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Clinical prediction models for patients diagnosed with breast cancer: A systematic review

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Background: Clinical prediction models provide insight in the probability of an event based on the combination of multiple predictor variables. Predicted probabilities may support clinical decision making. It is currently uncertain how many prediction models exist to support decision making in breast cancer care, which outcomes can be predicted, and which predictor variables are necessary to predict these outcomes. We aimed to systematically review prediction models that may be used to guide clinical decision making in patients who have been diagnosed with breast cancer.

Methods: Medline and Embase were searched systematically to identify existing prediction models published between January 2010 and September 2019. Studies reporting on the development or update of models predicting outcomes in patients diagnosed with breast cancer were included. Data extraction was performed according to the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS). The potential risk of bias was assessed using the Prediction model Risk Of Bias ASsessment Tool (PROBAST).

Results: After screening 16004 studies on title and abstract, 913 studies were selected for full text screening where 553 studies were excluded for the full analysis. A total of 360 studies were included, reporting on 516 models. Numerous models predict similar outcomes (Table 1), but often differed on 1) the outcome definition (i.e. lymph node involvement (LNI) can comprise sentinel LNI and/or non-sentinel LNI), 2) the intended use of the model (i.e. model eligible only for triple negative breast cancer), and 3) the predictor variables used to predict the outcome (i.e. clinical or genetic). The majority of the models (>75%) were considered to contain high risk of bias on the PROBAST analysis domain. Approximately 25% of the models failed to report sufficient information to reproduce the model.

Table 1 Number of models per outcome

Outcome	N (%) total = 516
Overall survival	165 (32.0%)
Breast cancer specific survival	40 (7.8%)
Recurrence free disease	111 (21.5%)
Lymph node involvement	103 (20.0%)
Pathologic complete response	38 (7.4%)
Complication or adverse event	28 (5.4%)
Lymphedema	14 (2.7%)
Menses recovery	7 (1.4%)
Surgical margin	5 (1.0%)
Quality of life	4 (0.8%)
Healthcare expenditure	1 (0.2%)

Conclusions: The number of available prediction models for breast cancer is abundant. Models often require the same predictor variables to calculate the same outcome. Still, the clinical utility of most of these models remains unclear as a substantial number of models were not reported according to established reporting guidelines or showed methodological flaws in the development and validation of the model. Development of new models is undesirable before current promising models have been thoroughly assessed on their impact in clinical practice.

No conflict of interest.

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Factors affecting locoregional recurrence rate of breast conserving surgery in patients with neoadjuvant chemotherapy

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Background: Breast conserving surgery(BCS) is preferred over traditional mastectomy for better cosmetic and non-inferior oncological outcome. BCS is best indicated for early stage breast cancer with relatively small tumor size. Neo-adjuvant chemotherapy(NAC) helps downstaging locally advanced breast cancer and increase the possibility for BCS. However, recent meta-analysis from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) showed a higher locoregional recurrence(LLR) rate in the NAC group than in the adjuvant chemotherapy group. Thus, the aim of this study was to retrospectively explore the factors affecting the LRR rate in breast cancer patients receiving BCS after NAC.

Materials and Methods: During 2005–2017, we retrospectively collected 1047 breast cancer patients underwent BCS or mastectomy after NAC in Chang Gung Memorial Hospital, Linkou. We obtained information about patient and tumor characteristics, chemotherapy regimen, clinical tumor response, tumor molecular subtypes and pathology complete response (pCR) status, type of surgery and recurrence retrospectively.

Results: A total of 1047 patients underwent NAC, 22.2% patients (n = 232) achieved pCR while the other were non-pCR (77.8%, n = 815). The BCS rate is 41% (n = 432) and the rest of patients received mastectomy (59%, n = 615). The median follow-up time is 45 months. During the follow-up period, 22.9% patients experienced tumor recurrence (n = 240), in which 8.6% was LRR (n = 90). The LLR rate in BCS group is 14.3% (n = 35) while in mastectomy group is 13.2% (n = 55). Amount the BCS group who had LLR, 4.3% (n = 6) is pCR vs 10.0% (n = 29) is non-pCR, ($p < 0.05$). Further investigation according to the breast cancer molecular subtype showed HER-2 overexpressing non-pCR group has significantly increased in LRR as compared with HER-2 overexpressing pCR group (22.2% vs 6.3%, $p < 0.05$) in post-NAC BCS patients. Triple-negative non-pCR group also noted a significant increase in LRR rate as compared with triple negative pCR group (0% vs 20.4%, $p < 0.005$) in post-NAC BCS patients. There was no LRR rate difference in between pCR and non-pCR groups of luminal type breast cancer.

Conclusions: The status of pathological response after NAC is related to the risk of developing LRR. LRR rate was higher in non-pCR group after NAC with BCS, especially in the HER2 positive and triple negative breast cancer. Therefore, both the status of pathological response and molecular subtype have to be taken into careful consideration when choosing candidates for BCS after NAC.

No conflict of interest.

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Circulating tumour DNA as a prognostic biomarker in predicting breast cancer outcomes: Systematic review and meta-analysis

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Background: Fragmented DNA is constantly released into the circulation by apoptosis and necrosis of both cancerous and non-cancerous cell. When it is released by cancer cells, it is specifically known as circulating tumour DNA (ctDNA). We performed a systematic review and meta-analysis to determine the clinical utility of ctDNA as a prognostic biomarker in predicting breast cancer outcomes.

Methods: A meta-analysis of nine relevant studies was performed. Primary outcome was the association of ctDNA with breast cancer disease free survival/relapse free survival. Secondary outcomes focused upon a subgroup analysis of the survival implications of ctDNA detection in early breast cancer and metastatic breast cancer. Statistical analysis was performed using Revman 5.

Results: Nine studies reported on 661 cases in total. ctDNA detection (both pre and post treatment) was significantly associated with worse disease free survival (DFS) (HR 3.53, CI 1.47–8.49, P = <0.00001). ctDNA detection was significantly associated with a reduction in disease free survival in the early breast cancer subgroup (HR 8.32, CI 3.01–22.99, P = <0.0001). ctDNA in the metastatic group was not associated with significance (HR 1.86, CI 0.43–1.34, P = 0.61). Pre and post-treatment plasma sample collection was analysed in both early and metastatic groups. Pre-treatment plasma detection of ctDNA was significantly associated with reduced DFS (HR 3.30, CI 1.98–5.52, P = <0.00001). Post-treatment sampling of ctDNA failed to achieve statistical significance (HR 4.31, CI 0.14–136.23, P = 0.41).

Conclusion: Circulating tumour DNA is an important prognostic biomarker of reduced breast cancer disease free survival. Detection of elevated plasma ctDNA can predict patients at high risk of relapse and therefore may provide an excellent method to stratify risk and personalize patient follow-up.

No conflict of interest.