Received: 25 September 2017 | Revised: 5 March 2018 | Accepted: 5 March 2018

DOI: 10.1002/pon.4702

PAPER

WILEY

Sense of coherence is a predictor of survival: A prospective study in women treated for breast cancer

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Funding information
Percy Falk Foundation; Jakob och Johan Söderberg Foundation; Swedish BC Survivor Association (BRO)

Abstract

Objective: Sense of coherence (SOC) reflects a person's overall orientation to life. Sense of coherence guides the person in finding and utilizing resources to maintain health and manage stress. Previously, we demonstrated SOC's stability over time among breast cancer (BC) patients, and in the present article, SOC's predictive value for survival is tested.

Methods: A cohort of 487 women underwent surgery for invasive BC and completed preoperatively the SOC-13 within a multicenter trial. Hazard ratios (HRs) were performed to identify significant independent predictors and their association with increase in SOC.

Results: Over a median follow-up time of 10 years, patients with a higher SOC had 63% lower risk of BC progression (HR 0.63; 95% CI, 0.11 to 0.85, *P* .03), 80% lower risk of BC mortality (HR 0.80; 95% CI, 0.38 to 0.96, *P* .00), and 80% lower risk of all-cause mortality (HR 0.80; 95% CI, 0.47 to 0.93, *P* .00) than patients with a lower SOC. The mortality risk declined by 2.3% for every 1-unit increase in SOC, both for BC mortality (HR 0.98; 95% CI, 0.96 to 0.99, *P* .01) and for all-cause mortality (HR 0.98; 95% CI, 0.96 to 0.99, *P* .00). The risk of progression declined by 1.4% for every 1-unit increase in SOC (HR 0.99; 95% CI, 0.97 to 1.00, *P* .03).

Conclusions: This study provides evidence of SOC's predictive value for disease progression and BC-caused and all-cause mortality. Sense of coherence provides a complement when designing individual plans that aims to support patients during their treatment.

KEYWORDS

breast cancer, cancer, mortality, oncology, progression, sense of coherence, SOC

1 | BACKGROUND

The ability to manage stressful situations has been elaborated by Antonovsky among others. Antonovsky defined a person's sense of coherence (SOC) to be central to this ability to manage stressful situations.[1,2] Sense of coherence reflects a person's overall orientation to life which guides the person in finding and utilizing resources to maintain health especially during times of considerable strain.[1] The concept comprises 3 well-defined interrelated components: comprehensibility, manageability, and meaningfulness, which together contribute to the unity of SOC. Antonovsky hypothesized SOC as being a stable trait and having a stress-buffering effect.[1] Studies confirmed that SOC is rather stable in adult life.[3] A systematic review of Antonovsky's opinion of the SOC construct concurred that a higher degree of SOC was positively related to psychological well-being,[4] less pain and distress,[5] reduced levels of symptom burden,[6] perceived health and mental

well-being after surgery,[7] and quality of life after treatment[8,9] and was a determinant for successful adaptation to stressful situations.[10] Higher SOC has also shown to be associated with a decreased risk of all-cause mortality in population-based studies.[11-13] This was to the best of our knowledge, not studied in relation to breast cancer (BC). The specific aim with this study was to investigate the SOC's predictive value in BC patients regarding disease progression and BC mortality in a 10-year perspective.

2 | METHODS

2.1 | Study inclusion

The present study stems from a multicenter trial with its primary endpoint of subjective and objective assessment of arm morbidity after different types of BC surgeries at the time of introducing the sentinel node biopsy concept, a minimally invasive surgical procedure of the axilla. Four university-affiliated breast units participated in a multicenter trial addressing arm morbidity after different types of axillary surgery.[14,15] The inclusion period was 1999 to 2004, the enrollment was on a consecutive basis, and the median follow-up time for the present study was 10 years (range 8-12 years). The recommended surgical and adjuvant treatment was based on the National and Regional guidelines.[16,17] Eligible patients had primary invasive BC. Exclusion criteria were bilateral BC, previous axillary surgery or clinically fixed axillary metastases, inability mentally or physically to participate in the pre- and postoperative evaluation, or difficulty in understanding the Swedish language. Patients were informed about the study by the surgeon and, after oral informed consent, a research nurse at each center administrated the baseline questionnaires (including the SOC-13) to the patients before surgery. In total, 557 women were included in the multicenter trial. The 487 patients (87%) who answered a complete SOC-13 questionnaire (described below) preoperatively formed the sample of the present study.

2.2 | Data sources

The 13-item SOC scale is a self-assessment questionnaire that consists of 13 items that measure SOC. The questionnaire utilizes a 7-point scale with 2 anchoring responses. Five items are reversed when aggregated to reflect a total SOC score ranging from 13 to 91 points. A higher score indicates a higher degree of SOC. The SOC-13 scale has demonstrated validity and reliability in several cultural contexts. In a recent publication, the stability of the SOC scale over time was assessed and measured at baseline and at follow-up visits up to 3 years postoperatively. This study suggested that SOC was stable over time.[18] A review concluded that SOC changes very little over time.[19] Thus, only 1 point of measurement could be used in the current study.

Demographic data (age, employment, and marital status at surgery) and medical data (type of breast surgery, tumor size, lymph node status, and type of adjuvant treatment given) were collected from medical charts.

Data on disease progression (including first local/regional/distant event) were obtained from the National Cancer Registry[20] and mortality data (including date and cause of death) through the Cause of Death Registry.[21]

Ethical approval from the Regional Ethics Committee was obtained (Dnr 500: 16 979/99, 2011 1916: 32). Written informed consent was not required at the time of the study. All patients were orally informed about the study by the breast surgeon. The patients were also informed that they were free to discontinue their participation at any time, without having to give a reason for this, and that withdrawal would not affect their medical treatment or care. Whenever patients declined participation, they were excluded from further analysis.

2.3 | Statistical methods

The subjects were followed from inclusion to disease progression, and then to death by BC or by all other causes, or to the end of the study, whichever came first. The analyses were performed for each event separately. Progression-free survival was defined as the time elapsing from surgery to progression or death caused by BC. Breast cancer survival was defined as the time elapsing from surgery to death caused by BC. Overall survival was defined as the time elapsing from surgery to death from all other causes. End of follow-up represented a censoring event. The Kaplan-Meier method was used for assessing progression-free survival and survival in 3 equal sized groups of SOC (SOC sum 20-52 low, 53-74 medium, and 75-90 high).

Univariate and multivariate analyses were performed to identify significant independent predictors. We estimated the crude (univariate) and adjusted (multivariate) hazard ratios (HRs and aHRs) associated with 1-unit increase in SOC with Cox proportional-hazard regression. The linearity of the relationship between the log-hazard and SOC was assessed by means of natural cubic spline variables. When introduced in the regression model, the relationship between log-hazard and SOC can be nonlinear. The spline variables were not significant, which indicated that the linear model could represent an adequate approximation. The assumption of proportionality of the hazards was tested by including a time-varying interaction between time and SOC. No evidence of lack of proportionality was detected. The adjusted model included the following significant predictors in the univariate analysis in addition to SOC: age (26-51, 52-57, 58-65, and 66-89 years), married/cohabitant (yes or no), employed (yes or no), breast surgery (sector resection or mastectomy), and axillary lymph node status (positive or negative).

To cross-validate SOC as a predictor, we calculated the recalibration coefficient for the estimates for the hazard ratio associated with 1-unit increase in SOC with a thousand bootstrap samples.[22]

Finally, we estimated the probability of experiencing disease progression, death of BC, and death of all causes within 5 years after inclusion with logistic regression; because no data were censored before this time (ie, follow-up time for the present study was 8-12 years). To evaluate SOC's value as a predictor, we calculated the area under the receiver operating characteristic (ROC) curve (AUC), which summarizes sensitivity and specificity of the predictive model. For all analyses, the statistical software Stata version 14 (Statacorp, College Station, TX) was used.

3 | RESULTS

Demographic and clinical data for the patients (n = 487) are presented in Table 1. The patients' mean age at inclusion was 58.8 years (SD 10.6, range 26-89 years). Most had breast conserving surgery, approximately one-third of the patients were lymph node positive, and most had received postoperative adjuvant therapy. During the follow-up time, 101 disease progression events were observed, with a rate of 0.03 disease progressions/person-year (95% CI, 0.03 to 0.04), 75 BC caused deaths with a mortality rate of 0.02 deaths/person-year (95% CI, 0.01 to 0.02), and a total of 96 deaths with a mortality rate of 0.02 deaths/person-year (95% CI, 0.02 to 0.03).

TABLE 1 Demographic and clinical data of the study sample (n = 487)

Age[a]		
Mean, (SD)		58.8 (10.6)
Range		26-89
	n	%
Married/cohabitants[a]		
Yes	328	67.4
No	159	32.6
Employed[aa]		
Yes	284	58.3
No	203	41.7
Breast surgery		
Breast conserving surgery	354	72.7
Mastectomy	133	27.3
Tumor size (mm)		
≤20	319	65.5
21-50	155	31.8
>50	13	2.7
Lymph node status		
Negative	320	65.7
Positive	167	34.3
Postoperative adjuvant treatment[b]		
Antihormonal treatment		
Yes	378	77.6
No	109	22.4
Chemotherapy		
Yes	183	37.6
No	304	62.4
Radiotherapy		
Yes	409	84.0
No	78	16.0
Disease progression[c]		
No	386	79.3
Yes	101	20.7
Deceased[cc]		
BC	75	15.4
Other reason	21	4.3

[a]At inclusion.

[b]More than one regime could be given.

[c]8 to 12 years.

The mean SOC score, of the study cohort, at baseline was 67.21 (SD 13.4, range 20-90). Disease progression was more prevalent among the patients with the lowest SOC values (SOC sum 20-52). When assessing BC survival and overall survival, outcome was also statistically significantly worse in the group of patients with the lowest SOC values as presented in Figure 1.

The risk of progression and dying during the follow-up time declined as SOC increased. Patients who reported a high SOC (SOC = 90) had a 63% reduced risk of BC progression (HR 0.63; 95% CI, 0.11 to 0.85, *P* .03), a 80% reduced risk of BC caused mortality (HR 0.80; 95% CI, 0.38 to 0.96, *P* .00), and a 80% reduced risk of all-cause mortality (HR 0.80; 95% CI, 0.47 to 0.93, *P*.00) over the 10 years of follow-up compared with those reporting a low SOC (SOC = 20) (Table 2 and Figure 2).

The HR and aHR associated with SOC from the proportional hazard regression as shown in Table 2 revealed that the risk of progression declined by 1.4% for every 1-unit increase in SOC (HR 0.99; 95% CI, 0.97 to 1.00, *P* .03). The association was slightly weaker and became borderline statistically nonsignificant, when adjusted for the significant predictors in the univariate analysis (high age, unmarried/not cohabitant, unemployed, having a mastectomy, and having positive lymph nodes). The adjusted decline was 0.7% (aHR 0.99; 95% CI, 0.98 to 1.01, *P* .29).

The risk of dying (both BC mortality and all-cause mortality) declined by 2.3% for every 1-unit increase in SOC (BC mortality HR 0.98; 95% CI, 0.96 to 0.99, *P* .01 and all-cause mortality HR 0.98; 95% CI, 0.96 to 0.99, *P* .00). The statistically significant association persisted with adjustment for the significant predictors in the univariate analysis. The decline was 1.7% (BC) (aHR 0.98; 95% CI, 0.97 to 1.00, *P* .05) and 1.5% (all-cause) (aHR 0.99; 95% CI, 0.97 to 1.00, *P* .04).

The cross validation of SOC as a predictor was based on 1000 Monte Carlo bootstrap sampling draws, and the recalibrated adjusted coefficient was 0.99 indicating acceptably low over-optimism in the coefficient estimates.

In ROC analyses including SOC as the only predictor for the probability of progression-free survival and surviving 5 years, the AUC for progression-free survival was 0.58 (95% CI, 0.51 to 0.65). With a cut-off value of SOC = 70, sensitivity and specificity were 50.2% and 58.4%, respectively. The AUC for BC and overall survival was 0.61 (95% CI, 0.52 to 0.70). With a cut-off value of SOC = 70, sensitivity and specificity were 50.0% and 62.2%, respectively.

To quantify the predictive value of SOC per se, we excluded SOC but included all the other predictors listed in Table 2 in the multivariate analysis. We found that when SOC is included, the risk for progression in 6.8% of the patients (95% CI, 4.7% to 9.4%) would be classified more accurately. Likewise, having SOC included in the analysis showed a more accurate risk classification: both for the risk of BC caused mortality in 23.8% (95% CI, 20.1% to 27.9%) and that of the risk of all-cause mortality in 17.5% (95% CI, 14.2% to 21.1%) of the patients.

4 | DISCUSSION

A higher SOC, when explained as a single predictor, showed an 80% reduced risk of BC-related mortality, and all-cause mortality.

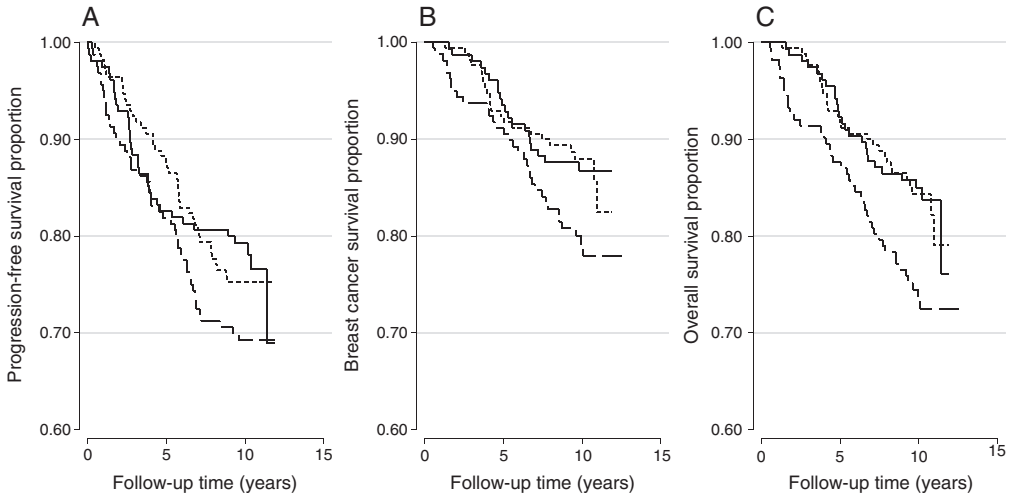

FIGURE 1 Kaplan-Meier survival curves for (A) progression-free survival, (B) breast cancer survival, and (C) overall survival, by 3 groups of sense of coherence: 20 to 52 (long dash), 53 to 74 (short dash), and 75 to 90 (solid line)

TABLE 2 Estimated crude (univariable model) and adjusted (multivariable model) hazard ratios and 95% confidence intervals associated with 1-unit increase in sense of coeherence for progression-free survival, breast cancer survival, and overall survival

	Progression-Free Survival			Breast Cancer Survival			Overall Survival		
Univariable		**(95% CI)**	***P* Value**		**(95% CI)**	***P* Value**		**(95% CI)**	***P* Value**
SOC	0.99	(0.97-1.00)	.03	0.98	(0.96-0.99)	.01	0.98	(0.96-0.99)	.00
Multivariable									
SOC	0.99	(0.98-1.01)	.29	0.98	(0.97-1.00)	.05	0.99	(0.97-1.00)	.04
Age (years)									
26 to 51	1.00			1.00			1.00		
52 to 57	0.76	(0.44-1.31)	.32	1.24	(0.59-2.57)	.57	1.29	(0.67-2.48)	.45
58 to 65	0.86	(0.52-1.44)	.57	1.37	(0.69-2.71)	.37	1.19	(0.63-2.25)	.59
66 to 89	1.03	(0.63-1.71)	.89	1.38	(0.68-2.79)	.37	1.54	(0.83-2.85)	.17
Married/cohabitant									
Yes	1.00			1.00			1.00		
No	1.46	(1.02-2.09)	.04	1.45	(0.91-2.32)	.12	1.64	(1.09-2.48)	0.02
Employed									
Yes	1.00			1.00			1.00		
No	1.92	(1.32-2.79)	.00	1.82	(1.12-2.95)	.02	2.25	(1.45-3.47)	0.00
Breast surgery									
Breast conserving surgery	1.00			1.00			1.00		
Mastectomy	1.23	(0.84-1.81)	.30	1.76	(1.09-2.84)	.02	1.40	(0.90-2.17)	.13
Lymph node status									
Positive	1.65	(1.14-2.38)	.01	2.05	(1.27-3.31)	.00	1.74	(1.14-2.66)	.01
Negative	1.00			1.00			1.00		

95% Confidence intervals in brackets.

Moreover, a higher SOC showed a 63% reduced risk of disease progression. The results support the importance of SOC in predicting mortality and progression as being independent of, and often stronger than, several other tumor and treatment variables.

Our results are in line with the population-based studies that have reported higher SOC to be associated with a decreased risk of all-cause mortality.[11-13] Poppius et al[23] found after adjustment for potential cofounders an increased overall cancer incidence in a cohort of 5800 men with low SOC, which led to the assumption that a high SOC could putatively delay cancer onset. When SOC's predictive value for overall cancer mortality was studied, a higher SOC was associated with a 30% reduced cancer mortality in men.[24]

Even though the studies are countable, they indicate that increasing SOC seems to have a protective role in how people manage life strain. Haukkla et al[25] showed that the association between higher SOC and a lower risk of all-cause mortality became non-significant after adjustment for depressive symptoms. The question of whether the concepts of SOC and mental health are closely

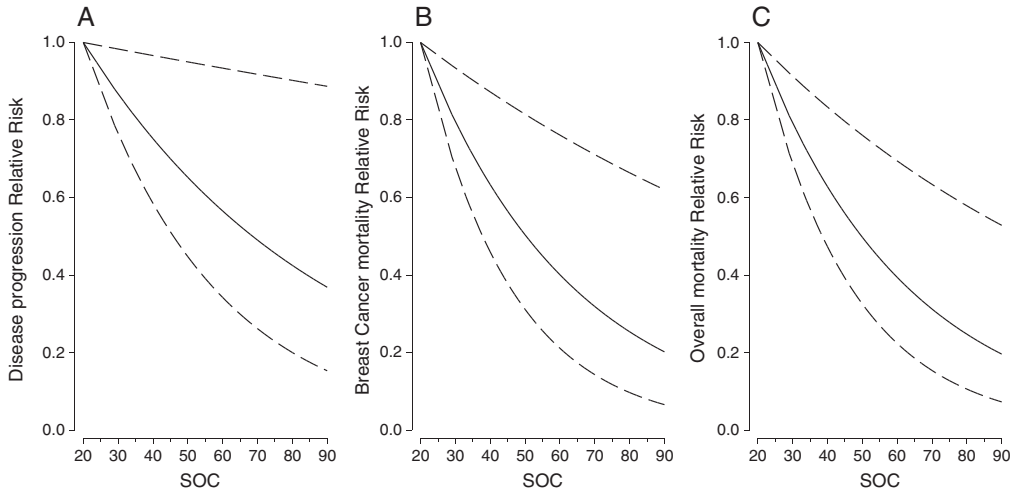

FIGURE 2 Estimated relative risk (solid line) and 95% confidence intervals (dashed lines) of (A) disease progression, (B) breast cancer mortality, and (C) overall mortality

interrelated has been raised, but studies indicate that, although interrelated, they can be considered as independent concepts.[26,27] Previous studies support that SOC is implicated in successful coping with life stress, anxiety, and depression.[28,29] Furthermore, SOC mediated how patients with BC rated their emotional distress before and 6 months after treatment.[8] The ability to manage stressful life experiences according to Antonovsky is stronger in individuals with a higher SOC.[1] In our study, a clear cut-off was seen between those patients with the lowest SOC values (SOC sum 20-52) and the rest of the cohort. A link between low SOC and increased mortality may coincide with how they cope with disease and treatment. A systematic review concluded that despite proven clinical efficacy of adjuvant hormonal therapy, many BC patients fail to adhere to or persist in long-term treatment.[30] One could speculate whether patients with low SOC may be overrepresented among the noncompliers. Patients with a low SOC may not understand the need of the hormonal treatment (comprehensibility), do not have tools or support enough to handle side effects (manageability), and/or do not have enough motivation (meaningfulness) to adhere with the hormonal therapy because of severe side effects. Therefore, considering each patient's SOC during the first clinical patient appointment could provide a complement when designing individual plans that aims to support patients during their treatment. Measurements of SOC are stable and therefore valid. Baseline measurements as shown by our previous studies and by others can be safely used.[18,19]

The strengths of the study are the clinical setting, the large cohort size, the long follow-up time (10-year median), and the reliability of registers[31] (the National Cancer Registry[20] and Cause of Death Registry[21]) used. The sample is representative regarding age, tumor stage, and treatment according to the Regional BC Registers[32] from each region at time of inclusion and is also representative regarding BC mortality in Sweden.[33] The mean values of SOC in this study are comparable to other studies that include women with BC.[10] Of the 557 included in the multicenter trial, available demographic (age, employment, and marital status at surgery), and medical baseline data (type of breast surgery, tumor size, lymph node status, and type of adjuvant treatment given) did not differ between responders and no responders of the SOC scale.

5 | CONCLUSIONS

Our study provides evidence of SOC's predictive value for disease progression, BC-caused mortality, and for all-cause mortality among women with BC. Sense of coherence provides a complement when designing individual plans that aims to support patients during their treatment.

5.1 | Study limitations

Some limitations should be mentioned. At the time of inclusion, clinical practice was more focused on prognostic rather than on treatment predictive markers, and only hormonal therapy for estrogen receptor positive tumors were used as predictive markers. To what extent that information may have had an impact on treatment decisions, disease progression, and survival for the included patients remains unclear. Although our previous results confirm SOC's stability over a 3-year period,[18] knowledge of how reproducible our results would be in another patient population with more advanced disease needs further evaluation. Although statistically, these data are robust, a larger sample size might have strengthened the results.

There may be other unmeasured confounding factors, which we did not control for, for example, comorbidity, such as depression or unaccounted psychosocial variables. However, SOC is considered to reflect successful coping with stressful situations.[10]

5.2 | Clinical implications

Considering every patient's level of SOC during the initial planning and during follow-up could be of support to better individualize patient care and treatment. For example, patients with low SOC at diagnosis

might benefit from additional support from health-care providers to handle symptoms that are disease or treatment related to reduce morbidity, enhance health related quality of life, and in the long-term prolong survival. A future study targeting this could give us more strength to our findings.

ACKNOWLEDGEMENTS

The study was supported by the Swedish BC Survivor Association (BRO), Jakob och Johan Söderberg Foundation, and Percy Falk Foundation, Sweden. The authors acknowledge the following who participated in the initial planning, recruitment of patients, and data collection: Leif Bergkvist, Li Bjelkebo, Lena Boman Engqvist, Yvonne Brandberg, Fuat Celebiuglo, Staffan Eriksson, Inga-Lill Fredriksson, Jan Frisell, Göran Liljegren, and Viveca Åberg.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

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How to cite this article: Lindblad C, Langius-Eklöf A, Petersson L-M, Sackey H, Bottai M, Sandelin K. Sense of coherence is a predictor of survival: A prospective study in women treated for breast cancer. *Psycho-Oncology*. 2018;27:1615–1621. https://doi.org/10.1002/pon.4702