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REVIEW

The relation between stressful life events and breast cancer: a systematic review and meta-analysis of cohort studies

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Abstract

Purpose Breast cancer is the most common cancer among women with high rate of mortality. This systematic review and meta-analysis was conducted to investigate the relation between stressful life events and breast cancer.

Methods We searched PubMed, Scopus, ScienceDirect, and Google scholar databases from their inception until June 2018. The keywords and phrases we used in the search were (life events AND stress AND breast cancer OR neoplasm) to identify potentially relevant cohort studies that reported relative risk estimates and confidence intervals of this association. Pooled Risk ratio and 95% confidence intervals (CIs) were calculated using random effects model.

Results Out of 168 potentially relevant publications, 11 documents met the inclusion criteria. The results showed that history of stressful life events slightly increases the risk of breast cancer [pooled Risk Ratio: 1.11 (95% CI 1.03 to 1.19)].

Conclusions History of stressful life events could be associated with a moderate increase in the risk of breast cancer. We advise that receiving psychological and counseling services after occurrence of stressful life events of women should be taken seriously.

Keywords Stress · Life events · Neoplasm · Breast cancer · Psychological distress

Introduction

Breast cancer is the most common type of cancer among women that involves 1.5 million women annually. The death rates of breast cancer is also significant such that according to a report provided by the World Health Organization in 2015, 570,000 deaths occurred due to breast cancer around the world which accounted for 15% of total amount of deaths by different cancers among women [1]. According to the report announced by International Agency for Research on Cancer, breast cancer accounts for 25% of all cancers and 15% of deaths due to all cancers among women [2]. The American Cancer society has predicted that in 2018 about 266,120 American women will get breast cancer and 40,920 deaths will occur due to breast cancer in the United States [3].

Numerous studies have been conducted on breast cancer risk factors in which different factors such as age, family history, early menarche, late menopause, use of contraceptives, environmental factors, and lifestyle are reported as breast cancer risk factors [4–10]. Some studies have investigated the role of stress or other psychological distress in cancer occurrence [11–15]. Their results were quite contradictory,

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and some of them denied the existence of any relation between the stressful life events and breast cancer [16, 17], but some others have reported strong and significant relations between them [18–22]. These inconsistent results can be attributed to the use of different methodology, the way of controlling confounding variables, the study population, or the different research designs, and ways of measuring stressful life events.

These serious contradictions in studying the relation between stressful life events and breast cancer have motivated some researchers to conduct systematic review and meta-analysis studies on this topic. The results of systematic review and meta-analysis studies were quite contradictory, and furthermore, there was no similar procedure in selection of included studies in such a way that these included a wide range of cross-sectional studies, case–control studies, prospective studies, or a combination of different studies [23–26]. It seems that one of the important reasons for the contradictory results between systematic review and meta-analysis studies was the selection of studies with heterogeneous methodologies.

Since cohort studies provide stronger evidences in comparison with other noninterventional studies, this systematic review and meta-analysis study was conducted with the aim of investigating the results of cohort studies on relation between stressful life events and breast cancer.

Materials and methods

In this study, we followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [27].

Inclusion and exclusion criteria

Literature search was performed to identify cohort studies which investigated the relation between stressful life events and breast cancer. Inclusion criteria of selected articles were (1) original peer-reviewed articles published in English language; (2) the articles should describe the association between stressful life events and breast cancer risk; (3) they reported measure of association between stressful life events and cancer such as Risk Ratio, Rate Ratio, Odds Ratio, and the related Standard Error (SE) or 95% confidence intervals (CI) or provided enough raw data to calculate them; (4) They studied on women of 18 years old or older with first occurrence of breast cancer. Review Articles, editorials, debates, letters, case reports, meeting abstracts, and non-peer-reviewed articles were excluded. Also studies examining the relation between breast cancer and anxiety and other psychological disorders were excluded.

Search strategy

A systematic literature review was conducted using the PubMed, Scopus, ScienceDirect, and Google scholar from their inception until June 2018. The keywords and phrases we used in the search were (life events AND stress AND breast cancer OR neoplasm) in the title, abstract, or keywords.

To find any additional published study, the reference lists of all retrieved articles and related review articles were searched manually. All searches were performed by two independent reviewers, and disagreements were resolved by consensus and, if necessary, by consulting with the third party.

Data extraction

The titles and abstracts of articles were evaluated for the selection of eligible studies. Some articles were excluded as they did not satisfy inclusion criteria. Then the full-texts of selected articles were evaluated to decide whether they fulfill the inclusion criteria. The data were extracted according to predefined checklist including article title, authors, year of publication, setting, sample size, age of participants and main results including Risk Ratio (RR), and 95% confidence intervals. Data extraction was done independently by the first and second authors.

Quality assessment

All the selected articles were examined in terms of quality based on Newcastle–Ottawa Quality Assessment Scale for cohort studies [28]. Newcastle–Ottawa Scale for Cohort Studies is examined in terms of interrater reliability and construct validity in the previous study, and has reported a high degree of agreement across its domains [29]. This scale has eight items and three domains including Selection, Outcome, and Comparability categories. A study can be awarded a maximum of one or two stars for each numbered item. The total score can be given between 0 and 13 stars [28]. We stratified all studied based on their scores into three levels:

(1) ‘High-quality studies’: studies scoring 75% or more of maximum attainable stars (score $\geq$ 10 stars).
(2) ‘Moderate-quality studies’: studies scoring between 50 and 75% of attainable stars (stars between 7 and 9).
(3) ‘Low-quality studies’; studies scoring lower than 50% attainable stars (stars $\leq$ 6).

Quality assessment was conducted independently by two investigators.

Statistical analysis

Risk ratios and rate ratios, and 95% confidence intervals were considered as measures of effect in this meta-analysis. Heterogeneity among studies was evaluated via the I^2 statistic (the proportion of total variance due to between-studies variance) and the Q test, in which a p value < 0.1 was considered as statistically significant. For pooling the effect size estimates, we used the fixed effects model, when there was no heterogeneity between studies and the random effects model otherwise.

Cumulative meta-analysis was conducted to identify any trend in estimates across time. The Begg's rank correlation and the Egger's weighted regression methods were used to statistically assess publication bias. A p value < 0.05 was considered statistically significant for tests of publication bias. We also visually assessed publication bias using funnel plot. STATA 12 (Stata Corp, College Station, TX, USA) was used for statistical analysis.

Results

Characteristics of included studies

We found a total of 11 cohort studies [22–32] until June 2018. The main characteristics of the studies included in this meta-analysis are summarized in Table 1. The flow diagram of search strategy and reasons of exclusion are presented in Fig. 1.

Association between stressful life events and breast cancer

There were evidences of heterogeneity among studies. Based on I^2, the proportion of total variance attributed to between-studies variance was about 53%. What is more, Q test for heterogeneity was significant ($\chi^2 = 21.47$, $p = 0.01$). After pooling the data based on random effects model, we observed that history of stressful life events slightly increases the risk of breast cancer [pooled Risk Ratio: 1.11(95% CI 1.03 to 1.19)]. The individual and pooled estimates of effect size are presented in Fig. 2. We did not perform any subgroup analysis because of the small number of studies and/or low variability in potentially modifier variables such as age group, area of study, and quality score. Cumulative meta-analysis by the year of publication showed that the first constant significant relation was revealed after the study by Helgesson in 2003 (RR = 1.17, 95%CI 1.03 to 1.33). Adding other studies neither changed the direction nor strength of association, but increased the precision of the effect size (Fig. 3). Although the Egger's and Begg's test showed no evidence of publication bias (p values = 0.11 and 0.3, respectively), the funnel plot of effect size of the studies was slightly skewed to the right (Fig. 4).

Discussion

The results of our systematic review and meta-analysis suggested that history of stressful life events is associated with a moderate increase in the risk of breast cancer.

Some previous studies have also reported results consistent with the present meta-analysis. For instance, Lin et al. (2013) conducted a meta-analysis of seven case–control studies and reported that breast cancer has a borderline increase after stressful life events [24]. Kocic et al. (2015) have also reported in a case–control study that stressful life events can justify a part of cancer breast etiology [21]. Moreover, some other studies have confirmed the relation between breast cancer and stress [41–43].

The relation between stressful life events and breast cancer is supported based on some assumptions. According to one assumption, the stress caused by such events can affect hypothalamic–pituitary–adrenal axis and cause disorders in the endocrine system, and therefore the amount of cortisol is increased and anti-neoplastic activity is inhibited [44–46]. Another assumption on this matter is that the high anxiety that is followed by stressful events, increase the breast cancer risk by suppressing the immunity system [47, 48]. These assumptions are supported by the results of some studies which elucidate that psychological treatments during the occurrence of stressful life events can decrease breast cancer [24].

There is another linkage between stressful life events and breast cancer via intermediate endpoints such as inflammatory markers, cytokines, interleukins, etc. Previous studies about psychological stress outcomes have reported the profound effects of stress on immune system function depending on the severity, kind and duration of the stressor, etc [49, 50]. One of the most important responses of the immune system is increasing the circulating level of cytokines especially IL-6, TNF-α, and IL-1β [51, 52]. Also several studies have reported increasing levels of IL-2, 4, 10, and IFN-γ [49, 53]. On the other hand, some studies about the etiology of breast cancer suggested that the imbalance of cytokines can suppress the function of the immune system and lead to several disorders including infections or neoplastic growth. Cancer cells communicate with the host cells via cytokines and utilize this communication system to shape tumor microenvironment and promote metastasis activity [54]. Also the role of interleukins in breast cancer has been explained clearly. Circulating levels of IL 6 and IL8 in breast cancer women are much higher than in normal people and are also related to the stage and mortality rate of breast cancer [55].

Table 1 Main characteristics of cohort studies included in the meta-analysis of Stressful Life Events and Breast Cancer

Authors, Year	Country	Type of stressful life event	Assessment instruments	Sample size	Age	Duration of follow-up	RR (95% CI)	Quality score
Jacobs, 2000 [30]	USA	Maternal death in childhood	Interview	1213	N/A	10 years	2.56 (1.59–4.35)	9
Lillberg, 2001 [31]	Finland	Stress of daily activities	Stress of daily activities questionnaire	10,519	> 18 years	20 years	1.07 (0.79–1.44)	11
Price, 2001 [32]	Australia	Life stressors	Brown and Harris Life Event and Difficulties Schedule	239	> 40 years	Previous 2 years	1.04 (0.94 –1.16	11
Graham, 2002 [33]	United Kingdom	Stressful life experience	Bedford College life events and difficulties Schedule	222	< 60 years	18 months before and 5 years after diagnosis or	1.01 (0.58–1.74)	7
Li, 2002 [34]	Denmark	Death of a child	Denmark Register of Birth and Death Statistics	21,062	N/A	18 years	1.18 (1.01–1.37)	11
Lillberg, 2003 [35]	Finland	Stressful life events	A researcher made questionnaire	10,808	> 24 years	15 years	1.07 (1.00–1.15)	12
Helgesson, 2003 [36]	Sweden	Stressful events	A researcher made stress scale (score: 1 to 6)	1462	38–60 years	5 years	2.1 (1.2–3.7)	12
Michael,2009 [37]	USA	Stressful life events	A modified life events inventory	84,334	50–79 years	Previous 1 year	1.12 (1.01–1.25)	10
Olsen, 2012 [38]	Denmark	Death of cohabiting partner	Danish Central Population Register and Danish Breast Cancer Cooperative Group	21 213	> 30 years	14 years	1.10 (0.95–1.27)	11
Kennedy, 2014 [39]	Sweden	Parental death during early adulthood (18 years)	Swedish Multi-Generation Register, Swedish Causes of Death and Cancer Registers	345,882	> 40 years	40 years or less	1.1 (1.0–1.3)	11
Schoemaker, 2016 [40]	United Kingdom	Stressful life Events	A researcher made questionnaire	1783	16 years or older	11 years	0.93 (0.77–1.12)	12

However, the results of systematic review and meta-analysis studies on relation between stressful life events and breast cancer are contradictory, and a range of no-to-strong relation is reported. Some meta-analysis studies have reported no significant relation between stressful life events and breast cancer. For instance, Santos et al. conducted a systematic review and meta-analysis study on cohort and case–control articles. They reported that there is no association between stressful life events and breast cancer [56]. In another meta-analysis conducted by Duijts et al. [25], retrospective case–control, prospective case–control studies, and limited perspective cohort and prospective cohort studies were included. Although in this study, a moderate relation between the death of the spouse

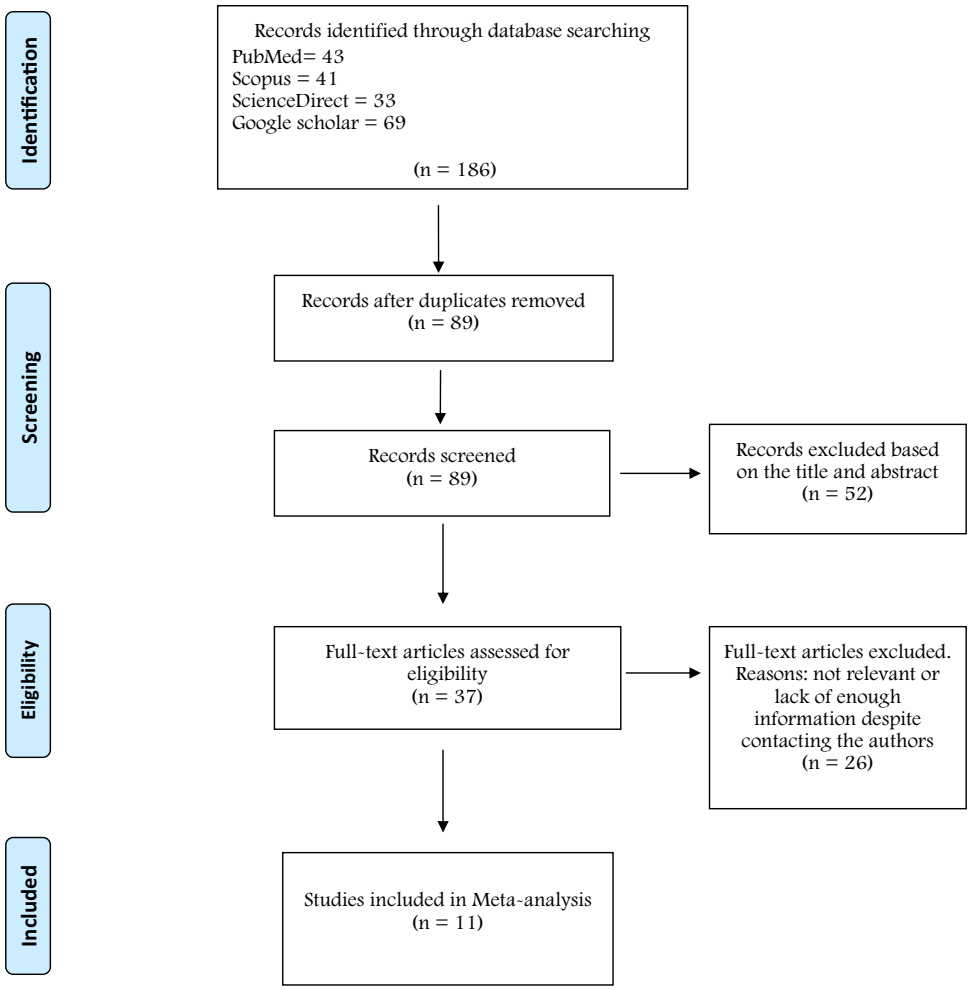

Fig. 1 Flowchart of study-selection progress in the meta-analysis of Stressful Life Events and Breast Cancer

and breast cancer was reported, the overall results of this study did not show relation between stressful life events and breast cancer. Similar results in older study conducted by Petticrew et al. was reported in a meta-analysis of a retrospective cohort study, 14 case–control studies and 14 limited perspective studies [57].

As some assumptions confirm the relation between cancer and stress, some other mention dubious evidences on this issue. One of the ambiguities about the association between stress and breast cancer is the fact that while high levels of estrogen is known as a certain risk factor of breast cancer, how chronic stress which inhibits the synthesis of estrogen can be associated with breast cancer? [25]. Moreover, this question is posed about the assumption of protective effect of immune system suppression in the occurrence of cancer that considering this severe suppression in the recipients of organ donation, how is it that several cancers will not occur? [47, 48].

These contradictory results in different studies can be due to diversity in the types of included studies. Some important contradictions among these studies were found in the method of assessing the stressful life events and in the different definitions of these events. In these studies, different events such as divorce, spouse or child death, parent death, severe illness of children are considered as stressful events.

Another important factor that can be the reason of contradiction in the study results and be the missing link in the design of these studies is that the amounts of perceived stress as a result of events defined as stressful life events can be different in various people—in other words, the important point is the stress experienced due to stressful events, not merely the existence or nonexistence of these events. Furthermore, according to what has been reported in some studies, coping strategies to stressful life events and coping skills can play an important role in reducing the adverse consequences of stress [58–60]. However, these issues did not receive attention in any of the previous studies, and it seems that more studies with stronger methodologies and considering the role of intervening variables such as perceived stress or rate of using coping skills in investigation of relation between stressful life events and breast cancer need to be conducted.

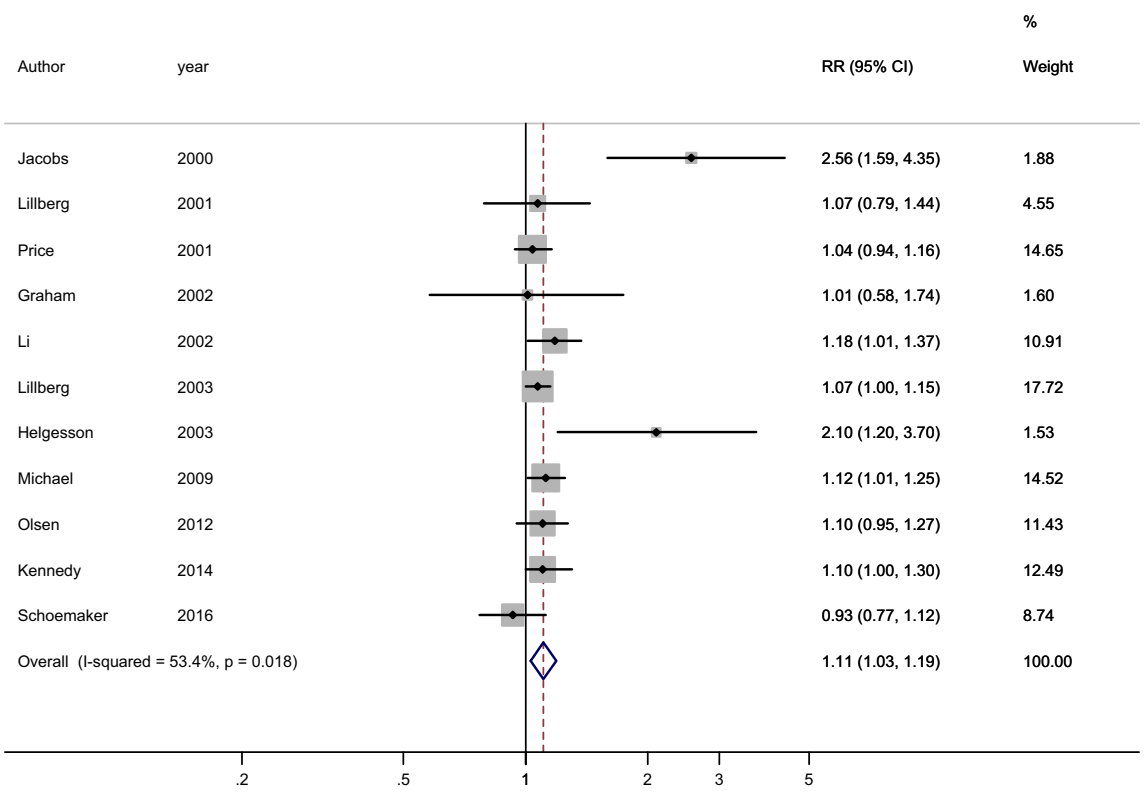

Fig. 2 Forest plot for association between stressful life events and breast cancer based on random effects model

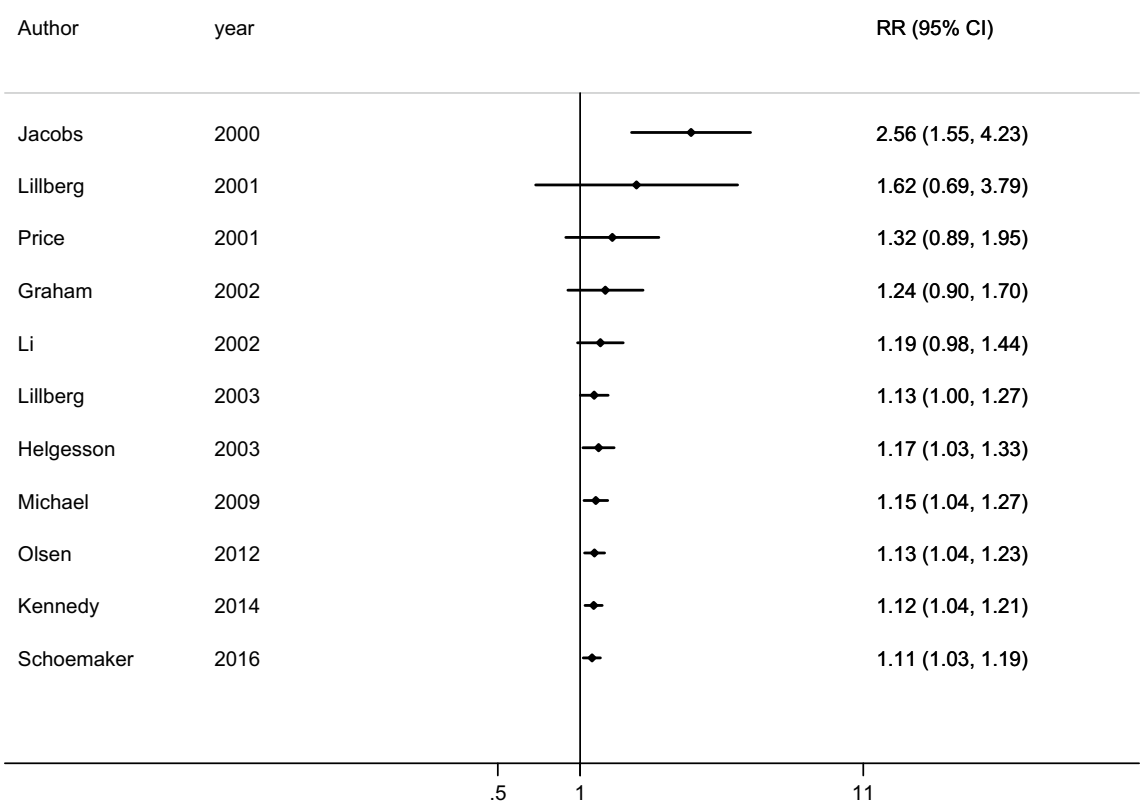

Fig. 3 Cumulative forest plot for association between stressful life events and breast cancer based on random effects model

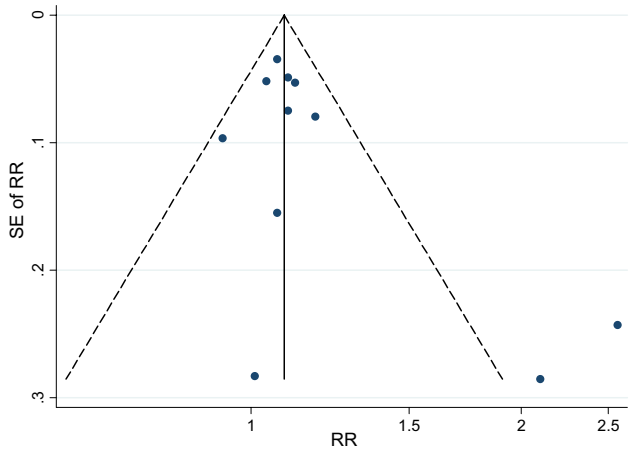

Fig. 4 Funnel plot of association between stressful life events and breast cancer

In the present study, although the formal tests did not show any evidence of publication bias, the funnel plot was slightly skewed to the right. It shows that we cannot simply ignore the possibility of publication bias and have to interpret the results with caution. However, to prevent this bias, we comprehensively searched electronic databases and manually checked the reference list of included articles.

Conclusion

The overall results of this systematic review and meta-analysis elucidated that stressful life events slightly increases the risk of breast cancer. According to these results, we strongly advise that receiving psychological and counseling services after occurrence of stressful life events of women should be taken seriously. However, conducting more extensive studies considering the perceived stress and assessing the rate of using coping skills is suggested in this field.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. World Health Organization. Breast cancer. http://www.who.int/cancer/prevention/diagnosis-screening/breast-cancer/en/. Accessed 18 Mar 2018
2. International Agency for Research on Cancer. Estimated incidence, mortality and 5 year prevalence: both sexes. http://gco.iarc.fr/today/fact-sheets-populations?population=900&sex=0. Accessed 10 Mar 2018
3. Siegel RL, Miller KD, Jemal A (2018) Cancer statistics, 2018. CA Cancer J Clin 68(1):7–30. https://doi.org/10.3322/caac.21442
4. Rudolph A, Chang-Claude J, Schmidt MK (2016) Gene-environment interaction and risk of breast cancer. Br J Cancer 114(2):125–133. https://doi.org/10.1038/bjc.2015.439
5. Autier P, Boniol M, Smans M, Sullivan R, Boyle P (2016) Observed and predicted risk of breast cancer death in randomized trials on breast cancer screening. PLoS ONE 11(4):e0154113. https://doi.org/10.1371/journal.pone.0154113
6. Rojas K, Stuckey A (2016) Breast cancer epidemiology and risk factors. Clin Obstet Gynecol 59(4):651–672
7. Moslehi R, Freedman E, Zeinomar N, Veneroso C, Levine PH (2016) Importance of hereditary and selected environmental risk factors in the etiology of inflammatory breast cancer: a case-comparison study. BMC Cancer 16:334. https://doi.org/10.1186/s128-2369-016-.z
8. Santen RJ, Boyd NF, Chlebowski RT, Cummings S, Cuzick J, Dowsett M et al (2007) Critical assessment of new risk factors for breast cancer: considerations for development of an improved risk prediction model. Endocr Relat Cancer 14(2):169–187
9. Cedolini C, Bertozzi S, Londero AP, Bernardi S, Seriau L, Concina S, Cattin F, Risaliti A (2014) Type of breast cancer diagnosis, screening, and survival. Clin Breast Cancer 14(4):235–240. https://doi.org/10.1016/j.clbc.2014.02.004
10. Yiannakopoulou E (2014) Etiology of familial breast cancer with undetected BRCA1 and BRCA2 mutations: clinical implications. Cell Oncol (Dordr) 37(1):1–8. https://doi.org/10.1007/s13402-013-0158-0
11. Cormanique TF, Almeida LE, Rech CA, Rech D, Herrera AC, Panis C (2015) Chronic psychological stress and its impact on the development of aggressive breast cancer. Einstein (Sao Paulo) 13(3):352–356. https://doi.org/10.1590/S1679-45082015AO3344
12. Lee TY, Chen HH, Yeh ML, Li HL, Chou KR (2013) Measuring reliability and validity of a newly developed stress instrument: Newly Diagnosed Breast Cancer Stress Scale. J Clin Nurs 22(17–18):2417–2425. https://doi.org/10.1111/jocn.12107
13. Payne JK (2014) State of the science: stress, inflammation, and cancer. Oncol Nurs Forum 41(5):533–540. https://doi.org/10.1188/14.ONF.533-540
14. Hassan S, Karpova Y, Baiz D, Yancey D, Pullikuth A, Flores A (2013) Behavioral stress accelerates prostate cancer development in mice. J Clin Invest 123(2):874–886. https://doi.org/10.1172/JCI63324
15. Zhao L, Xu J, Liang F, Li A, Zhang Y, Sun J (2015) Effect of chronic psychological stress on liver metastasis of colon cancer in mice. PLoS ONE 10(10):e0139978. https://doi.org/10.1371/journal.pone.0139978
16. Surtees PG, Wainwright NW, Luben RN, Khaw KT, Bingham SA (2010) No evidence that social stress is associated with breast cancer incidence. Breast Cancer Res Treat 120(1):169–174. https://doi.org/10.1007/s10549-009-0454-6
17. Protheroe D, Turvey K, Horgan K, Benson E, Bowers D, House A (1999) Stressful life events and difficulties and onset of breast cancer: case-control study. BMJ 319(7216):1027–1030

18. Kruk K, Aboul-Enein HY (2004) Psychological stress and the risk of breast cancer: a case-control study. Cancer Detect Prev 28(6):399–408. https://doi.org/10.1016/j.cdp.2004.07.009
19. Tas F, Karalar U, Aliustaoglu M, Keskin S, Can G, Cinar FE (2012) The major stressful life events and cancer: stress history and cancer. Med Oncol 29(2):1371–1377. https://doi.org/10.1007/s12032-011-9927-7
20. Ollonen P, Lehtonen J, Eskelinen M (2005) Stressful and adverse life experiences in patients with breast symptoms; a prospective case-control study in Kuopio, Finland. Anticancer Res 25(1B):531–536
21. Kocic B, Filipovic S, Vrbic S, Pejcic I, Rancic N, Cvetanovic A, Milenkovic D (2015) Stressful life events and breast cancer risk: a hospital-based case-control study. J BUON 20(2):487–491
22. Kruk J (2012) Self-reported psychological stress and the risk of breast cancer: a case-control study. Stress 15(2):162–171. https://doi.org/10.3109/10253890.2011.606340
23. Nielsen NR, Grønbaek M (2006) Stress and breast cancer: a systematic update on the current knowledge. Nat Clin Pract Oncol 3(11):612–620. https://doi.org/10.1038/ncponc0652
24. Lin Y, Wang C, Zhong Y, Huang X, Peng L, Shan G, Wang K, Sun Q (2013) Striking life events associated with primary breast cancer susceptibility in women: a meta-analysis study. J Exp Clin Cancer Res 32(1):53. https://doi.org/10.1186/1756-9966-32-53
25. Duijts SF, Zeegers MP, Borne BV (2003) The association between stressful life events and breast cancer risk: a meta-analysis. Int J Cancer 107(6):1023–1029. https://doi.org/10.1002/ijc.11504
26. Antonova L, Aronson K, Mueller CR (2011) Stress and breast cancer: from epidemiology to molecular biology. Breast Cancer Res 13(2):208. https://doi.org/10.1186/bcr2836
27. PRIZMA: preferred reporting items for systematic reviews and meta-analyses. http://www.prisma-statement.org/. Accessed 25 Jan 2019
28. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf. Accessed 28 Jun 2019
29. Hartling L, Hamm M, Milne A, Vandermeer B, Santaguida PL, Ansari M (2012) Validity and Inter-Rater Reliability Testing of Quality Assessment Instruments. Agency for Healthcare Research and Quality (US), Rockville (MD). Report No.: 12-EHC039-EF. https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0077153/. Accessed 23 June 2019
30. Jacobs JR, Bovasso GB (2000) Early and chronic stress and their relation to breast cancer. Psychol Med 30(3):669–678
31. Lillberg K, Verkasalo PK, Kaprio J, Teppo L, Helenius H, Koskenvuo M (2001) Stress of daily activities and risk of breast cancer: a prospective cohort study in Finland. Int J Cancer 91(6):888–893
32. Price MA, Tennant CC, Butow PN, Smith RC, Kennedy SJ, Kossoff MB, Dunn SM (2001) The role of psychosocial factors in the development of breast carcinoma: Part II. Life event stressors, social support, defense style, and emotional control and their interactions. Cancer 91(4):686–689
33. Graham J, Ramirez A, Love S, Richards M, Burgess C (2002) Stressful life experiences and risk of relapse of breast cancer: observational cohort study. BMJ 324(7351):1420
34. Li J, Johansen C, Hansen D, Olsen J (2002) Cancer incidence in parents who lost a child: a nationwide study in Denmark. Cancer 95(10):2237–2242. https://doi.org/10.1002/cncr.10943
35. Lillberg K, Verkasalo PK, Kaprio J, Teppo L, Helenius H, Koskenvuo M (2003) Stressful life events and risk of breast cancer in 10,808 women: a cohort study. Am J Epidemiol 157(5):415–423
36. Helgesson O, Cabrera C, Lapidus L, Bengtsson C, Lissner L (2003) Self-reported stress levels predict subsequent breast cancer in a cohort of Swedish women. Eur J Cancer Prev 12(5):377–381. https://doi.org/10.1097/01.cej.0000090600.09882.60
37. Michael YL, Carlson NE, Chlebowski RT, Aickin M, Weihs KL, Ockene JK, Bowen DJ, Ritenbaugh C (2009) Influence of stressors on breast cancer incidence in the Women's Health Initiative. Health Psychol 28(2):137–146. https://doi.org/10.1037/a0012982
38. Olsen MH, Bidstrup PE, Frederiksen K, Rod NH, Grønbaek M, Dalton SO, Johansen C (2012) Loss of partner and breast cancer prognosis—a population-based study, Denmark, 1994-2010. Br J Cancer 106(9):1560–1563. https://doi.org/10.1038/bjc.2012.96
39. Kennedy B, Valdimarsdóttir U, Sundström K, Sparén P, Lambe M, Fall K, Fang F (2014) Loss of a parent and the risk of cancer in early life: a nationwide cohort study. Cancer Causes Control 25(4):499–506. https://doi.org/10.1007/s10552-014-0352-z
40. Schoemaker MJ, Jones ME, Wright LB, Griffin J, McFadden E, Ashworth A, Swerdlow AJ (2016) Psychological stress, adverse life events and breast cancer incidence: a cohort investigation in 106,000 women in the United Kingdom. Breast Cancer Res 18(1):72. https://doi.org/10.1186/s13058-016-0733-1
41. Palesh O, Butler LD, Koopman C, Giese-Davis J, Carlson R, Spiegel D (2007) Stress history and breast cancer recurrence. J Psychosom Res 63(3):233–239. https://doi.org/10.1016/j.jpsychores.2007.05.012
42. Peled R, Carmil D, Siboni-Samocha O, Shoham-Vardi I (2008) Breast cancer, psychological distress and life events among young women. BMC Cancer 22(8):245. https://doi.org/10.1186/1471-2407-8-245
43. Black AR, Woods-Giscombé C (2012) Applying the Stress and 'Strength' Hypothesis to Black women's breast cancer screening delays. Stress Health 28(5):389–396. https://doi.org/10.1002/smi.2464
44. Glaser R, Kiecolt-Glaser JK (2005) Stress-induced immune dysfunction: implications for health. Nat Rev Immunol 5(3):243–251. https://doi.org/10.1038/nri1571
45. Schernhammer ES, Hankinson SE, Rosner B, Kroenke CH, Willett WC, Colditz GA, Kawachi I (2004) Job stress and breast cancer risk: the nurses' health study. Am J Epidemiol 160(11):1079–1086. https://doi.org/10.1093/aje/kwh327
46. Obeid EI, Conzen SD (2013) The role of adrenergic signaling in breast cancer biology. Cancer Biomark 13(3):161–169. https://doi.org/10.3233/CBM-130347
47. Vajdic CM, van Leeuwen MT (2009) Cancer incidence and risk factors after solid organ transplantation. Int J Cancer 125(8):1747–1754. https://doi.org/10.1002/ijc.24439
48. Adami J, Gäbel H, Lindelöf B, Ekström K, Rydh B, Glimelius B, Ekbom A, Adami HO, Granath F (2003) Cancer risk following organ transplantation: a nationwide cohort study in Sweden. Br J Cancer 89(7):1221–1227. https://doi.org/10.1038/sj.bjc.6601219
49. Dhabhar FS (2014) Effects of stress on immune function: the good, the bad, and the beautiful. Immunol Res 58(2–3):193–210. https://doi.org/10.1007/s12026-014-8517-0
50. Clark SM, Song C, Li X, Keegan AD, Tonelli LH (2019) CD8 + T cells promote cytokine responses to stress. Cytokine 113:256–264. https://doi.org/10.1016/j.cyto.2018.07.015
51. Cheng Y, Jope RS, Beurel E (2015) A pre-conditioning stress accelerates increases in mouse plasma inflammatory cytokines induced by stress. BMC Neurosci 7(16):31. https://doi.org/10.1186/s12868-015-0169-z
52. Steptoe A, Hamer M, Chida Y (2007) The effects of acute psychological stress on circulating inflammatory factors in humans: a review and meta-analysis. Brain Behav Immun 21(7):901–912. https://doi.org/10.1016/j.bbi.2007.03.011
53. McKim DB, Weber MD, Niraula A, Sawicki CM, Liu X, Jarrett BL (2018) Microglial recruitment of IL-1β-producing monocytes to brain endothelium causes stress-induced anxiety. Mol Psychiatry 23(6):1421–1431. https://doi.org/10.1038/mp.2017.64
54. Vinay DS, Ryan EP, Pawelec G, Talib WH, Stagg J, Elkord E et al (2015) Immune evasion in cancer: mechanistic basis and

therapeutic strategies. Semin Cancer Biol 35(Suppl):S185–S198. https://doi.org/10.1016/j.semcancer.2015.03.004
55. King J, Mir H, Singh S (2017) Association of cytokines and chemokines in pathogenesis of breast cancer. Prog Mol Biol Transl Sci 151:113–136. https://doi.org/10.1016/bs.pmbts.2017.07.003
56. Santos MC, Horta BL, Amaral JJ, Fernandes PF, Galvão CM, Fernandes AF (2009) Association between stress and breast cancer in women: a meta-analysis. Cad Saude Publica 25(Suppl 3):S453–S463
57. Petticrew M, Fraser J, Regan MF (1999) Adverse lifeevents and risk of breast cancer: a meta-analysis. Br J Health Psychol 4:1–17
58. Stagl JM, Lechner SC, Carver CS, Bouchard LC, Gudenkauf LM, Jutagir DR (2015) A randomized controlled trial of cognitive-behavioral stress management in breast cancer: survival and recurrence at 11-year follow-up. Breast Cancer Res Treat 154(2):319–328. https://doi.org/10.1007/s10549-015-3626-6
59. Würtzen H, Dalton SO, Christensen J, Andersen KK, Elsass P, Flyger HL (2015) Effect of mindfulness-based stress reduction on somatic symptoms, distress, mindfulness and spiritual wellbeing in women with breast cancer: results of a randomized controlled trial. Acta Oncol 54(5):712–719. https://doi.org/10.3109/0284186X.2014.997371
60. Mojalli M, Karimi Moonaghi H, Khosravan S, Mohammadpure A (2014) Dealing with coronary artery disease in early encountering: a qualitative study. Int Cardiovasc Res J 8(4):166–170