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Short Communication

# Breast Cancer Screening in High-Risk Women

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## INTRODUCTION

There is circumstantial evidence that population-based screening programmes can reduce breast cancer mortality in women aged 40–70 years old. The value of screening in high-risk groups such as women with a positive family history of breast cancer is unproven.

In the meantime a rapidly increasing number of high-risk women seek counselling about strategies to reduce their risk of breast cancer death, such as intensive surveillance. As for ethical reasons no randomized trials can be performed, the effect of screening these women has to be evaluated by means of observational studies. In several specialized centers in the Netherlands, women with a more than 2 times increased risk of breast cancer (BC) (lifetime > 15%) are being screened regularly.

In this study the first results of screening high-risk women in the Rotterdam Cancer Center/ University Hospital are described.

## PATIENTS AND METHODS

According to Dutch national guidelines, high-risk women are screened by (at least) biannual clinical breast examination (CBE) and yearly mammography. The minimum age at entry is 25 years. When indicated, additional investigations by ultrasound and/or MRI are performed. A database was set up in which family and individual characteristics, screening data and final outcome of screening are registered. To date, 810 women were screened at least once.

By means of DNA-diagnosis or genetic-epidemiologic tables [1], three risk groups were defined (see Table 1).

Table 1

| | Risk group | Lifetime risk of BC | Criteria | No. of women |
|---|---|---|---|---|
| 1 | Carriers | 60–85% | proven carriers of a BRCA1/2 mutation (DNA-analysis) | 71 |
| 2 | High risk | 35–50% | * HBOC<br>* ≥ 3 close relatives with BC<br>* 2 relatives with BC < 50 | 531 |
| 3 | Moderate risk | 15–35% | all others not fulfilling the above mentioned criteria | 208 |

HBOC = hereditary breast and ovarian cancer; BC = breast cancer.

Table 2
Clinical and pathological characteristics of 18 breast cancers diagnosed during screening

| Patient | Age at diagnosis | Risk category | Screening round | Mode of detection | Histology | Tumour size (mm) | Nodal status |
|---|---|---|---|---|---|---|---|
| 1 | 28 | 1 | interval | BSE | ductal | 40 | 2/13 |
| 2 | 44 | 1 | interval | BSE | ductal | 12 | 0/19 |
| 3 | 39 | 1 | interval | BSE | ductal | 7 | 3/21 |
| 4 | 70 | 2 | 13th incident | mammography | DCIS | n.m.[1] | n.d. |
| 5 | 66 | 2 | 9th incident | mammography | DCIS | 7 | n.d. |
| 6 | 25 | 2 | 14th incident | mammography | ductal | 6 | 2/34 |
| 7 | 44 | 2 | 3rd incident | mammography | ductal | n.m.[1] | 0/6 |
| 8 | 35 | 2 | 12th incident* | CBE + mammography | ductal | 12 | 0/22 |
| 9 | 38 | 2 | 6th incident* | CBE + mammography | ductal | n.m.[2] | 7/13 |
| 10 | 43 | 2 | prevalent | CBE + mammography | ductal | 9 | 0/13 |
| 11 | 35 | 2 | prevalent | CBE + mammography | ductal | 8 | 1/18 |
| 12 | 60 | 2 | 2nd incident | CBE + mammography | ductal | 10 | 0/10 |
| 13 | 29 | 2 | 8th incident | mammography | medullar | 15 | 0/16 |
| 14 | 58 | 2 | 2nd incident | mammography | DCIS | n.m.[1] | n.d. |
| 15 | 48 | 2 | interval | BSE | ductal | 20 | 0/18 |
| 16 | 49 | 2 | 6th incident | CBE + mammography | ductal | 20 | 0/15 |
| 17 | 56 | 3 | 17th incident | CBE + mammography | ductal | 15 | 0/21 |
| 18 | 51 | 3 | 8th incident* | CBE + mammography | lobular | 12 | 1/11 |

*symptomatic at the time of screening; [1]multifocal tumour; [2]ill-defined border.
Abbreviations used: BSE = breast self examination; CBE = clinical breast examination; DCIS = ductal carcinoma in situ; n.m. = not measurable; n.d. = not done.

Table 3
Observed and expected numbers of breast cancer

| Risk group | Mean age at 1st screening (range) | Observed no. of breast cancers* | No. of person-years at-risk | Detection rate per 1000 | Expected no. of breast cancers** | Ratio observed/ expected |
|---|---|---|---|---|---|---|
| BRCA1/2 carriers (1) | 37 (25–63) | 3 | 136 | 22 | 0.2 | 15 |
| High risk (2) | 38 (25–68) | 10 | 1159 | 9 | 1.7 | 6 |
| Moderate risk (3) | 37 (25–67) | 2 | 458 | 4 | 0.7 | 2.5 |
| Overall/total | 37 | 15 | 1753 | 8.5 | 2.6 | 5.5 |

*DCIS excluded. ** for population aged 40–50 according to National Cancer Registry 1990–1995.

## FOLLOW-UP

Two patients (1 and 9) relapsed; both died of metastatic disease 2.5 and 4 years, respectively, after the diagnosis. One additional patient (4) died of another cause (CML).

## SUMMARY MEASURES

See Table 4.

## CONCLUSIONS

It is possible to identify young women at high familial risk for breast cancer. The number of cancers detected in this population was on average 5 times greater than expected and related to the risk category.

Data will be included in a national multi-centre study to assess the short-term results of screening and predict long-term effects, such as mortality reduction. Further, the value of MRI as a

Table 4

| | | | |
|---|---|---|---|
| Nodal status[1]: | negative | 60% | (9/15) |
| | positive | 40% | (6/15)[2] |
| Tumour size[1,3]: | < 10 mm | 31% | (4/13) |
| | 10–20 mm | 61% | (8/13) |
| | > 20 mm | 8% | (1/13) |
| Sensitivity = a/a + c with a defined as: | | | |
| | 1) all screen-detected tumours (n = 14) | 78% | (14/18) |
| | 2) asymptomatic screen-detected (n = 11) | 61% | (11/18) |

[1]invasive tumours only; [2]two pN1a; [3]two tumours with unknown size.

potential alternative for mammography will be investigated.

## References

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