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Original article

Performance of four published risk models to predict sentinel lymph-node involvement in Australian women with early breast cancer

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ABSTRACT

Background: Sentinel lymph-node biopsy has reduced the need for extensive axillary surgery for staging. It still exposes women to associated morbidity. Risk models that use clinical and pathology information of the primary tumour to predict sentinel lymph-node metastasis may allow further improvements in care. This study assessed the performance of four published risk models for predicting sentinel lymph-node metastasis in Australian women with early breast cancer; including one model developed in an Australian population.
Methods: The Sentinel Node Biopsy Versus Axillary Clearance (SNAC) trial dataset was used to assess model discrimination by calculating the area under the receiver-operating-characteristic curve (AUC) and the false-negative rate for sentinel lymph-node metastasis using model-predicted risk cut-points of 10%, 20%, 30%, and calibration using Hosmer-Lemeshow tests and calibration plots.
Results: The sentinel node was positive in 248 of 982 (25.2%) women (158 macrometastasis, 90 micrometastasis). The AUCs of risk models ranged from 0.70 to 0.74 for prediction of any sentinel-node metastasis; 0.72 to 0.75 for macrometastasis. Calibration was poor for the three models developed outside of Australia (lack-of-fit statistics, $P < 0.001$). For women with a model-predicted risk of sentinel lymph-node metastasis $\leq$10%, observed risk was 0–13% (three models <10%), false-negative rate 0–9%; 1–17% of women were classified in this range.
Conclusion: All four models showed good discrimination for predicting sentinel lymph-node metastasis, in particular for macrometastasis. With further development such risk models could have a role in the provision of reassurance to low risk women with normal nodes sonographicaally for whom no axillary surgery is contemplated.

Introduction

Sentinel lymph-node biopsy is the current recommended procedure to assess axillary lymph-node metastasis in women with early breast cancer and clinically negative nodes [1–3], but still exposes women to morbidity [4]. The SLN is negative in up to two-thirds of women and trials of adjuvant therapy strategies that may allow women to avoid SLN biopsy are currently under way [5]. Methods to classify a women's risk of axillary metastasis would be valuable.

Mathematical risk prediction models have been developed to address this clinical need. They combine known clinical and pathological risk factors for nodal metastasis by weighting each factor to predict the probability of SLN involvement. They can be presented graphically (nomogram) to assist in preoperative counselling of patients and planning management. Four published risk models for predicting SLN metastasis have been developed by the Memorial Sloan Kettering Cancer Center (MSKCC) in a United States breast cancer population [6], the Shanghai Cancer Hospital (SCH) in China [7], Yeniay et al. in Turkey [8], and Coombs et al. in an Australian breast cancer screening population [9].

The 0performance of a risk model can vary when applied to a different population from the one in which it was developed requiring calibration for use in different settings. We aimed to compare the performance of the MSKCC [6], SCH [7], Yeniay [8], and Coombs [9] models in Australian women with newly diagnosed early breast cancer.

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Methods

Data source

Sentinel Node Biopsy versus Axillary Clearance (SNAC-1) trial data were used. Trial design and outcomes [3,10] and analysis of SLN identification in SNAC-1 have been reported [11]. Table 1 shows the key clinicopathological variables for SNAC and the published models.

Missing data for model predictors were imputed. Imputation maintained consistency in the population to which the risk models were applied, ensuring comparability of findings.

Outcome

A positive SLN was defined as the presence of SLN macrometastases (>2 mm) or micrometastases (>0.2–2 mm). Isolated tumour cells (≤0.2 mm) were classified as SLN negative. In secondary analyses, SLN positivity was defined as macrometastasis alone, with micrometastasis and isolated tumour cells classified as SLN negative, matching the definition used in current surgical practice. For further validation of the MSKCC model, isolated tumour cells were included in the definition of SLN positive, consistent with the definition used for model development.

Model development studies

The SNAC study and two of the four model development studies defined a positive SLN as a metastasis identified by any one results of immunohistochemistry, serial sectioning and standard H&E. The SCH study did not include immunohistochemistry and the Coombs study did not report histopathology methodology.

The number of model predictors ranged from two factors for the Coombs model to nine for the MSKCC model (Appendix 1). The MSKCC and SCH studies externally validated their model in an independent population.

The SCH [7], Yeniay [8] and Coombs [9] model equations were extracted from the publication (Appendix 2). The nomogram for the MSKCC model appears in the paper [6] and is available online. MSKCC statisticians used their mathematical model to independently calculate the risk of SLN involvement for women in SNAC.

Statistical analysis

To assess the predictive performance of each risk model, we applied the model to the SNAC population to compute the predicted probabilities of SLN metastasis (present, absent) for each SNAC patient, and report on model discrimination and calibration.

Model discrimination refers to the ability of the model to differentiate between patients who do and do not have a SLN metastasis. We calculate the area under curve (AUC) of the receiver-operating-characteristic (ROC) curve as an overall measure of discrimination to compare the four models. AUC is interpretable as the probability that the risk score orders the risk of a randomly chosen woman with positive SLN above that of a randomly chosen woman with negative SLN. In clinical terms, an AUC of 0.5 is consistent with prediction of SLN status that can be achieved by chance alone, and 1.0 indicates perfect discrimination. Odds of correct ordering by risk score of the random pair are 4:1 for AUC of 0.8, 3:1 for AUC 0.75, and 2:1 for AUC 0.67. AUC 0.7–0.8 indicates good discrimination. In practice, prediction models are not used to order random pairs of patients with and without the condition of interest (SLN metastases). As such, AUC values do not provide a clinical meaningful measure of model discrimination. Thus, we also estimate the clinical accuracy of the models to inform clinical decisions such as for SLN biopsy. Given the main potential clinical use of the model may be to rule out axillary metastases in women classified as low risk who may avoid SLN biopsy, we report the false negative rate is the primary measure of clinical accuracy. The false negative rate as the proportion of women with SLN metastases who have a model calculated probability of SLN ≤10% that would be missed if a model-predicted risk of ≤10% is used as a threshold for clinical decisions to avoid SLN biopsy. Further calculations were performed at thresholds of ≤5, ≤20 and ≤ 30%.

Model calibration refers to the agreement between predicted and observed risks. This is shown graphically in a calibration plot by categorising patients in deciles of model-predicted probability of SLN metastasis on the x-axis and plotting observed risks and standard errors for each group on the y-axis. We present the calibration plot for each model for groups with a predicted risk of 0.0–0.5. Calibration was assessed using the Hosmer-Lemeshow test [12,13], Calibration plots were characterised by intercept a and slope b in logistic regression. In the model development populations, $a = 0$, $b = 1$. Estimates of a in the SNAC cohort differing from 0 suggest predictions systematically too low or too high (termed bias, or failure of 'calibration-in-the-large' [14]), while $b < 1$ reflects lesser association between risk score and SLN metastasis in the SNAC cohort than was the case in the original modelling development cohort. To provide a clinically meaningful measure of model calibration, we report the proportion of women with a model calculated risk of ≤10% who have true SLN metastases; an observed risk >10% would be considered clinically unacceptable.

Statistical analyses used rms, pROC and knitr in R, version 3.2.5, and SPSS (version 21.0; SPSS Inc., Chicago, IL, USA).

Ethics approval

The SNAC trial and this secondary study were approved by the appropriate institutional ethics committees.

Results

SNAC cohort

SLNs were detected in 1024 of 1088 patients in the SNAC trial, of whom 982 were eligible for the present analysis. Exclusions were 34 patients with ductal carcinoma in situ and 8 with missing information about tumour size. Overall, 69 (7%) of patients required some data imputation for missing values. Imputations were: histology grade ($n = 5$); lymphovascular invasion ($n = 1$); ER status ($n = 4$); PR status ($n = 66$).

The distribution of tumour characteristics and SLNB technique varied between the SNAC cohort and model development populations are shown in Table 1.

SLN metastases

In the SNAC cohort, the median number of SLNs removed was 2 (range 1–8). Overall, 277 patients had SLN metastases identified (macrometastases 158, micrometastases 90, isolated tumour cells 29, Table 1). For the assessment of risk model performance, SLN was classified as positive in the 248 patients (25.3%) with micro- or macrometastasis.

Model performance

The AUCs of each model ranged from 0.70 to 0.74 (Table 2, Fig. 1). The MSKCC, SCH, and Yeniay models failed to provide calibration-in-the-large for SNAC women ($P < 0.001$), and the Coombs model result was borderline ($P = 0.05$). The SCH and Yeniay models calibrated poorly on slope ($P < 0.001$), indicating overoptimism concerning the

Table 1
Patient characteristics for SNAC cohort and model development populations and SLNB technique.

Characteristic	SNAC (Australia)[a]	MSKCC (USA)	SCH (China)	Coombs (Australia)	Yeniay (Turkey)
No. of patients	982[b]	3786	1000	4585	932
Recruitment period	2001–2005	1996–2002		1996–1999	2003–2011
Age, years					
Median	57.5	56	50	NR	52
Range	28–83	20–91	20–87	50–69	19–85
Tumour size, mm					
T1 ≤ 20	782 (79.6)	3098 (81.8)	645 (64.5)[c]	3674 (80.1)	630 (67.6)[c]
T2 21–50	190 (19.3)	655 (17.3)	344 (34.4)	911 (19.9)	278 (29.8)
T3 >50	10 (1.0)	33 (0.9)	11 (1.1)	0	5 (0.5)
Tumour type				NR	
DCIS	0	0[c]	34 (3.4)[c]	–	0[c]
Ductal	808 (82.3)	3244 (85.7)	907 (90.7)	–	718 (77.0)
Lobular	95 (9.7)	372 (19.8)	11 (1.1)	–	48 (5.2)
Other		170 (4.5)	48 (4.8)	–	158 (17.0)
Tumour location				NR	NR
Upper outer quadrant	492 (50.1)	2154 (56.9)[c]	500 (50)[c]	–	–
Upper inner quadrant	173 (17.6)	564 (14.9)	234 (23.4)	–	–
Central	108 (11.0)	285 (7.5)	47 (4.7)	–	–
Lower inner quadrant	80 (8.1)	271 (7.2)	89 (8.9)	–	–
Lower outer quadrant	129 (13.1)	480 (12.7)	130 (13)	–	–
Histologic grade					
I	310 (31.6)	331 (8.7)[c]	52 (5.2)[c]	1610 (35.1)[c]	118 (12.7)
II	423 (43.1)	1033 (27.3)	709 (70.9)	2031 (44.3)	207 (22.2)
III	244 (24.8)	1782 (47.1)	231 (23.1)	944 (20.6)	69 (7.4)
Unknown	5 (0.5)	311 (7.1)	8 (0.8)		538 (57.7)
Nuclear grade	NR		NR	NR	
I	–	298 (7.9)	–	–	144 (15.5)
II	–	1732 (45.7)	–	–	562 (60.3)
III	–	1073 (28.3)	–	–	118 (12.7)
Unknown	–	311 (8.2)	–	–	108 (11.6)
Estrogen receptor status				NR	
Positive	803 (81.8)	2471 (65.3)	780 (78.0)	–	704 (75.5)[c]
Negative	175 (17.8)	640 (16.9)	200 (20.0)	–	224 (24.0)
Unknown	4 (0.4)	675 (17.8)			
Progesterone receptor status				NR	
Positive	654 (66.6)	1866 (49.3)[c]	762 (76.2)[c]	–	625 (67.0)[c]
Negative	262 (26.7)	1230 (32.5)	216 (21.6)	–	303 (32.5)
Unknown	66 (6.7)	690 (18.2)	22 (2.2)	–	4 (0.4)
Lymphovascular invasion				NR	
Yes	218 (22.2)	797 (21.1)	187 (18.7)	–	163 (17.5)[c]
No	763 (77.8)	2989 (78.9)		–	769 (82.5)
Multifocality				NR	
Yes	64 (6.5)	843 (22.3)[c]	29 (2.9)[c]	–	95 (10.2)[c]
No	918 (93.5)	2943 (77.7)	971 (97.1)	–	836 (89.7)
SLN metastasis					
Present	248 (25.3)	1100 (29.1)[d]	295 (29.5)	1089 (23.8)	271 (29.0)
Macrometastases (>2 mm)	158 (16.1)	869 (23.0)[d]	NR	NR	196 (21.0)
Micrometastases (0.2–2 mm)	90 (9.2)	231 (6.1)[d]	–	–	75 (8.0)
Absent (nil or isolated tumour cells)	705 (71.8)	2686 (70.9)[d]	–	–	661 (70.9)
Isolated tumour cells	29 (3.0)	151 (4.0)[d]	–	–	36 (3.9)
SLNB Technique					
Scintigraphy	Y	Y	Y	N	Y
Blue Dye	Y	Y	N	N	Y
cN0	Y	U/K	Y	U/K	Y

DCIS = ductal carcinoma in situ; NR = not reported; SLN = sentinel lymph node.
Percentages may not add to 100%, indicating patient data not available or not reported.
[a] Validation cohort.
[b] Excluding 8 patients with unreported tumour size.
[c] Indicates that the difference between the model development cohort and the SNAC cohort was statistically significant ($P < 0.05$).
[d] As advised by MSKCC. van la Parra et al. have shown the proof of principle that to optimize application of the MSKCC model in a population with SLN size rather than method of detection, the following equivalencies should be made: isolated tumour cells = immunohistochemistry; micrometastases = serial sectioning; macrometastases = routine hematoxylin & eosin and frozen section [19].

strength of the association with metastasis. Findings were similar in secondary analyses of prediction of macrometasis alone, and for the MSKCC model, for prediction of SLN metastasis including isolated tumour cells (Table 2). The Coombs model provided the best calibration statistics of these models, although the Hosmer-Lemeshow test of discrepancy between observed SLN metastasis and risk estimate decile was statistically significant ($P = 0.03$).

On examination of model performance for prediction of SLN metastasis in the low risk range (probability 0.0–0.5), Fig. 2 shows the proportion of women in each decile of predicted risk up to 0.5 varied between models (Fig. 2 barplot). The SCH model generally underestimated risk with observed risk higher than predicted risk for most decile groups; whereas for all other models, the observed risk for each group did not exceed the predicted risk (Fig. 2 calibration plot). The Coombs model showed the closest agreement between observed and predicted risk across this range.

For prediction of risk <10%, the SCH model classified more women (167, 17.0%) in this range than other models, but also

Table 2
Comparison of the predicted probabilities of sentinel lymph-node metastasis with observed sentinel lymph-node metastases in the SNAC cohort.

Study	Discrimination			Calibration						Lack of fit	
	AUC	SE (AUC)	95% CI	Intercept a	SE, a	*P*	Slope b	SE, b	*P*	H-L X^2	*P*
Prediction of SLN micro- and macrometastasis, *n* = 248											
MSKCC	0.73	0.02	0.70–0.77	−0.51	0.09	<0.001	0.89	0.08	0.19	40.3	<0.001
SCH	0.71	0.02	0.67–0.75	−0.41	0.10	<0.001	0.62	0.06	<0.001	62.6	<0.001
Coombs	0.70	0.02	0.66–0.73	−0.24	0.12	0.05	1.03	0.13	0.81	17.3	0.03
Yeniay[a]	0.74	0.02	0.70–0.77	−0.64	0.09	<0.001	0.76	0.07	<0.001	74.9	<0.001
Prediction of SLN macrometastasis, *n*=158											
MSKCC	0.75	0.02	0.71–0.79	−1.16	0.10	<0.001	0.91	0.09	<0.001	164.7	<0.001
SCH	0.73	0.02	0.69–0.78	−1.03	0.10	<0.001	0.07	0.07	<0.001	133.2	<0.001
Coombs	0.72	0.02	0.68–0.76	−0.81	0.12	<0.001	1.09	0.13	0.49	103.6	<0.001
Yeniay	0.75	0.02	0.70–0.79	−1.32	0.09	<0.001	0.72	0.07	<0.001	256.7	<0.001
Prediction of any SLN metastasis[a]											
MSKCC	0.72	0.02	0.68–0.76	−0.36	0.09	<0.001	0.84	0.08	0.04	22.3	0.004

AUC = area under the curve; SE = standard error; CI = confidence interval; H-L=Hosmer-Lemeshow; SLN = sentinel lymph node; SNAC= Sentinel Node Biopsy Versus Axillary Clearance; AUC = area under the curve; SE = standard error; MSKCC = Memorial Sloan Kettering Cancer Center; SCH= Shanghai Cancer Hospital.
[a] Including isolated tumour cells.

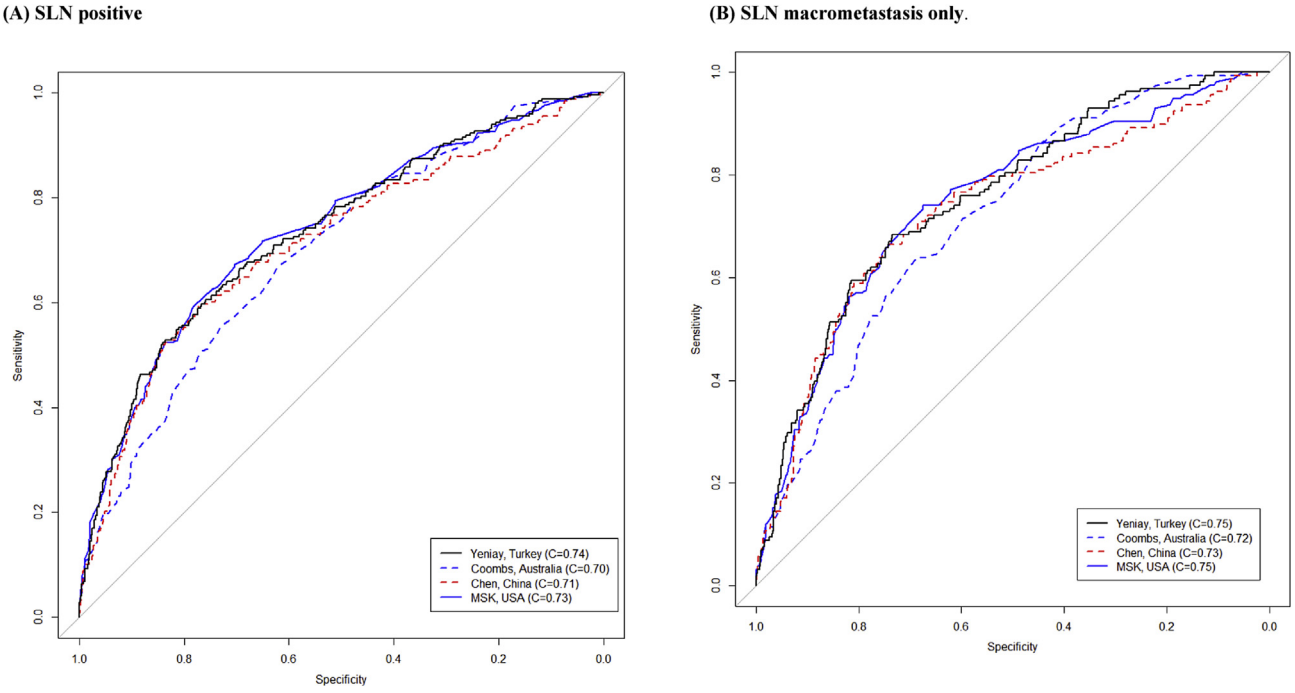

Fig. 1. Receiver operator characteristic curves and areas under the curves for risk models: a. sentinel-lymph-node positive; and B. sentinel-lymph-node macrometastases.

underestimated risk for this group. For the MSKCC, Coombs and Yeniay models, the group of women with a predicted risk <10% also had an observed risk <10%. Of these models, the MSKCC model classified 90 (9.2%) women in this range, compared with 27 (2.7%) for the Coombs model, and 7 (0.7%) for the Yeniay model (Table 3). For assessment of model discrimination for prediction of SNB metastases at this 10% risk cut-point, the false-negative rate of each model for detection of SLN metastases in women with a predicted risk of ≤10% was less than 10%, and 0–2% in the MSKCC, Coombs, and Yeniay models.

Discussion

All models provide good overall discrimination for SLN status, in particular for women with SLN macrometastases. Although calibration of model-predicted risk across the range from low to high risk was generally poor, the MSKCC, Coombs, and Yeniay models demonstrated good calibration to identify women with a low risk of SLN metastases ≤10%, with low rates of false negatives.

Validation of published models in different populations is recommended to identify and support the wider implementation of models that perform well outside the development population but this is rarely undertaken [15]. We selected the SNAC cohort as the reference population to validate the performance of the risk models for use in Australian women because it represents a population in whom the model is likely to be used. We included assessment of model performance for detection of SLN macrometastases, since micrometastases are currently regarded as node negative for key management decisions such as complete axillary dissection [16,17].

Model performance can be degraded when a model is used in different populations, unexplained by differences in technical and pathological factors alone. This may explain the variation in results when the MSKCC nomogram is validated in other populations [18,19,20].

The model validation AUCs of 0.70–0.74 are considered to indicate good model discrimination, and are comparable with those reported for widely used nomograms in oncology, such as Oncotype DX and Adjuvant Online [20]. However, the false-negative rate provides

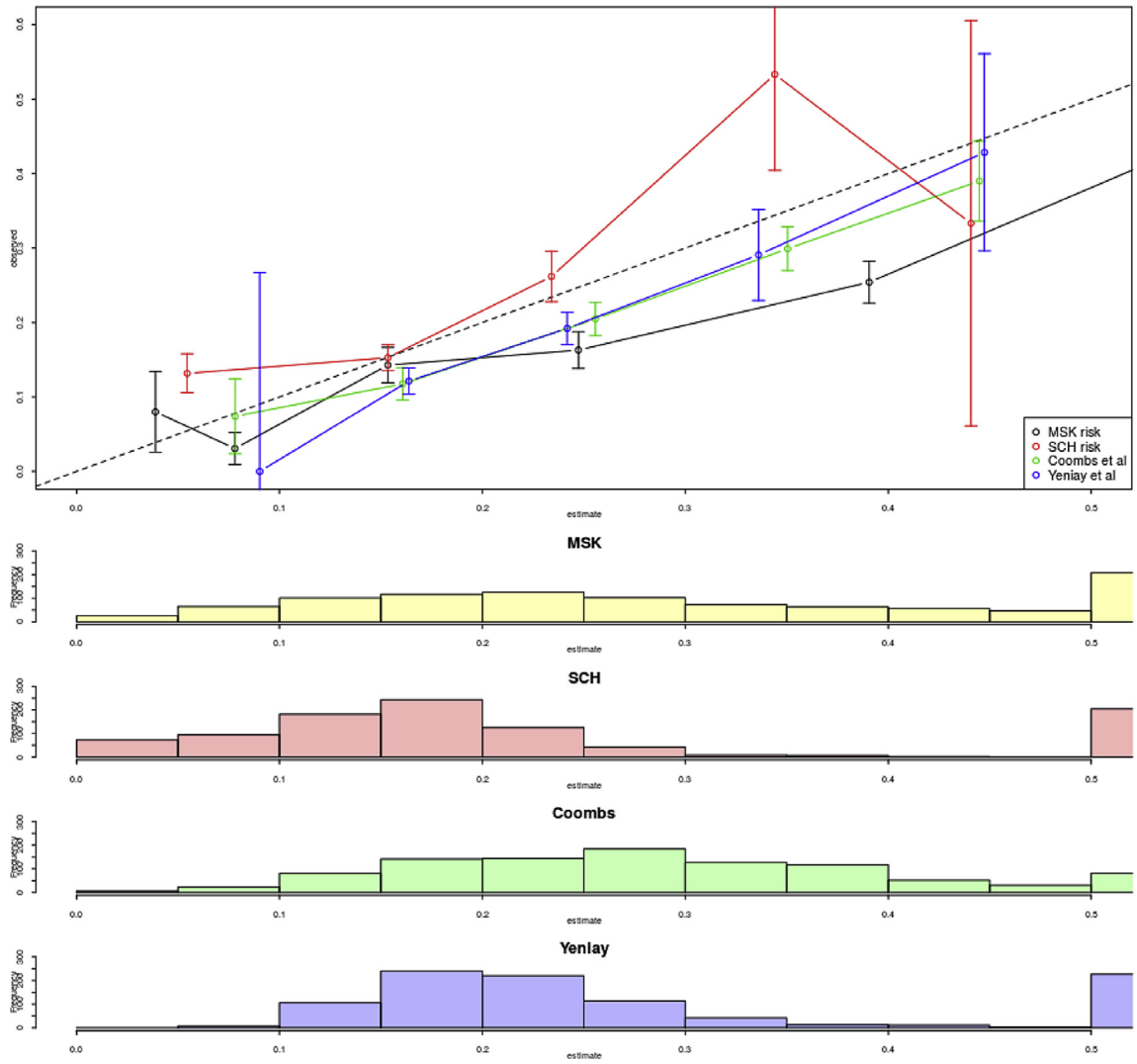

Fig. 2. Validation plots in Sentinel Node Biopsy Versus Axillary Clearance (SNAC) cohort for risk models, with standard errors of observed rates and histogram of assessed risk probabilities of each model for women with a predicted risk <0.5. Below this, four barplots show the distributions of assessed risk: numbers of women placed in 10 equally spaced risk classes (from 0 to 0.5 probability of positive sentinel lymph node) according to the risk model, together with number of women assessed at probability above 0.5 (final bar) for each risk model.

more meaningful information about the discrimination of the risk model for clinical use. Of 248 women with SLN metastases in the SNAC cohort, the four models classified between 226 and 248 (91–100%) as having a risk of SLN metastases greater than 10%, corresponding to a false negative rate of less than 10%. The false negative rate considered adequate varies, depending on what clinical decisions the model will be used to inform, the size of the benefit for those who are correctly classified, and the consequences for those who are not. For three models (MSKCC, Coombs, Yeniay), the FNR was less than 2%, indicating excellent discrimination at this threshold. Further, for each of these three models, women with a model calculated risk <10% also had an observed risk of true SLN metastases less than 10% (range 0–7%) – demonstrating very good calibration. In contrast, the SCH model was not as well calibrated at this level with an observed risk of SLN metastases of 13%. The MSKCC nomogram also showed good calibration between predicted and observed outcomes at thresholds of ≤10%, ≤20% and ≤30%. A similar finding was reported by van la Parra et al. in a low-risk group, despite an AUC of 0.69. Calibration was poorer for the higher-risk groups where there was greater variation between observed and predicted risk.

For each model, the majority of women without SLN metastases also had a model calculated risk of ≤30% (range 62%–86%). However relatively few of these women had a model calculated risk of ≤10% (range 1–20%, data shown in Table 3). This means that if using the threshold of 10% risk to rule out the need for SLN biopsy, most women without SLN metastases would still proceed to a biopsy. Future models could be developed to improve discrimination such that a larger proportion of women without SLN metastases have a predicted probability in this range to avoid SLN biopsy.

The strengths of this report include the quality of the SNAC trial data, eligibility criteria, and strict guidelines for SLN biopsy and processing, allowing transparent validation of existing model performance. Limitations include changes in clinical presentation, staging, SLNB techniques and pathology reporting since SNAC recruitment took place. Participation in the national screening program has remained constant at around 54%. Axillary staging has changed since the recruitment of the SNAC cohort and a more relevant population for model validation in current practice would include those women with a negative axillary ultrasound. We have addressed the matter of changes in classification of nodal metastases by analysing macrometastases specifically.

Current trials are evaluating the outcome of treatment in

Table 3
Numbers estimated at low risk, observed number of false negatives, and false negative rate among patients with metastases in the MSKCC, SCH, Coombs and Yeniay models at four predictive probability cut points and the number of patients with macrometastasis classified in low-risk categories by MSKCC, SCH and Coombs models at the same predictive probability cut points.

Model cut-point	Cumulative *n* (%)	Micrometastases and macrometastases ($n = 248$)			Macrometastases only ($n = 158$)		Including isolated tumour cells ($n = 277$)	
		n	Probability of metastasis	False-negative rate	*n*	False-negative rate	*n*	False-negative rate
MSKCC								
≤0.05	25 (2.5)	2	0.08	0.01	0	0.00	2	0.01
≤0.10	90 (9.2)	4	0.04	0.02	1	0.01	7	0.03
≤0.20	307 (31.3)	35	0.11	0.14	14	0.09	44	0.16
≤0.30	534 (54.4)	76	0.14	0.31	40	0.25	88	0.32
SCH								
≤0.05	73 (7.4)	10	0.14	0.04	5	0.07	14	0.19
≤0.10	167 (17.0)	22	0.13	0.09	13	0.08	29	0.17
≤0.20	592 (60.3)	87	0.15	0.35	44	0.07	104	0.18
≤0.30	760 (77.4)	131	0.17	0.53	74	0.10	153	0.20
Coombs								
≤0.05	5 (0.5)	0	0.00	0.00	0	0.00	0	0.00
≤0.10	27 (2.7)	2	0.07	0.01	0	0.00	2	0.01
≤0.20	248 (25.3)	29	0.12	0.12	10	0.06	35	0.13
≤0.30	575 (58.6)	101	0.18	0.41	55	0.35	117	0.42
Yeniay								
≤0.05	0 (0.0)	0	0.00	0.00	0	0.00	0	0.00
≤0.10	7 (0.7)	0	0.00	0.00	0	0.00	0	0.00
≤0.20	353 (35.9)	45	0.13	0.18	22	0.14	51	0.18
≤0.30	686 (69.9)	115	0.17	0.46	63	0.40	135	0.49

women with T1 cancer and clinically and sonographically negative lymph nodes who are randomised to SLNB or no axillary surgery [21]. We propose a well performing risk model would help counsel women as an adjunct to conventional staging to inform decisions for axillary surgery. This group represents the majority of women with a new diagnosis of early breast cancer in Australia, where over 50% of breast cancers are currently detected by mammography; and >50% of such women have cancers <15 mm in diameter. At least 80% of screening populations are lymph-node negative and could potentially be spared axillary surgery [21].

A separate issue is the decision for ALND following a positive SLNB. Currently this decision is informed by the results of three trials; ACOSOGZ0011 in which women with 1 or 2 positive SLN derived no benefit from completion of ALND [22]; AMAROS which demonstrated survival equivalence for ALND and axillary irradiation following a positive SLNB with reduced morbidity with irradiation [23], and IBCSG 23 which showed no benefit in those with micrometastases in the SLN [21]. Treatment decisions in this situation requires pathological confirmation of the number of positive SLN and/or the size of metastases and an accurate SLNB is the only way to obtain this information. The nomograms evaluated in this report do not perform well to identify high risk groups.

The main research implication of our findings is the need to develop and validate a nomogram with good calibration to classify risk across the range from low to high risk. In countries with breast screening programs such as Australia, where screening mammography has resulted in increased numbers of small cancers, and axillary ultrasound is widely used, a model should be developed in a population sharing these characteristics.

Disclosures

None.

Synopsis

This validation study demonstrates three published risk models for prediction of axillary node metastasis in women with early breast cancer perform well for correctly identifying Australian women with a risk of metastases below 10%, but not across the risk range.

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Appendix 1. Predictors included in published risk models

Characteristic	Bevilaqua, MSKCC, USA	Lee, SCH, China	Coombs, Australia	Yeniay, Turkey
Age	●	●		
Tumour size	●	●	●	●
Tumour type	●	●		
Tumour site	●	●		
Lymphovascular invasion	●	●		●
Estrogen-receptor positive	●			
Progesterone-receptor positive	●			●
Multifocality	●			
Grade, nuclear or histologic	●		●	

Appendix 2. Published risk models for prediction of SLN metastasis

Model 1: Bevilacqua, USA (MSKCC)[6]

Probabilities for the MSKCC model are available by using the web calculator at http://nomograms.mskcc.org/breast/BreastSLNodeMetastasisPage.aspx.

Model 2: Chen, China (SCH)[7]

Probability = 1/[1 + exp(−LP)] with LP = −4.605 + 0.0373^{c} TP

where TP (total points) are points summed from the table below (by measurement from Chen et al., Fig. 2):

Factor	Points
Size, cm	8.29
Tumour type	
Lobular	39
Ductal	65
mixed (other)	69.5
ductal cancer in situ_M (ref)	0
Location	
upper outer quadrant	15
lower inner quadrant	23
central	25
upper inner quadrant (ref)	0
Lymphovascular invasion	58
Age	−0.15

Model 3: Yeniay, Turkey[8]

Probability = 1/1 + exp(−LP) with

LP = 2.414−0.048 × tumour size (mm) − 0.533 × PR (0 = no, 1 = yes) − 2.157 × LVI (0 = no, 1 = yes)

LVI = lymphovascular invasion, PR = progesterone receptor

Authors confirmed the correction to published model with '−' signs for all three risk factors.

Model 4: Coombs, Australia[9]

G I primary tumour: probability (%) = 1.5 × tumour size (mm) + 2

G II primary tumour: probability (%) = 1.5 × tumour size (mm) + 6

G III primary tumour: probability (%) = 1.5 × tumour size (mm) + 10

G = tumour grade; tumour size is restricted to < 50 mm

(For validation in the SNAC cohort, we substituted size as 50 mm for larger tumours).

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