up and initial recurrence time were 29 (range 1–165) and 10 (range 2–61) months, respectively. For the low-risk PPR group, median follow-up and initial PPR time were 36 (range 1–165) and 27 (3–50) months. For the high-risk PPR group, median follow-up and initial PPR time were 25 (3–124) and 9 (2–61) months (Figure 3B).

The 3-year RFS rates were 98.1% (95% CI, 92.8–99.9) and 65.7% (95% CI, 55.5–74.9) for the low- and high-risk PPR groups, respectively ($P < 0.0001$; Figure 3B). The 3-year overall survival rates were 94.4% (95% CI, 87.9–98.0) and 57.8% (95% CI, 47.5–67.6) for the low- and high-risk PPR groups.

Evaluation of existing risk stratification systems used in EC management. The current RSS were tested to evaluate their accuracy to predict PPR (Table 5). The concordance indexes of the FIGO classification, ESMO/ESGO/ESTRO classification, GOG-99 criteria, PORTEC 1 criteria, and SEPAL study were 0.69 (0.59–0.779), 0.70 (0.60–0.788), 0.61 (0.507–0.706), 0.58 (0.474–0.678), and 0.685 (0.584–0.774), respectively.

Clinical utility of our prediction model. Our model could be used to design a clinical trial to test the efficacy of systemic chemotherapy or chemoradiation therapy to reduce the risk of PPR. We assumed a 50% risk reduction by adjuvant treatment. If a trial included all patients without any selection criteria, then 92.75% of patients would receive unnecessary treatment and suffer from severe complications. However, a scenario can be suggested based on our risk model. If we enrolled cases with an estimated risk of more than 15%, then the percentage of unnecessarily treated patients and the required size of the study population would both be reduced by 56.5%, whereas the proportion of benefited patients among enrolled patients would increase by 49%. Figure 3C shows how the model could be used to design a clinical trial to test the efficacy of adjuvant treatment to reduce the risk of PPR after adjuvant treatment.

DISCUSSION

The results of the present study demonstrate that our nomogram accurately predicts which women with FIGO stage I–III EC are at risk of PPR. It would appear to be more accurate than the current RSS that are used worldwide to adapt surgical strategies and indications for adjuvant treatments. On the basis of these results, women may be divided into two groups that are highly predictive of PPR. We believe this tool can help select candidates for trials designed to evaluate the efficacy of adjuvant treatment in EC.

Several RSS based on clinical and pathological factors have been developed to standardise EC management (Creutzberg *et al*, 2000; Keys *et al*, 2004; Todo *et al*, 2010). These RSS guide clinicians in their decision-making by grouping women according to their risk group for recurrence. They also form the basis of international guidelines for surgical staging and adjuvant therapies (Todo *et al*, 2010; Querleu *et al*, 2011; Colombo *et al*, 2013; Colombo *et al*,

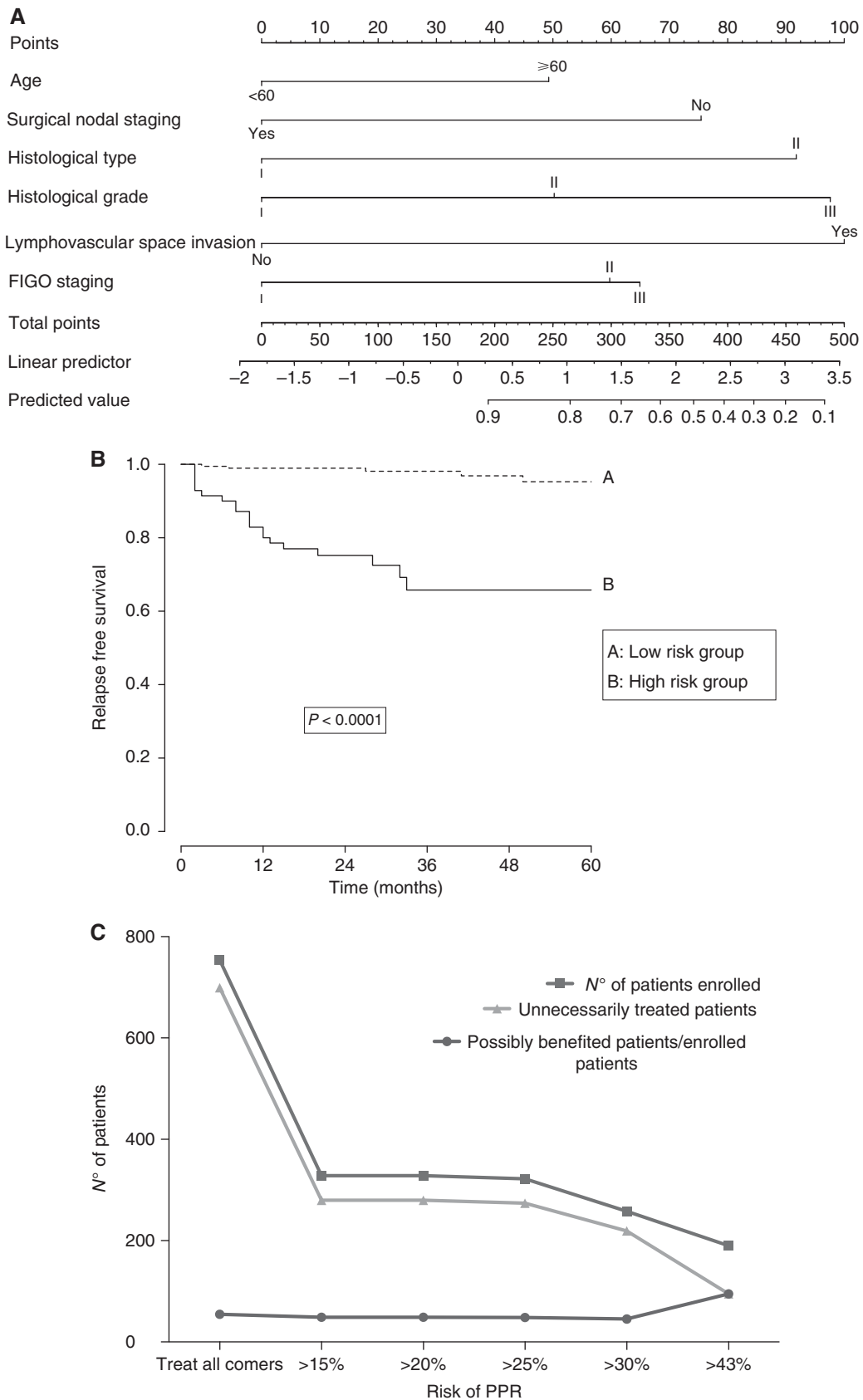


Figure 3. Nomogram presentation. (A) Nomogram for predicting 3-year probability of poor prognosis recurrence (PPR) for women with I–III FIGO stage endometrial cancer. To estimate risk, calculate points for each variable by drawing a straight line from patient’s variable value to the axis labelled ‘Points’. Sum all points and draw a straight line from the total point axis to the 3-year recurrence axis. (B) Recurrence-free survival according to nomogram optimal threshold. (C) Graph showing how the prediction model could be used to design a clinical trial testing the efficacy of systemic chemotherapy with or without radiation in endometrial cancer.

Table 5. Evaluation of existing Risk Stratification Systems used in EC management

	Concordance index (95% CI)
FIGO	0.69 (0.59–0.779)
ESMO	0.715 (0.616–0.801)
GOG-99	0.61(0.507–0.706)
SEPAL	0.685 (0.584–0.774)
PORTEC	0.58 (0.474–0.678)
ESMO-ESGO-ESTRO	0.70 (0.60–0.788)

Abbreviations: CI = confidence interval; EC = endometrial cancer; FIGO = International Federation of Gynecology and Obstetrics.

2016a). However, such an approach is based on the assumption that all women within a risk group are at equal risk, whereas recent studies have demonstrated that the RSS are not accurate enough to predict recurrence (Bendifallah *et al*, 2015). To address this limitation, individual characteristics of the woman (such as age and genetic susceptibility) should be taken into account when deciding on a treatment option in addition to tumour biology. In this specific setting, predictive models such as nomograms have been shown to provide reasonable personalised risk estimates that facilitate management-related decisions (Shariat *et al*, 2009). Hence, optimising outcome in women with EC will require individualised tailoring of care based on multiple clinical and biological risk factors.

Approximately 70% of all EC recurrence occurs within the first 3 years after primary surgery (Fung-Kee-Fung *et al*, 2006; Ben Arie *et al*, 2012; Kilgore *et al*, 2013). We found that women with PPR decline rapidly during the initial 2 years (median time to PPR was 9 months), whereas those with other recurrence sites decline gradually over the years. In fact, more than 50% of women with PPR die during the first year and fewer than 30% survive more than 5 years after recurrence (Bouros *et al*, 1996; Salani *et al*, 2011). However, although authors agree that distant metastases are associated with reduced overall survival (Creutzberg *et al*, 2003), there is no clear consensus to define PPR. In the current study, the PPR group, consisting of women with distant metastases and peritoneal carcinomatosis, had the lowest 3-year overall survival when compared with other sites of recurrence. There are limited data about prognostic factors and outcomes of women whose EC recurs with peritoneal carcinomatosis. This recurrence site has been previously grouped with other sites under the terms: extravaginal (Moschiano *et al*, 2014), abdominal (Esselen *et al*, 2011), and extrapelvic (Odagiri *et al*, 2011; Robbins *et al*, 2012). When considering peritoneal carcinomatosis as a separate entity, we found a 3-year survival rate of 33.1%. Indeed, the finding that these women had the lowest overall survival rate suggests that further intensification of systemic treatment and exploration of novel therapies may be needed for this group. Women with PPR are generally considered incurable except in the setting of operable situations (e.g., isolated metastases to the liver or lung that can be resected and women with peritoneal carcinomatosis who can undergo successful cytoreduction and have no macroscopic residual disease (Morice *et al*, 2016). In fact, most of these women are candidates for systemic palliative therapy, but the choice between hormonal treatment and chemotherapy rely on histopathological and clinical features at an individual level. Indeed, progestogens, tamoxifen alternated with megestrol, gonadotropin-releasing hormone analogues, selective oestrogen receptor modulators, and aromatase inhibitors have been used with response rates ranging from 11 to 56% (Panici *et al*, 2008).

There is a persistent debate about the rationale of adjuvant chemotherapy in standard management of high-intermediate- and

high-risk ECs. Although chemotherapy seems to be recommended for high-risk women with lymph node metastasis, its indication for those without is more questionable. The recent European guidelines state that adjuvant systemic therapy is still under investigation for women with type 1 EC at increased risk of recurrence with negative nodal staging or without nodal staging. The results of both ongoing and future trials are expected to further clarify the place of adjuvant chemotherapy or chemoradiation for this subgroup of women. In this specific setting, the current prediction model may be useful to select candidates for such clinical trials, for example, a women who's age is over 60 years (50 points) in whom lymphadenectomy was not performed (75 points) could be identified with a probability of not having a PPR probability of 25% (or a probability of 75% of having a PPR) based on the definitive pathology results if the tumour was type I (0 points), grade 2 (60 points) with LVSI (100 points) and a FIGO stage II. The personalised risk estimate is of particular interest in that case if substantial comorbidities are present because it informs the discussion of the benefits of adjuvant treatment based on her health status and PPR risk. Indeed, in our scenario, we could reduce unnecessary treatment by 60% using a probability of 15% as a cutoff for study enrolment. Moreover, this selective enrolment strategy could also reduce the number of women to be enrolled by 56.5% as well as reducing the required sample size and the population size to be screened. If all women at high risk were enrolled, 377 would be required for each arm at a power of 90% and an alpha error of 0.25. However, if we only enrolled high-risk women with a probability of recurrence > 15% according to the reported optimal threshold, the required sample size would decrease to 164 women for each arm at the same power. Thus, our prediction model may help to reduce the resources required for trials.

The strengths of our study lie in its multicenter nature and the large number of women included. However, some limits deserve to be mentioned. First, we cannot exclude an inherent bias linked to its retrospective nature. Second, during the data collection period, modifications occurred in staging modalities (FIGO classification) and surgical techniques such as lymph node staging (Panici *et al*, 2008; Pecorelli and Sergio, 2009; Ballester *et al*, 2011). Finally, our cohort included women from several centres and discrepancies in patient management might have affected our results. However, all included centres were regional referral centres applying the current French guidelines.

In conclusion, we have developed a nomogram to predict PPR in women with FIGO stage I–III EC. It could be used as an additional tool to better select women requiring adjuvant treatment. Our model may also facilitate the design of clinical trials for systemic chemotherapy in EC by selecting a population at high risk of PPR in high-risk EC women.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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