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EPIDEMIOLOGY

Differences in breast cancer biological characteristics between ethnic groups in New Zealand

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Abstract *Objective* To investigate differences in breast cancer biological characteristics between ethnic groups in Auckland, New Zealand. *Design* Prospective cohort study. *Setting* Auckland Breast Cancer Study Group. *Participants* All people diagnosed with breast cancer in the greater Auckland area between 2000 and 2005 who agreed to participate (1,577). *Main outcome measures* Size, grade, lymph node status, estrogen receptor (ER), progesterone receptor (PR), lymphovascular invasion (LVI), grade allowing for size, all compared with ethnicity. *Results* NZ Maori and Pacific Island participants had larger tumours ($P < 0.0001$), higher grade tumours ($P < 0.0001$) with more involved lymph nodes ($P < 0.0001$). When allowing for size, there was still an indication that NZ Maori people had higher grade tumours ($P = 0.03$). There was no difference in ER, PR and LVI between ethnic groups. *Conclusion* These data suggest differences in tumour biology related to ethnicity in the Auckland population and this has implications for breast cancer screening and management.

Keywords Breast Cancer · Ethnicity · Maori · Hormone receptors

Introduction

Initially thought to be a disease of affluence breast cancer is becoming a disease of the disadvantaged with higher mortality rates amongst indigenous people and those of lower socioeconomic status [1]. This trend is seen worldwide and its cause is believed to be multifactorial. Possible explanations include differences in access to breast cancer diagnosis and treatment services as well as genetic differences in tumour biology and behaviour [1–4].

Breast cancer follows skin cancer as the leading cause of cancer death for New Zealand females [5]. Within New Zealand (NZ) there are ethnic disparities in breast cancer mortality despite similar registration rates; In 1997 'European and other' women had a mortality rate of 22 per 100,000, and NZ Maori women a rate of 33 per 100,000 [5, 6].

New Zealand's population has changed over recent decades from a largely bicultural to an ethnically diverse population. The indigenous NZ Maori and the NZ European populations have been joined by many Asian and Pacific Island subgroups. Previous NZ studies have looked at Maori versus Non-Maori figures, while international studies often include Asian and Pacific Island people together as one group. In NZ it is becoming more relevant to investigate differences between these groups as well as differences between Maori and Non-Maori [7].

Potential differences in tumour biological characteristics as a cause for ethnic disparities in breast cancer have not been investigated in NZ to date. Using data from the Auckland Breast Cancer Study Group database we investigated differences in breast cancer biological characteristics between ethnic groups in Auckland on the premise that ethnic disparities in outcome from breast cancer might be due to one group having a biologically more aggressive tumour than others.

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Methods

The study population

All complete data from the Auckland Breast Cancer Study Group database was used, which included data from 2000 to 2005. This prospective database was established in 2000 and includes 85% of both screen detected and non-screen detected male and female breast cancers from the greater Auckland area. Inclusion in the database is by consent and ethnicity is self-assigned.

People of many ethnic groups were involved and participants were grouped into four broad groups: NZ European, NZ Maori, Pacific Island (Samoan, Tongan, Niuean, Fijian, Cook Island Maori, Tokelauan, other Pacific Islander and Pacific Island not further determined), and Asian (Chinese, Southeast Asian, Other Asian and Asian not further determined). Participants of ethnicities that did not fit under these headings were excluded. The Asian group excluded people from South Asian countries such as India or Pakistan as these people were felt to be ethnically different to the Asian group, but too small a group to be used alone. We did not look at age as it has already been demonstrated that there is a similar age-specific incidence of breast cancer across ethnic groups in New Zealand [8].

For those participants with multiple foci of cancer or bilateral cancers only the first cancer on the database was included, the remaining cancer/s excluded. For those participants who had recorded multiple ethnicities only the first ethnic group recorded was used, the others were disregarded.

Participants were excluded from each analysis if their data was incomplete or non-sensical.

Statistical analysis

Using SAS software (SAS Institute Inc, Carey, North Carolina, USA) the data were tested to see whether there were any differences between the ethnic groups in markers indicative of tumours with poorer prognosis. This included tumour size, tumour grade, lymph node involvement, estrogen receptor (ER), progesterone receptor (PR) and lymphovascular invasion (LVI). HER2 receptor status was not included as this was not consistently measured in the earlier years of the study population.

A chi square test for independence was performed for ER, PR and LVI.

A Kruskal Wallis analysis of variance was performed for tumour size and tumour grade. A Kruskal Wallis analysis of variance was performed for lymph node involvement by dividing the number of involved lymph nodes into groups of 0, 1–3, 4–9 and >10. This analysis did not take into account the number of lymph nodes analysed in each participant.

To investigate whether any ethnic difference in tumour grade could be explained by the size of the tumour an ordinal logistic regression was performed with tumour grade as the ordinal outcome and tumour size and ethnicity as explanatory variables. The proportional odds assumption for this analysis was not met, i.e.: the relationship between explanatory variables and grade was not proportional across grade. To overcome this two binary logistic regressions were run, the first comparing grade 1 with grade 2 and 3, and the second comparing grade 1 and 2 with grade 3.

Results

The total study population was 1,577, made up of NZ European 1,220, NZ Maori 133, Pacific Island 128 and Asian 96. These were proportionally felt to be representative of the Auckland population.

There was no difference between ethnic groups in ER, PR or LVI, with P values being 0.72, 0.94 and 0.98 respectively.

There was strong evidence of a difference in size between ethnic groups, with NZ Maori and Pacific Island groups having larger tumours ($P < 0.0001$) (Fig. 1).

There was strong evidence of a difference in tumour grade between ethnic groups, with NZ Maori and Pacific Island groups having higher grade tumours ($P < 0.0001$) (Fig. 2).

There was a difference between ethnic groups in numbers of involved lymph nodes with NZ Maori and Pacific Island groups having more involved lymph nodes ($P < 0.0001$) (Fig. 3).

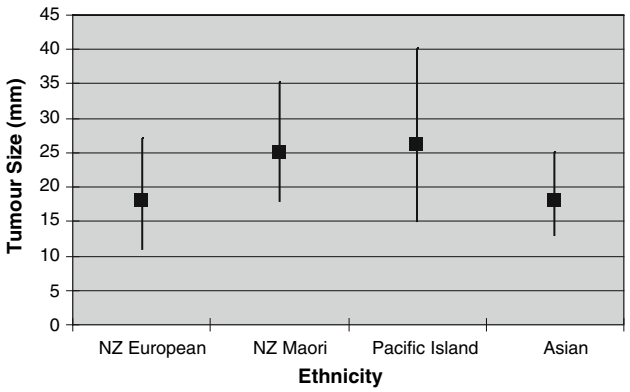

Fig. 1 Tumour size by ethnicity. Bars indicate interquartile range, squares indicate median

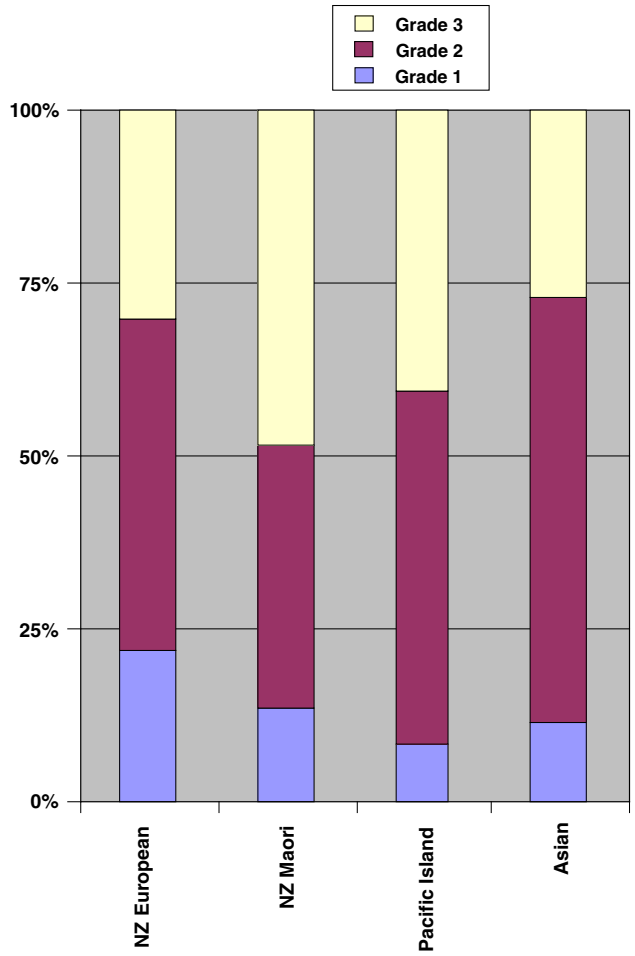

Fig. 2 Grade by ethnicity: proportions grade 1, grade 2 and grade 3

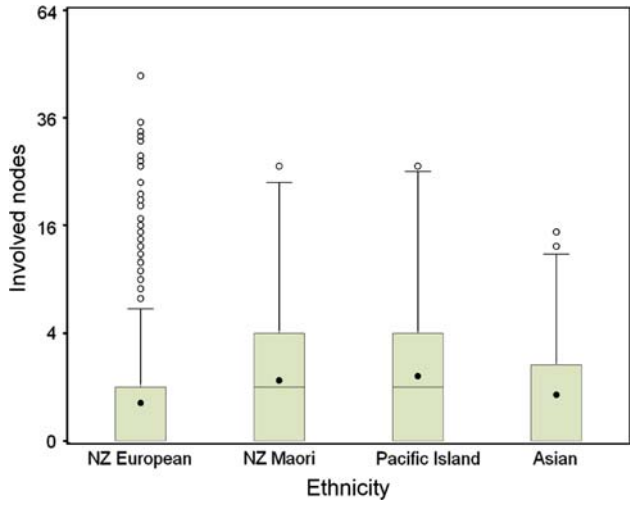

Fig. 3 Involved lymph nodes by ethnicity. Box indicates interquartile range with median, black dots indicate mean, circles indicate values beyond the whiskers which extend to the last value within 1.5X interquartile range

A difference in tumour grade 1 versus grade 2 and 3, and grade 1 and 2 versus 3, allowing for size, both showed evidence of an effect of ethnicity (both $P = 0.03$) with the NZ European group having more grade 1 tumours and the NZ Maori group having more grade 3 tumours than the other groups.

Discussion

This study confirms that there is a difference in breast cancer biological characteristics between ethnic groups in NZ. Our analyses revealed a significant difference in size, grade and lymph node status, with NZ Maori and Pacific Island groups having larger, higher grade tumours with more positive lymph nodes. Furthermore when allowing for delay in presentation, by allowing for size, the NZ Maori group had more grade 3 tumours, suggesting more aggressive disease. There were no significant differences in ER, PR or LVI between ethnic groups.

International studies have shown differences in biological characteristics of breast cancers between ethnic groups. In 2001 Furberg et al reported the results of their population based case control study comparing the biological characteristics of tumours in White and African American women. They found pathologically advanced tumours (large size, high grade, high stage, ER/PR negative) were significantly more common among young and African American women [9].

Similar results were found in study by Cunningham and Butler in 2004 and in addition they found that when controlling for T-stage, African American women were more likely to have high grade and/or ER negative disease [2].

Until now there has been no convincing evidence of NZ Maori having biologically worse disease. However several studies have suggested this may contribute to the poorer breast cancer outcomes in NZ Maori compared to other ethnic groups. Results from the Auckland Breast Cancer Study Group in 1992 suggested Pacific Island women presented more frequently with large tumours and metastases, and Maori women were more frequently node positive. Increased body mass index could explain the former finding but the frequency of large tumours in Pacific Island women is still higher when compared with European and Maori women weighing more than 75 kg [10, 11].

Studies investigating ethnic differences are challenged by the inherent variability in measurement and interpretation of ethnicity [12]. We utilised self-assignment of ethnicity and did not allow for participants selecting multiple ethnicities. Others have utilized slightly different techniques for assigning ethnicity in New Zealand but we believe that this is unlikely to have influenced our findings significantly [8].

Similarly the study was not able to allow for those with multifocal or multicentric cancers and used only the reference cancer in the analysis. This may have underestimated the severity of some cancers and also resulted in an underestimate of cancer size.

There is a possibility that the results of this study are due to a delay in presentation or difference in access to health care across various ethnic groups. While this study did not specifically address these issues, and are beyond the scope of this paper, we think that this is unlikely and that the differences are most likely to be largely due to biological characteristic of the tumours. This is based on the assumption that breast cancers do not dedifferentiate with time and on the fact that grade, allowing for size (a proxy for delay in presentation), was significantly different between groups. The view that breast cancer grade does not change with time has been challenged by some however. Anderson et al. [13] and Korsching et al. [14] have reported results of breast cancers showing phenotypic drift of cancer grade, with cancers becoming less differentiated over time. This theory is yet to replace conventional pathological doctrine.

This study has important implications for breast cancer screening and education. NZ Maori have been shown to have more aggressive disease, and when this is combined with a tendency for delayed presentation and lower screening coverage rates the outcomes are invariably worse. The breast cancer screening program in NZ (BreastScreen Aotearoa) involves screening mammography every two years between the ages of 45 and 69. Attendance rates are 39% for Maori compared to 59% for non-Maori/non-Pacific women [8]. Decreasing the screening interval for NZ Maori might improve the likelihood of diagnosing a biologically more aggressive tumour at an earlier stage, however this approach would be unlikely to make any significant improvements for the population as a whole.

Improving access to screening mammography and treatment services, education by Maori for Maori about the importance of breast cancer screening, and addressing cultural safety issues may be a more effective approach.

In conclusion this is the first study of its kind in NZ investigating potential differences in biological behaviour of breast cancers between ethnic groups. It has shown a tendency towards larger, higher grade tumours with more positive lymph nodes in NZ Maori and Pacific Island people and, allowing for size, a tendency to higher grade tumours in NZ Maori. This has implications for screening and treatment.

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