Can we save the morbidity of Axillary Clearance in Sentinel Node Positive breast cancer patients?

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Introduction

Axillary Nodal Clearance (ANC) is performed in breast cancer patients for regional control, prognostic information and adjuvant treatment planning, but has the potential to cause significant morbidity. Sentinel Node Biopsy (SNB) has been shown to be highly accurate at predicting axillary involvement with much less morbidity[1]. Our aim was to try to identify a subgroup of patients in whom axillary clearance could be avoided by determining the risk of further nodal involvement given a positive sentinel lymph node using the Memorial Sloan-Kettering Cancer Center (MSKCC) nomogram as a predictive tool.

Methodology

The Auckland Breast Cancer Register was searched for all patients who underwent SNB with subsequent ANC between January 2000 and July 2011 in the Auckland region (across both public and private centres). A retrospective audit was conducted, excluding those with a histological diagnosis other than infiltrating ductal or lobular carcinoma (e.g. DCIS, mucinous), participants of the SNAC trial, and those where complete data was unavailable. Tumour characteristics and sentinel node pathological details were entered into the MSKCC nomogram and the percentage probability of women having further positive nodes was calculated. This predicted likelihood was then compared with the actual observed percentage of further nodes on ANC. A receiver operating characteristic (ROC) curve was constructed and the area under the curve (AUC) calculated. Analyses were performed using the John Hopkins University online ROC analysis tool[3].

Results

A total of 734 patients were analyzed. The median tumour size for the population was 20.0mm (range 1.0-130.0mm). The median number of sentinel nodes harvested was 2 (mean 2.63, range 1-13) and a median of 16 nodes removed on axillary clearance (mean 16.9, range 2-50). A total of 413 (56%) patients did not have further involved lymph nodes on ANC.

The probability of further involved nodes as predicted by the nomogram and as was actually observed is summarized in Table 1. This demonstrates a linear correlation between the two values. The MSKCC nomogram predicted the likelihood of non-sentinel node metastases with an AUC of 0.7238 (95% CI 0.705-0.7426) in our population compared to an AUC of 0.76 in the original MSKCC study [4].

In the subgroup of patients with a calculated likelihood of additional nodes of greater than 80%, 82.7% of women (43/52) had confirmed metastatic nodes on axillary clearance. Conversely, only 20% in the lowest subset of 30% or less (26/131) had non-sentinel involved nodes on ANC.

Discussion

ANC is considered to be the definitive treatment for patients with axillary metastasis detected by SNB. Unfortunately it can be associated with complications including seroma, wound infection, nerve injury, reduced shoulder mobility and lymphoedema in up to 40% of cases. The SNAC trial, conducted throughout Australasia, demonstrated that SNB followed by ANC only after a positive node was identified resulted in accurate axillary staging with significantly less associated morbidity than routine axillary clearance [1].

Nomogram predicted probability (%)	Actual observed incidence (%)	Number of patients in subgroup	Patients with further nodal mets on ANC
>80	82.7	52	43
71-80	67.7	65	44
61-70	64.3	98	63
51-60	48.5	130	63
41-50	36.4	140	51
31-40	26.3	118	31
<30	19.9	131	26

Table 1. Predicted probability of further nodal metastases versus actual observed incidence on ANC.

Recently, a randomised controlled trial by Giuliano et al [2] outlined that SNB alone compared with ANC did not result in inferior survival with respect to overall cancer outcomes in a selected group of patients. In addition, as a result of screening and other methods of early detection of breast cancer, lymph node metastasis has become less common with a rising proportion of women having an ANC with no further nodal metastases identified, even with a sentinel node positive for metastasis. This was indeed the case in our study, where 56% of women had no further nodal metastasis detected on ANC.

It follows that since the introduction of SNB-based management, many authors have endeavoured to define a subset of SNB-positive patients in whom omission of axillary clearance may be deemed appropriate without compromising the information (prognosis, adjuvant planning) and therapeutic benefits (regional control and overall survival) obtained by performing an ANC.

The MSKCC nomogram uses eight histopathological variables of the primary breast tumour and sentinel node to calculate the likelihood of additional nodal metastases in patients with a positive SNB. It was proven to be accurate and discriminating, as demonstrated by the AUC of 0.76 in the original study [4]. The nomogram has subsequently been studied several times in many countries with varying results, ranging from "insufficient performance" (van den Hoven et al, Netherlands, AUC 0.68) [5], to "very accurate" (Degnim et al, LA, California and Soni et al, NSW, Australia; AUCs of 0.72-0.86) [6,7]. Our study results are consistent with the latter; AUC 0.72 which indicates a fair level of accuracy.

One limitation of the nomogram is that it relies on parameters such as tumour size and multifocality, which can only be reliably obtained from the final pathology report, rather than being available at the time of surgery following SNB when a decision whether to proceed with ANC needs to be made.

In view of current evidence, it is likely that increasing numbers of women with early breast cancer will be managed with SNB alone. In such women, use of the MSKCC nomogram to determine the probability of further positive axillary nodes will be useful in providing prognostic information, and in planning adjuvant treatment and surveillance for regional recurrence.

Across all subgroups, including those with a predictive probability of >80%, there were cases with no further lymph nodes involved on ANC, thus outlining that it is almost impossible to accurately identify a subgroup or an individual who will have no further nodal involvement.

Based on our results if ANC is not performed on those with a predictive probability of <30%, almost 80% of such women could be spared the morbidity associated with ANC. However this assumption has to accept that 20% of these women may have residual regional disease with unknown implications for clinical recurrence and overall survival.

The main strength of our study is its size; a significantly large number of patients were analyzed over the Auckland region, both public and private sectors, over a ten-year period. One limitation is that our study is confined to a retrospective analysis only. Another limitation acknowledged is that frozen section analysis was used in the nomogram as the mode of sentinel node processing for all cases; one centre however used imprint cytology in addition to this, and another imprint cytology only.

Conclusion

Our analysis of 734 Auckland women over the last 10 years has shown that 56% of SNB positive breast cancer patients have no further involved axillary nodes on ANC. The MSKCC nomogram was found to be accurate in our population in predicting the probability of further involved axillary nodes. There was no group identified with no risk of further axillary nodal disease, however the nomogram did allow stratification of individual risk. The MSKCC nomogram can be used in our population to assist surgeon and patient in their decision whether to proceed to ANC in the setting of a positive sentinel node.

References

1. Gill, G. and the SNAC Trial Group of the Royal Australasian College of Surgeons (RACS) and NHMRC Clinical Trials Centre. Sentinel-lymph-node based management or routine axillary clearance? One-year outcomes of sentinel node biopsy versus axillary clearance (SNAC): A randomized controlled surgical trial. *Annals of Surgical Oncology* 2009; 16:266-275
2. Giuliano, A.E., Hunt, K.K., Ballman, K.V., Beitsch, P.D., Whitworth, P.W., Blumencranz, P.W. et al. Axillary dissection vs. no axillary dissection in women with invasive breast cancer and sentinel node metastasis: A randomized clinical trial. *Journal of American Medical Association* 2011;305(6):569-575
3. Eng, J. ROC analysis: web-based calculator for ROC curves. *John Hopkins University* 2006. Retrieved 02/10/12, from http://www.jrocfit.org.
4. Van Zee, K.J., Manasseh, D-M.E., Bevilacqua, J.L.B., Boolbol, S.K., Fey, J.V., Tan, L.K. et al. A Nomogram for predicting the likelihood of additional nodal metastases in breast cancer patients with a positive sentinel node biopsy. *Annals of Surgical Oncology* 2003; 10(10):1140-1151
5. van den Hoven, I., Kuijt, G.P., Voogd, A.C., van Beek, M.W.P.M., Roumen,R.M.H. Value of Memorial Sloan Kettering Cancer Center nomogram in clinical decision making for sentinel lymph node-positive breast cancer. *British Journal of Surgery* 2010;97:1653-1658
6. Soni, N.K., Carmalt, H.L., Gillett, D.J., Spillane, A.J. Evaluation of a breast cancer nomogram for prediction of non-sentinel lymph node positivity. *European Journal of Surgical Oncology* 2005;31:958-964
7. Degnim, A.C., Reynolds, C., Pantvaidya, G., Zakaria, S., Hoskin, T., Barnes,S. et al. Nonsentinel node metastasis in breast cancer patients: assessment of an existing and a new predictive nomogram. *The American Journal of Surgery* 2005; 190:543-550

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