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Stressful life experiences and risk of relapse of breast cancer: observational cohort study

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Abstract

Objective To confirm, using an observational cohort design, the relation between severely stressful life experiences and relapse of breast cancer found in a previous case-control study.

Design Prospective follow up for five years of a cohort of women newly diagnosed as having breast cancer, collecting data on stressful life experiences, depression, and biological prognostic factors.

Setting NHS breast clinic, London; 1991-9.

Participants A consecutive series of women aged under 60 newly diagnosed as having a primary operable breast tumour. 202/222 (91%) eligible women participated in the first life experiences interview. 170 (77%) provided complete interview data either up to 5 years after diagnosis or to recurrence.

Main outcome measure Recurrence of disease.

Results We controlled for biological prognostic factors (lymph node infiltration and tumour histology), and found no increased risk of recurrence in women who had had one or more severely stressful life experiences in the year before diagnosis compared with women who did not (hazard ratio 1.01, 95% confidence interval 0.58 to 1.74, P=0.99). Women who had had one or more severely stressful life experiences in the 5 years after diagnosis had a lower risk of recurrence (0.52, 0.29 to 0.95, P=0.03) than those who did not.

Conclusion These data do not confirm an earlier finding from a case-control study that severely stressful life experiences increase the risk of recurrence of breast cancer. Differences in case control and prospective methods may explain the contradictory results. We took the prospective study as the more robust, and the results suggest that women with breast cancer need not fear that stressful experiences will precipitate the return of their disease.

Introduction

Between a quarter and a third of women diagnosed with operable breast cancer will have a recurrence of their disease within five years of it being diagnosed. Several biological factors, such as axillary lymph node involvement and histological grade, are known to influence breast cancer prognosis, yet women with apparently similar tumours at the time of presentation differ markedly in their disease-free survival and overall survival. This raises the possibility that such differences in outcome may be explained by host and environmental factors, which could include psychological and social variables. A mechanism by which stressful life experiences could influence recurrence of disease has been identified by preliminary immunological data. These data indicate that downregulation of the immune system occurs, via reduced activity of natural killer cells, after exposure to a variety of environmental stressors.[1] Furthermore, some data suggest that psychological interventions can improve survival for women with metastatic breast cancer,[2 3] although a relation has yet to be shown conclusively.[4]

Studies that have investigated the relation between stressful life experiences and cancer progression provide conflicting data.[5–11] All the studies are subject to methodological weaknesses. The single population based study to be carried out to date failed to find any increased risk of recurrence or death among over 14 000 women with cancer who had lost either a spouse or a child.[12 13] From examining studies carried out to date it is clear that the question of whether stressful life experiences influence disease recurrence remains unanswered.

The aims of this study were to investigate the relation between stressful life experiences and relapse of breast cancer in a methodologically robust way. We collected data on stressful life experiences prospectively by using a standardised, interview based instrument; we controlled for the main biological factors known to influence prognosis of breast cancer; and we used a relatively long follow up period.

Participants and methods

Participants

We approached a consecutive series of 222 women who had been diagnosed with a primary operable breast tumour at Guy's Hospital between May 1991 and July 1994. We excluded women at low risk of recurrence (women with a very small tumour (< 1 cm) and no lymph node involvement) and women older than 60 years, because older women have relatively fewer stressful life experiences than younger women.[14]

Methods

We collected data from the women on stressful life experiences and depression. Interviews, which were tape recorded and transcribed, were carried out every 18 months and covered the period from 12 months before diagnosis to five years after diagnosis. We identified details of the timing and nature of any recurrence through weekly examination of the breast unit's database and follow up records made by the clinic. We took the date of recurrence as the date of onset of a physical sign that was confirmed radiologically or histologically as a recurrence.[15] Our final interview with patients who had a recurrence took place approximately eight weeks after the diagnosis.

Instruments

We collected data on stressful life experiences by using the Bedford College life events and difficulties schedule.[14] This is a semi-structured standardised interview that inquires about discrete life events and more longstanding difficulties. Each stressful life experience is given a severity rating, reflecting the degree to which it would be threatening to a hypothetical woman in the same life circumstances.

Using this approach rather than the participant's subjective description of the threat associated with the experience reduces the bias that could arise from the participant's report of life experiences. An example of a severe event is divorce; a severe difficulty could be caring for a severely handicapped child. At each interview we elicited psychiatric symptoms by using the structured clinical interview with criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (third edition, revised), to enable us to identify episodes of persistent depression (lasting three months or longer) experienced by the women.[16]

Results

Of 202 (91%) women who completed an initial interview, 171 (77% of the original 222 eligible) provided complete interview data either up to five years after diagnosis or to recurrence. Patients with incomplete data were included in the analysis to preserve the consecutive series. Some patients died soon after recurrence; therefore, four of the final interviews after recurrence were completed by the woman's closest relative.

The overall five year relapse-free survival was 76% (95% confidence interval 68.6 to 81.1). Recurrence of disease was confirmed in 54 women. Disease factors were worse for women who subsequently had a recurrence; sociodemographic factors were similar in the two groups.

Associations between life experiences and recurrence

After the effects of lymph node infiltration and histological type were adjusted for, women who had one or more severely stressful life experiences in the year before diagnosis did not have an increased risk of recurrence compared with women without such experiences (table). Likewise, an episode of depression before diagnosis did not increase the risk of recurrence (hazard ratio 1.22, 0.38 to 3.92, P=0.7).

In the post-diagnosis period, after adjustment for nodes and histological type, women who had one or more severely stressful life experiences had a lower risk of recurrence than those who did not (table). Separate examination of life events and difficulties indicated that the effect was primarily caused by events (yes *v* no, 0.54, 0.30 to 0.96, P=0.04) rather than difficulties (yes *v* no, 0.79, 0.44 to 1.4, P=0.4). Having an episode of depression did not increase the risk of recurrence (0.88, 0.42 to 1.87, P=0.7).

Effect of severely stressful life experiences on risk of recurrence of breast cancer*

	Hazard ratio (95% CI)	P value
Before diagnosis:		
Severe life experience (yes *v* no)	1.01 (0.58 to 1.74)	0.99
Nodes involved (0, 1-3, 4-9, ⩾10)	1.66 (1.24 to 2.22)	0.001
Histological type (ductal grade III *v* other)	3.33 (1.92 to 5.79)	<0.001
After diagnosis:		
Severe life experience (yes *v* no)	0.52 (0.29 to 0.95)	0.03
Nodes involved (0, 1-3, 4-9, ⩾10)	1.68 (1.27 to 2.22)	<0.001
Histological type (ductal grade III *v* other)	3.45 (2.0 to 5.96)	<0.001

*Final Cox model.

Discussion

This study found no evidence that women who have a severely stressful life experience in the year before being diagnosed with breast cancer, or in the five years afterwards, are at any increased risk of developing a recurrence of their disease. In fact, women who had one or more severely stressful life experiences after diagnosis had a lower risk of recurrence than those who did not. It is perhaps a marginal association, with the upper limit of the 95% confidence interval close to 1. However, the only other study to use such detailed assessment of stressful life experiences reported a reduced risk of recurrence among women who had one or more severely stressful life experiences in the 12 months before surgery.[10] These intriguing findings are in the opposite direction to the outcome hypothesised, and it is difficult to formulate a rationale to explain how stressful life experiences might reduce a woman's chance of experiencing a recurrence of her disease.

Validity of the data

The data in this study were collected from a sufficiently large sample of women to enable identification of a doubling of the risk of recurrence after a severe life experience—a conservative estimate based on previous findings.[7] The follow up period was longer than that in the only other similar prospective study,[10] so, if stressful life experiences cause recurrence only after a latent period, the longer follow up would have increased the likelihood of an association being detected. The present study used a thorough measure of stressful life experiences, using a semi-structured interview to obtain details of experiences and a method of assessing the degree of threat posed by experiences, which takes into account the context in which they occur. The study used a prospective design, which meant that for most of the data collection, participant and interviewer were blind as to whether the disease would recur. Only for the final interviews of women who had a recurrence

What is already known on this topic

Women with apparently similar tumours at the time of presentation with breast cancer differ considerably in their disease-free survival and overall survival

Such differences in outcome may well be explained by host and environmental factors, which could include psychological and social variables

Data on the relation between severely stressful life experiences and cancer progression have been contradictory

What this study adds

Women who have a severely stressful life experience in the year before being diagnosed with breast cancer, or in the five years afterwards, do not seem to be at increased risk of developing a recurrence of the disease

Women with breast cancer need not fear that stressful experiences will precipitate the return of their disease.

was the outcome known, and this represented a small amount of the data. All of these factors would enhance the quality of the data and reduce the likelihood that the outcome is the result of bias.

Comparison with other studies

Of studies that have used a thorough assessment of stressful life experiences, studies with a prospective design (the current study, and that by Barraclough[10]) found no increase in the risk of recurrence of breast cancer, whereas the single case-control study found a strongly increased risk.[7] Differences in case-control and prospective methods may explain the contradictory results arising from these two types of study.

We took the prospective studies as the more robust, and these data indicate that women with breast cancer need not fear that stressful experiences in life are likely to bring about the return of their disease.

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Impact of preventive strategies on trend of occupational skin disease in hairdressers: population based register study

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Hairdressing is one of the occupations most hazardous to the skin.[1] Various efforts have been made in Germany in the past 10 years to reduce the incidence of occupational skin diseases among hairdressers.[2 3] Two legislative regulations introduced as Technical Rules for Hazardous Substances 530 "Hairdressing trade" and 531 "Endangerment of the skin by work in the wet environment (wet work)" came fully into force in September 1992 and September 1996.

Because of the high cost of medical treatment, professional retraining, and disability pensions for hairdressers with an occupational skin disease, the Statutory Accident Insurance Institution for the Health and Welfare Services (workers' compensation board) coupled the new technical rules with information campaigns and passed a resolution in 1994 to strengthen "secondary individual prevention," in accordance with the Ordinance on Industrial Disease. Sensitisation to glyceryl monothioglycolate is common, and in 1995 hair cosmetics manufacturers agreed with the hairdressers' guild to stop the use of this allergen in permanent wave solutions. The Health and Safety Authority in Bavaria started educational and enforcement activities to ensure that the new regulations were put into practice.

We analysed data from our register of occupational skin diseases in Northern Bavaria[1] to determine whether a downward trend in the annual incidence of occupational skin disease in hairdressers could be observed.

Methods and results

We identified hairdressers from all initial reports of occupational skin diseases (5285 cases) registered between 1990 and 1999. Of the 997 initial reports of occupational skin disease in hairdressers, 856 (85.9%) cases had a confirmed occupational cause.

Because of asymmetry, we used median and quartiles (Q1, Q3) for statistical description of distributions. We calculated incidences as the number of occupational skin diseases per 10 000 workers per year. We calculated asymptotic 95% confidence intervals according to standard theory. To test for linear trend of rates we used the Cochran-Armitage trend test.[4] We used SAS 8.1 (SAS Institute, Cary, NC) for data analysis.

The hairdressers with a stated occupational skin disease had a median age of 20 (Q1 18, Q3 22) years and a median occupational period of exposure of 24 (Q1 12, Q3 48) months. The annual incidence fell from 194 to 18 cases per 10 000 workers between 1990 and 1999 (figure), which is not only highly significant ($P < 0.0001$) but also of clinical importance as it corresponds to a 10-fold decline in the annual incidence.