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Left Handedness is Uncommon in Breast Cancer Patients

H. Olsson and C. Ingvar

Left handedness was found to be significantly less common among patients with breast cancer in southern Sweden (1.5%) than among a female referent population (5%) ($P<0.0025$). The findings lend support to theories suggesting that hormonal factors in early life are of importance both for handedness and for the risk of breast cancer.
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INTRODUCTION

THEORIES ON breast cancer have focused on the importance of events in the early reproductive years [1–9]. Trichopoulos has suggested that events in the prenatal and perinatal years could have an important bearing on breast cancer carcinogenesis [10]. Often only retrospective studies about factors for cancer development in these early periods are possible, since prospective studies would take generations.

Cerebral dominance of the left or right hemisphere, expressed as right or left handedness, could be partly dependent on the hormonal perinatal and prenatal environment [11–13]. Thus a higher rate of left handedness in the offspring could be caused by a more pronounced testosterone exposure to the fetus either by the mother or the fetus itself [11–13]. If a hormone exposure in early years would later have a bearing on the risk of developing breast cancer, an increased androgen exposure to the female fetus would reduce the risk of developing breast cancer. On the other hand, an increased oestrogen exposure instead would augment the risk [10].

In the present investigation, the frequency of left-handedness has therefore been investigated in a large group of breast cancer patients and female referents from the general Swedish population.

PATIENTS AND METHODS

Consecutive breast cancer patients (n = 395) at the Department of Oncology, University Hospital, Lund, were interviewed through a standardised structured questionnaire about handedness at their primary visit for postoperative radiation treatment. The median age of the patients was 62 (range 28–90) years. The department serves as the radiation treatment centre for the Southern Health Care Region in Sweden and has a catchment area of 1.2 million inhabitants. The recruitment is population-based. Except for ongoing randomised trials excluding approximately one third of postmenopausal women and one fifth of premenopausal women from radiation, the overall majority of breast cancer patients are seen. 5158 women interviewed through health care investigations from Swedish centres for Occupational Health in 1983–1984 was used as referents [14]. These women were occupationally active and their age ranged from 15–65 (median 41) years. Left handedness was defined as preferentially using the left hand when writing as an adult. Women using both hands equally were classified as right handed.

The Poisson distribution was used to compare the two groups.

RESULTS

Of the breast cancer patients, 6/395 (1.5%) were left handed compared with 258/5158 (5%) of the referents. This difference was highly significant ($P<0.00025$). 4 out of 6 (67%) left handed women with breast cancer also had a left sided breast cancer in comparison with 211/389 (54%) right handed women (OR = 1.7, 95% CI 0.3–12.7).

DISCUSSION

The present investigation shows that left handedness is less common among patients with breast cancer than among the general population. Theories have related prenatal and perinatal androgen exposure from the mother to the fetus as a possible cause for left handedness [11–13]. Our findings indicate that an increased exposure to testosterone in early life permanently reduces the risk of breast cancer for a woman and thus support theories on the age dependency of breast cancer carcinogenesis.

There are problems in determining handedness. First, there are individuals who are ambidextrous. By only classifying women preferentially writing with the left hand as left handed we hoped to avoid the possibility of a classification bias. Second, handedness was determined in adults and this is preferable since very young children may have a not fully developed cerebral

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dominance [11–13]. In this context, it is of interest that around 5% of fetuses favour the left thumb for sucking when assessed by ultrasound. This preference for a particular thumb is maintained during pregnancy and correlates highly with neonatal head position preference [15]. Using female referents is preferrable in a study of female subjects since among females there are somewhat fewer left handed individuals than among men [11–13].

Different interviewers were used for breast cancer patients and referents. This may introduce a potential bias. However it is unlikely to be the case in a study defined to determine handedness as described above.

Thus it appears unlikely that left handedness was overestimated or underestimated in our study. Further the figures from the literature on left handedness ranging from 5–10% [11–13] is well in accordance with the referent group.

To our knowledge only two previous investigations have assessed handedness in breast cancer patients [16, 17]. In one study [16], 3.5% of the breast cancer patients were left handed, again a figure lower than expected. In another study [17] no significant difference between cases and hospital referents could be seen regarding the frequency of left handedness. However, direct comparison with our study is precluded because the definition of handedness was not stated in the paper. As in our study, Hsieh *et al.* found in their investigation a suggestion of an association between breast cancer laterality and handedness [17].

It is interesting to speculate if the low percentage of left-handed women among breast cancer cases represent women with a retained left cerebral dominance for speech, since it has been shown that almost half of left handed individuals, and all right handed individuals use the left hemisphere as dominant for speech [11–13]. Several findings [11–13] indicate a sex difference in cerebral lateralisation. As stated above, left-handedness is more common in men than in females. Men show more developmental disorders regarding speech, language, cognition and emotion. On average women are superior verbally to men while men do better in spatial functions. As Geschwind *et al.* have pointed out there is evidence that sex hormones may cause this sex difference in cerebral function. Breast hypertrophy and breast cancer develop in an assymetrical manner, being more common in the left breast [11–13]. Whether this is in any way related to cerebral dominance is yet unresolved.

Could there be other explanations for the finding that patients with breast cancer are less likely to be left-handed? In one investigation a late age at first full-term pregnancy (another well-defined risk factor of breast cancer) in the mother was associated with a higher rate of left handedness in the offspring [18]. An early menarche has in some investigations been found to be a risk factor [19]. Women with late menarche have higher spatial scores than than those with early menarche [11–13]. This also underlines the possibility that hormonal factors may influence laterality and associated skills. In another investigation the mean age at menopause was found to be earlier among left handed than in right handed women [20]. It is unknown if other reproductive factors are associated with handedness, and if handedness thus potentially could covary with other breast cancer risk factors.

Thus the results of this study should prompt further investigations in patients with breast cancer on cerebral dominance and handedness in relation to reproductive and hormonal factors. Also studies of handedness in both female and male patients with other reproductive tumours as ovarian, endometrial, testicular and prostate carcinoma would have a high priority. From the present results, one could postulate that patients with prostate carcinoma may show a higher incidence of left handedness.

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