

The association between breast density & ethnicity

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Disclosures

This project received support in kind from Volparasolutions

The authors have no conflicts of interest to declare

Background

- Asian women are at lower risk of breast cancer compared with Caucasian women of the same age
- Asian women are thought to have higher breast density than Caucasian women of the same age
- Higher breast density is a risk factor for the diagnosis of breast cancer

Aim

To investigate the difference in breast density between women of Asian ethnicity and women of Caucasian ethnicity in a sample of women attending BreastScreen Victoria

Ethics approval

The study was approved by the Human Research Ethics Committee of Monash Health (project 15454L) with notification to the Monash University Human Research Ethics Committee



4cm

Data

Two data sets

- Retrospective (St Vincent's BreastScreen from 13/07/2012 to 20/08/2015)
one of two Siemens MAMMOMAT DR Inspiration machines
- Prospective (Monash BreastScreen 19/02/2016 and 15/10/2016)
Siemens MAMMOMAT DR Inspiration or Philips Sectra Microdose L30

Parameters explored in relation to breast density: (only routinely collected)

- age at the time of mammography
- ever exposure to hormone therapy (self reported)
- ethnicity:
 - Caucasian: born in Australia, UK, Greece, Italy, New Zealand, Germany or the Netherlands
 - Asian: born in China, Vietnam or Hong Kong
- body mass index was not available

Measurement of breast density



- Density was assessed using Volpara software (% dense tissue by volume)
- The volume of fibro-glandular tissue is summed across the breast, and the volumetric % density is the ratio of fibro-glandular tissue/total breast volume
- The 4th & 5th editions of the Volpara density estimate are correlated with the 4th & 5th editions of the ACR BI-RADS categories which use different cut-offs:

4th edition:

VDG1 <4.5%; VDG2 ≥4.5% & <7.5%; VDG3 ≥7.5% & <15.5%; VDG4 ≥15.5%

(mean density of both breasts)

5th edition:

VDG(a) <3.5%; VDG(b) ≥3.5% & <7.5%; VDG(c) ≥7.5% & <15.5%; VDG(d) ≥15.5%

(maximum density of L & R)

- The VDG 5th Edition was introduced in October 2015. We used both editions to allow direct comparison of our findings with previous studies which used the 4th edition and current and future studies using the 5th edition.

Sample size calculation



With over 16,000 women in the (combined) data set and the the estimated proportion of women with density 3 or 4 being 60%, the 95% CI would be $< +/-1%$

If 60% of Caucasian women had a breast density or levels 3 or 4, then with >9000 women (ratio of Caucasian to Asian of 10:1) we would have 80% power to detect a difference of 5% between groups

Exclusions

A small number of women with a past history of breast cancer or high risk lesions as well as a small number of diagnostic mammograms from the retrospective group were excluded from the analysis to ensure that the study was of women at average risk

Results

Retrospective data set:

9279 individual records - 38 “high risk” → 9241 in the analysis

Prospective data set:

7787 individual records - 47 “high risk” → 7740 in the analysis

Total in the merged data set was 16981

Density data missing for 38 women → 16943 in the analysis

Patient characteristics

A group of six diverse women of various ages are smiling together outdoors. They are dressed in casual to semi-formal attire, including blouses, jackets, and scarves. The background is a soft-focus green landscape.

- The mean age of the 16943 women was 59.1 (SD 8.2) years (range 40-92)
- 3455 of 16943 (20.4%) had ever taken hormone therapy

Distribution of breast density

| category | a 5 th edition | b 5 th edition | c 5 th edition | d 5 th edition | total |
|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|---------------|
| 1 4 th edition | 1781 | 3145 | 0 | 0 | 4926 29.1% |
| 2 4 th edition | 0 | 4752 | 490 | 0 | 5242 30.9% |
| 3 4 th edition | 0 | 5 | 4711 | 268 | 4984 29.4% |
| 4 4 th edition | 0 | 0 | 0 | 1791 | 1791 10.6% |
| total | 1781 10.5% | 7902 46.6% | 5201 30.7% | 2059 12.2% | 16943 |

76.9% have the same classification in both editions;
main difference is fewer women in group a in 5th edition

Age and breast density

(% by row)

| Age group years | 1 4 th edition | 2 4 th edition | 3 4 th edition | 4 4 th edition | Total |
|-----------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------|
| <50 | 249 (14.8%) | 372 (22.0%) | 634 (37.6%) | 433 (25.7%) | 1688 (10.0%) |
| 50-<75 | 4553 (30.7%) | 4705 (31.7%) | 4262 (28.7%) | 1334 (9.0%) | 14854 (87.7%) |
| 75+ | 124 (30.9%) | 165 (41.1%) | 88 (21.9%) | 24 (6.0%) | 401 (2.3%) |
| Total | 4926 (29.1%) | 5242 (30.9%) | 4984 (29.4%) | 1791 (10.6%) | 16943 |

| Age group years | a 5 th edition | b 5 th edition | c 5 th edition | d 5 th edition | Total |
|-----------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------|
| <50 | 112 (6.6%) | 461 (27.3%) | 639 (37.9%) | 476 (28.2%) | 1688 (10.0%) |
| 50-<75 | 1637 (11.0%) | 7206 (48.5%) | 4456 (30.0%) | 1555 (10.5%) | 14854 (87.7%) |
| 75+ | 32 (8.0%) | 235 (58.6%) | 106 (26.4%) | 28 (7.0%) | 401 (2.3%) |
| Total | 1781 (10.5%) | 7902 (46.6%) | 5201 (30.7%) | 2059 (12.2%) | 16943 |

Ethnicity and breast density

% by column

There were 13953 (82%) women classified as either Caucasian or Asian.

Asian women were more likely to have higher breast density than Caucasian women

| 4 th edition | Caucasian | Asian | 5 th edition | Caucasian | Asian |
|-------------------------|-----------------|----------------|-------------------------|-----------------|----------------|
| 1 | 3963 (31.1%) | 90 (7.5%) | a | 1480 (11.6%) | 16 (1.3%) |
| 2 | 3965 (31.1%) | 315 (26.3%) | b | 6091 (47.8%) | 352 (29.4%) |
| 3 | 3581 (28.1%) | 550 (45.9%) | c | 3752 (29.4%) | 554 (46.2%) |
| 4 | 1246 (9.8%) | 243 (20.3%) | d | 1432 (11.2%) | 276 (23.0%) |
| | 12755 | 1198 | | 12755 | 1198 |

Pearson chi square 4th edition $p < 0.001$; 5th edition $p < 0.001$

Mean age of Caucasian women 59.2(8.3) years, Asian women 57.5 (6.7) years (mean difference 1.7 (95%CI 1.3 to 2.1) years ($p < 0.001$), which may have confounded the association between breast density and ethnicity

Logistic regression analyses examining factors independently associated with breast density

| 4th edition | | OR | 95%CI for OR | P value |
|-------------------------------|-----------|-----------|---------------------|----------------|
| Cat 3+4 vs 1+2 | age | 0.942 | 0.938 to 0.946 | <0.001 |
| | ethnicity | 3.15 | 2.77 to 3.57 | <0.001 |
| | HT | 1.26 | 1.15 to 1.37 | <0.001 |
| Cat 4 vs 1+2+3 | age | 0.923 | 0.916 to 0.930 | <0.001 |
| | ethnicity | 2.30 | 1.97 to 2.69 | <0.001 |
| | HT | 1.29 | 1.12 to 1.49 | <0.001 |
| 5th edition | | | | |
| Cat c+d vs a+b | age | 0.944 | 0.940 to 0.949 | <0.001 |
| | ethnicity | 3.22 | 2.83 to 3.67 | <0.001 |
| | HT | 1.26 | 1.16 to 1.38 | <0.001 |
| Cat d vs a+b+c | age | 0.926 | 0.919 to 0.932 | <0.001 |
| | ethnicity | 2.32 | 2.00 to 2.69 | <0.001 |
| | HT | 1.28 | 1.12 to 1.47 | <0.001 |

Higher breast density was associated with being younger, being Asian and having taken hormone therapy (HT)

Summary: breast density & ethnicity

- The proportion of women with the highest density classification is 10-12% in both editions
- The lowest density category with the 4th edition is large (30% of women) compared with the 5th edition where the lowest density category includes only 10% of women
- Being of Asian (compared with Caucasian) ethnicity is associated with having higher breast density, independent of age and ever use of Hormone Therapy
- Our variable “ethnicity” is likely confounded by body mass index