A Pre- and Intraoperative Scoring System to Predict Nodal Metastasis in Endometrial Cancer

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ABSTRACT

Objective: The aim of this study was to identify risk factors to predict lymph node metastasis in patients with endometrial cancer, and to develop a scoring system that guides surgical decision-making regarding the need to perform lymphadenectomy.

Methods/materials: A retrospective multicenter study was performed of patients who underwent hysterectomy, bilateral salpingo-oophorectomy, and lymphadenectomy for endometrial cancer from 2003 to 2014. Pre- and intraoperative risk factors for lymph node involvement were analyzed by univariate and multivariate logistic regression. The relevant factors were used to develop a scoring system to predict lymph node metastasis.

Results: A total of 329 patients were assessed. The characteristics associated with nodal metastasis in univariate analysis included elevated CA-125 level, preoperative histological grade, increased endometrial thickness, and pathologic tumor features (size, extension in myometrium, cervix and adnexa, and lower uterine segment involvement). The following parameters remained significant on multivariate logistic regression analysis: preoperative histological grade, tumor extension, and lower uterine segment involvement. The resulting scoring system showed good accuracy with area under the receiving operating curve of 0.858 (95% confidence interval, 0.80 – 0.91). With a cut-off of 2 points, the calculated NPV (negative predictive value) of the model was 0.976, which corresponds to approximately 3% probability of positive lymph nodes.

Conclusions: A highly accurate scoring system was developed based on three pre- and intraoperative risk factors for predicting lymph node metastasis. If further validated, this model could greatly aid clinicians in the surgical management of endometrial cancer.
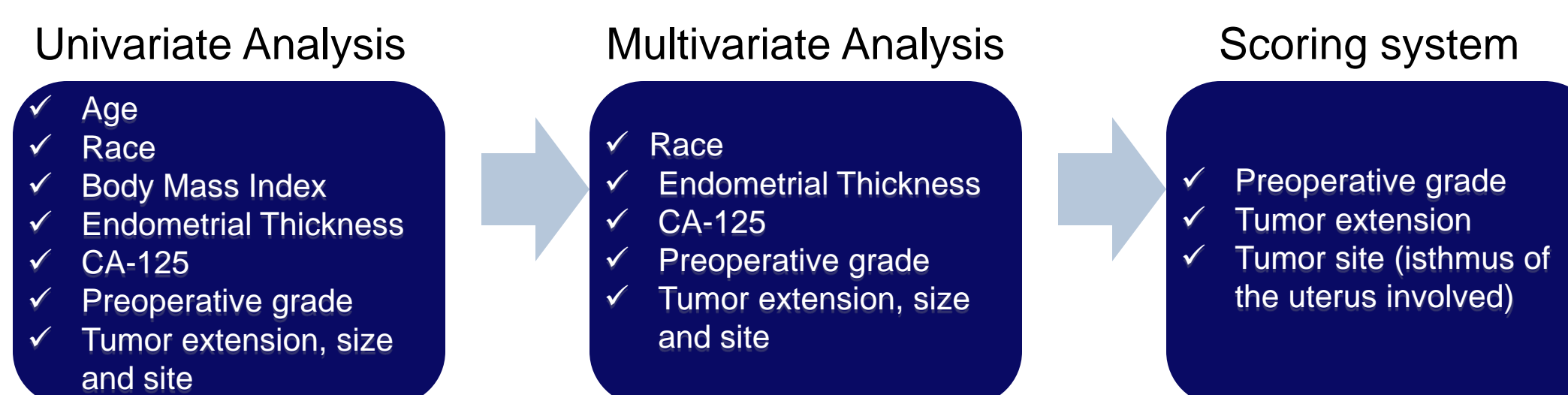
INTRODUCTION

The standard surgical approach for staging and treatment of endometrial cancer includes hysterectomy, bilateral salpingo-ophorectomy and para-aortic and pelvic lymphadenectomy. However, lymphadenectomy remains controversial, even though lymph node involvement is an important prognosis marker for survival. Considering that the vast majority of women with endometrial cancer are diagnosed in the early stages with no lymph nodes metastasis, this procedure causes an unnecessary risk of operative complications for these patients. The aim of this study was to develop a simple and accurate scoring system based on a multivariate logistic regression using pre- and intraoperative risk factors to predict lymph node metastasis in endometrial cancer.

METHODS

This multicenter, ethics committee approved (CEP 0751/11), retrospective study included 456 patients with histologically confirmed endometrial carcinoma treated from 2003-2014, and focused on the 329 surgically staged patients who underwent pelvic and para-aortic lymphadenectomy. Three Brazilian hospitals participated: Hospital São Paulo/ Universidade Federal de São Paulo (São Paulo, SP), Complexo Hospitalar do Vale do Paraíba/ Universidade de Taubaté (Taubaté, SP) and Hospital Erasto Gaertner (Curitiba, PR). Patients were divided into 2 groups: lymph node negative (LNN) and lymph node positive (LNP), according to the event occurrence.

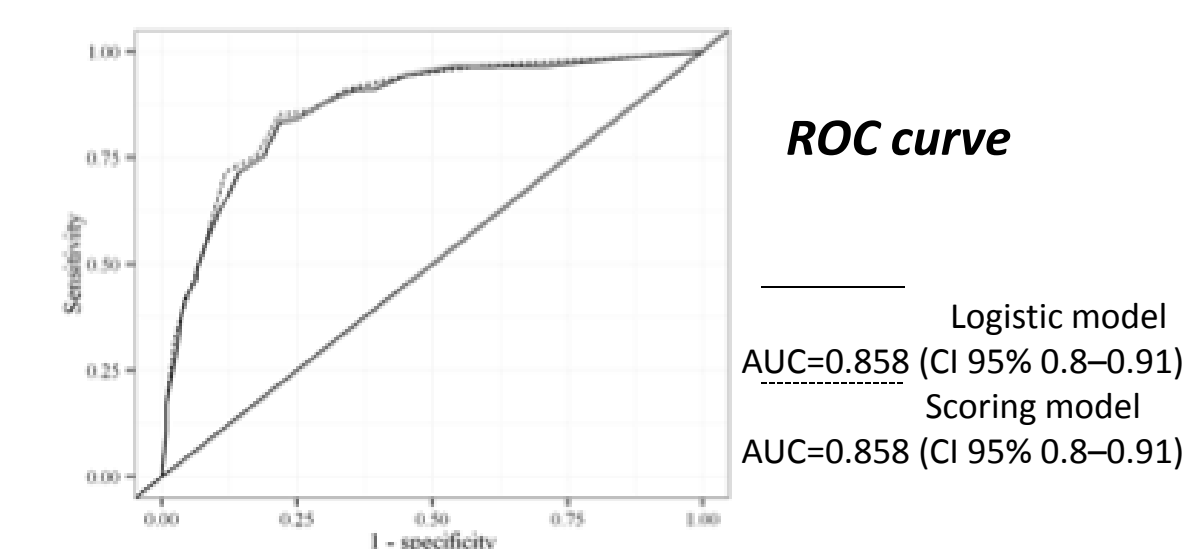### Risk factors evaluation steps for scoring system construction:

Univariate Analysis
- Age
- Race
- Body Mass Index
- Endometrial Thickness
- CA-125
- Preoperative grade
- Tumor extension, size and site

Multivariate Analysis
- Race
- Endometrial Thickness
- CA-125
- Preoperative grade
- Tumor extension, size and site

Scoring system
- Preoperative grade
- Tumor extension
- Tumor site (isthmus of the uterus involved)

RESULTS

Characteristics of the study patients – univariate analysis

Variable		LNN (258, 78.4%)	LNP (71, 21.6%)	Total (329)	P value
Age at diagnosis, y	Mean (SD)	63 (10)	64.1 (10.2)	63.2 (10.4)	0.381
Race (white/ non-white)		226 (89.7%)/ 26 (10.3%)	54 (78.2%)/ 15 (21%)	280 (87%)/ 41 (13%)	0.021
Body mass index	Mean (SD)	30.3 (7.3)	29 (6.5)	30 (7.2)	0.211
Number of lymph nodes removed		16 (18.4)	21 (22.6)	17 (9.3)	0.029
Endometrial thickness (mm)		16 (21.1)	20.1 (30.7)	16.4 (21.2)	0.012
CA-125 (U/mL)	Median (mean)	15 (54.2)	34.3 (274.2)	17 (101.3)	< 0.001
Preoperative histological grade Gx (Non-determined grade) G1 G2 G3		61 (24.2%) 108 (42.8%) 46 (18.3%) 37 (14.7%)	17 (24%) 16 (22.5%) 13 (18.3%) 25 (35.2%)	78 (24.1%) 124 (38.3%) 59 (18.3%) 62 (19.3%)	< 0.001
Tumor extension (FIGO 2009) I II III		204 (81.3%) 36 (14.3%) 11 (4.4%)	20 (32.2%) 22 (35.2%) 20 (32.3%)	224 (75.4%) 58 (26.2%) 31 (9.9%)	< 0.001
Tumor size (mm)	Median(mean)	35 (40.6)	50.5 (59.8)	40 (44.7%)	< 0.001
Tumor site (no isthmus/isthmus)		158 (68.4%)/ 71 (31.6%)	19 (29.2%)/ 46 (71%)	177 (60%)/ 119 (40%)	< 0.001

Multivariate logistic regression model for nodal metastasis prediction

Variables	OR (95% CI)	P value	Score
Preop grade			
G1	1		0
G2	3.7 (1.3 - 10.9)	0.0016	3
G3	5.33 (2 – 14.7)	0.001	5
Tumor extension			
IA	1		0
IB	2.4 (0.82 – 7.51)	0.117	2
II	7.43 (2.6 – 23.9)	<0.001	7
III	17 (5.43 – 60)	<0.001	12
Tumor site			
No isthmus	1		0
Isthmus	2.75 (1.2 – 6.37)	0.016	2

ROC curve

Logistic model
AUC=0.858 (CI 95% 0.8–0.91)
Scoring model
AUC=0.858 (CI 95% 0.8–0.91)

Prediction graph
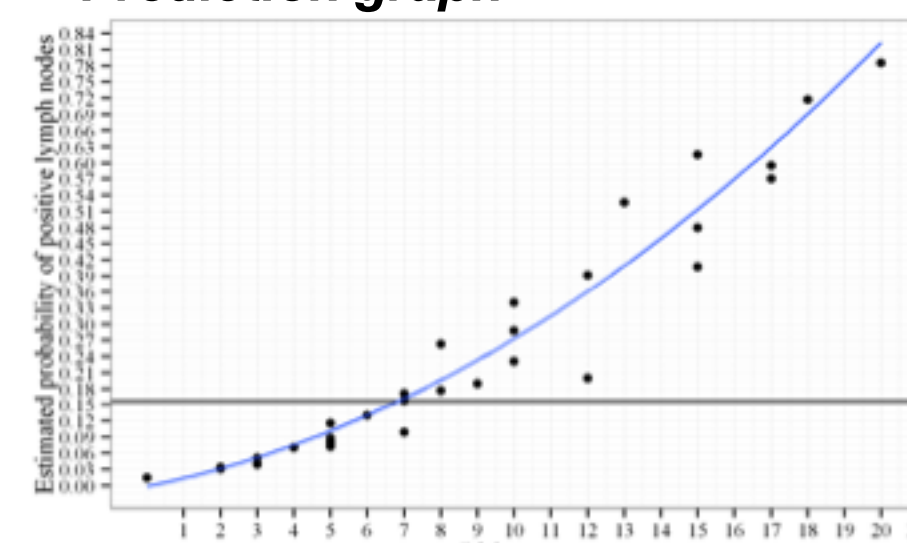
The probability of lymph node metastasis is calculated connecting the total score in *x* axis to its correspondent rate in *y* axis.

Prediction chart

Score	PPLN	Score	PPLN	Score	PPLN
0	<0.01	7	16.2%	14	46%
1	1.4%	8	19.6%	15	51.4%
2	3.2%	9	23.4%	16	57%
3	5.2%	10	27.3%	17	62.9%
4	7.6%	11	31.6%	18	69.1%
5	10.2%	12	36.1%	19	75.6%
6	13.1%	13	40.9%	20	82.3%

PPLN probability of positive lymph nodes

DISCUSSION/ CONCLUSION

Hypothetical case: a patient with preoperative histological grade 2 (3 points) with tumor extension more than 50% of myometrium or uterine stage IB (2 points) and isthmus of the uterus involved (2 points) would present a total sum of 7 points, which corresponds to 16.2% of lymph node m etastasis probability. In conclusion, this study developed a scoring system based on three variables obtained in pre- and intraoperative instances that accurately predicts individualized risk of lymph node metastasis in endometrial cancer.

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