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Mols, F.; Vingerhoets, A.J.J.M.; Coebergh, J.W.W.; van de Poll-Franse, L.V.

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Review

Quality of life among long-term breast cancer survivors: A systematic review

Floortje Mols^{a,b,*}, Ad J.J.M. Vingerhoets^b, Jan Willem Coebergh^{a,c},
Lonneke V. van de Poll-Franse^a

^a Comprehensive Cancer Centre South (IKZ), Eindhoven Cancer Registry, P.O. Box 231, 5600 AE Eindhoven, The Netherlands

^b Tilburg University, Department of Psychology and Health, Tilburg, The Netherlands

^c Department of Public Health, Erasmus University Medical Centre, Rotterdam, The Netherlands

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Abstract

The aim of this study was to review the literature on quality of life among long-term survivors of breast cancer and identify the specific aspects of quality of life that were affected in these survivors. We also describe predictors of quality of life. Published research reports were included if they described the quality of life of breast cancer survivors diagnosed at least five years earlier. The methodological quality of the 10 selected studies, conducted between 1997 and 2004, was high according to a list of predefined criteria. Most studies reported that long-term survivors of breast cancer experienced good overall quality of life. However, almost all studies reported that breast cancer survivors experienced some specific problems (*e.g.*, a thick and painful arm and problems with sexual functioning). The current medical condition, amount of social support and current income level were strong positive predictors of quality of life, and the use of adjuvant chemotherapy emerged as a negative predictor. More research on the specific medical and psychosocial needs of survivors is needed in order to be able to design appropriate intervention studies. If anything, this review shows that focusing on the long-term effects of breast cancer is important when evaluating the full extent of cancer treatment.

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Keywords: Breast cancer; Long-term survivors; Quality of life; Well-being

1. Introduction

Breast cancer is the most prevalent malignancy among women in the industrialized world. One out of every nine women will ultimately be diagnosed with breast cancer in the USA before the age of 85 [1], while this figure is 1 in 11 in Europe. The prevalence of breast cancer rises markedly with age from 3–4% at age 50–69 to 6% of women older than 70 [2]. The number of long-term survivors, defined by the American Cancer Society as every person who is still alive 5 years after diagnosis [1], is increasing rapidly due to the growing rates of

detection and incidence; the marked increase in the number and proportion of elderly; and improved survival [2,3]. This is in part also due to advances in cancer treatment. The relative survival of women with breast cancer at five years after initial diagnosis is now 86% [4]. All in all, this has led to increasing numbers of individuals who are either cured of their cancer or are living with it as a chronic disease [5].

The increasing numbers of long-term breast cancer survivors urge the examination of the long-term effects of breast cancer and specific treatments. The latter may need to be adapted in case of severe long-term side effects. In addition, specific medical and psychosocial needs of survivors should be assessed to be able to optimise aftercare. The goal of this review was to identify

* Corresponding author. Tel.: +40 2971616; fax: +40 2971610.

E-mail address: Research@ikz.nl (F. Mols).

the specific aspects of quality of life that were affected in long-term breast cancer survivors, and to identify predictors. We reviewed the literature on well-being of breast cancer survivors in a systematic way.

2. Methods

2.1. Search strategy

A computerised search of the literature was performed in Pubmed and PsychINFO from 1960 to May 2004. The term ‘breast cancer’ was used in combination with other key terms: survivors, long-term, quality of life, QoL, health-related quality of life, HRQoL, well-being. The reference lists of all identified publications were checked to retrieve other relevant publications, which were not identified by means of the computerised search.

2.2. Selection criteria

Studies were included if they described aspects of the quality of life in long-term breast cancer survivors. The search was limited to English, German and Dutch language studies. Studies that involved a variety of tumours were excluded. The American Cancer Society’s definition of long-term survival was used [1]; studies of survivors of less than five years after initial diagnosis were excluded. Quality of life had to be measured with a standardised or valid questionnaire. Studies not published in peer-reviewed journals were not taken into account.

The described inclusion criteria were applied to our initial 288 hits. Sixty-one articles met our criteria, but this selection was based on abstracts and titles of reviews and research articles only. The 61 selected studies were conducted between 1989 and 2004. Hard copies were ob-

tained of all studies. After inspection 10 articles fulfilled our selection criteria and were included in this review [6–15]. The flow chart of study selection is shown in Fig. 1.

2.3. Quality assessment

Two investigators (Mols and Vingerhoets) assessed the methodological quality of each of the 10 selected studies using a 14-item standardised checklist of predefined criteria. The checklist was a modified version of an established criteria list for systematic reviews [16–18]. The criteria are presented in Table 1.

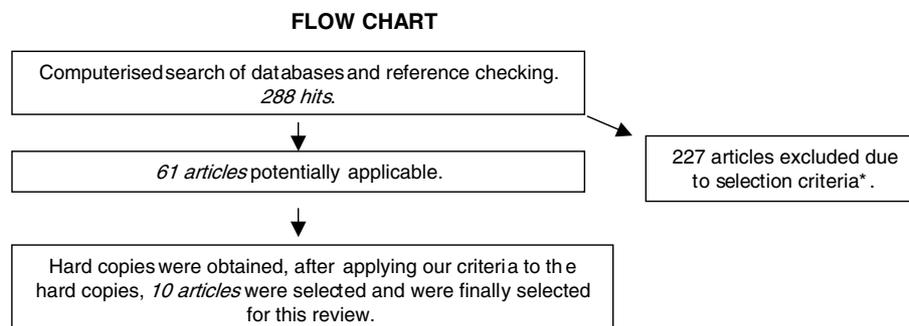
Each item of a selected study, which met our criteria, was assigned one point. If an item did not meet our criteria or was described insufficiently or not at all, zero points were assigned. The highest possible score was thus 14. Studies scoring 75% or more of the maximum attainable score (*i.e.* ≥ 10 points) were arbitrarily considered to be of ‘high quality’. Studies scoring between 50% and 75% were rated as ‘moderate quality’. Studies scoring lower than 50% were considered ‘low quality’.

Findings were considered consistent if $\geq 75\%$ of the studies that investigated a factor showed the same direction of the association. In Table 2, we defined five levels of evidence [19].

3. Results

3.1. Study characteristics

In total, 10 studies were included, all published after 1996. All but two [7,11] were conducted in the USA. The main findings are summarised in Table 3. Quality of life was a primary endpoint in all studies. Four studies compared the quality of life between breast cancer survivors and the general population [6,7,10,11]. Two studies



*Selection criteria:

1. Quality of life had to be a primary endpoint of the study.
2. Patients had to be alive at least five years after diagnosis.
3. Only breast cancer was selected; Studies of different tumours were excluded.
4. Study had to be published in a peer-reviewed journal.
5. Article had to be in English, German or Dutch language.

Fig. 1. Flow diagram of papers accepted and rejected during selection procedure.

Table 1
Criteria list for assessing the methodological quality of studies on quality of life among long-term breast cancer survivors

Positive if;	
A.	Socio-demographic and medical data is described (e.g., age, race, employment status, educational status, tumour stage at diagnosis etc.)
B.	Inclusion and/or exclusion criteria are formulated
C.	The process of data collection is described (e.g., interview or self-report etc.)
D.	The type of cancer treatment is described
E.	The results are compared between two groups or more (e.g., healthy population, groups with different cancer treatment or age, comparison with time at diagnosis etc.)
F.	Mean or median and range or standard deviation of time since diagnosis or treatment is given
G.	Participation and response rates for patient groups have to be described and have to be more than 75%
H.	Information is presented about patient/disease characteristics of responders and non-responders or if there is no selective response
I.	A standardized or valid quality of life questionnaire is used
J.	Results are not only described for quality of life but also for the physical, psychological and social domain
K.	Mean, median, standard deviations or percentages are reported for the most important outcome measures
L.	An attempt is made to find a set of determinants with the highest prognostic value
M.	Patient signed an informed consent form before study participation
N.	The degree of selection of the patient sample is described

Table 2
Levels of evidence

Strong	Consistent findings (≥75%) in at least 2 high quality studies
Moderate	Consistent findings (≥75%) in one high quality study and at least one low quality study
Weak	Findings of one high quality study or consistent findings (≥75%) in at least 3 or more low quality studies
Inconclusive	Inconsistent findings, or less than 3 low quality studies available
No evidence	No data presented

examined the quality of life between breast cancer survivors diagnosed at different ages [8,12]. In addition, one study specifically examined the role of ethnicity [9]; another study focused on the impact of primary treatment on survivors [13]; and two studies compared the quality of life at diagnosis and follow-up [14,15]. The time since diagnosis ranged between 5 and 23 years, 2169 survivors and 558 controls were included and the Rand SF-36 (also known as the MOS-SF 36) was the most frequently used assessment of quality of life.

3.2. Methodological quality

The evaluation of the methodological quality of the 10 studies by the two reviewers yielded the following re-

Table 3
Predictors

Possible predictors	Strong evidence	Weak evidence	Inconclusive evidence
Chemotherapy	X		
Medical condition	X		
Social support	X		
Income	X		
Employment status		X	
No children under age 18 at home		X	
Ethnicity		X	
Trait anxiety		X	
State anxiety		X	
Health perceptions		X	
Life stress		X	
Belief that the world is controllable		X	
Purpose		X	
Age at diagnosis			X
Current marital status			X
Time since diagnosis			X
Stage of disease			X

sults. On eight items, there was disagreement between the reviewers, mostly due to differences in interpretation. Item ‘L’ of Table 1, which represents an attempt to find a set of determinants with the highest prognostic value, yielded the most disagreements. These were solved through discussion in a consensus meeting.

The quality scores are shown in Table 4. They range from 10 to 14 points. The mean quality score was 11.4. All 10 studies attained scores above 75% of the maximum score. Methodological shortcomings concerned mainly the response rate and the lack of information on characteristics of non-responders.

3.3. Quality of life

In most studies, breast cancer survivors reported a good quality of life [14]. Physical and emotional well-being appeared to be excellent [15]. Scores on the CARES-SF global, physical, medical, psychosocial and marital subscales were all below 1, indicating that there were almost no problems in these areas [9]. In two studies, the quality of life of survivors and controls was almost similar [7,10]. Women who had survived longer after diagnosis of breast cancer reported better overall quality of life and better psychological and social well-being than women with fewer years of survival [9].

Other studies revealed problems in long-term survivors. Long-term survivors reported a lesser physical, psychological and general quality of life than the control group [6,11]. Survivors reported a lesser physical functioning than controls, but this did not affect their daily activities [10]. Survivors also reported a higher prevalence of symptoms of mild to moderate depression than

Table 4
Overview of studies on quality of life among long-term breast cancer survivors

Study	Study quality ^a	Participants	Age (yrs)	Time since diagnosis in years	Design	Population	Quality of life instruments	General conclusions
Weitzner (1997) [7]	10	60 survivors 93 controls	Mean = 53.8 (s.d. 8.8)	>5	Comparison	Selected	Ferrans and powers QoL index	Survivors exhibited a lower QoL than controls
Dorval (1998) [8]	11	124 survivors 262 controls	18% 30–49 26% 50–59 32% 60–69 25% 70–89	Mean = 8.8 (range 7.8–9.3)	Comparison	Unselected	A combination of different questionnaires	QoL of survivors and controls was the same, but survivors reported sexual problems and arm problems
Ferrell (1998) [9]	10	298 survivors	Mean = 58 (range 30–93)	Mean = 100 months Median = 75 months	Comparison	Unselected	QoL-breast cancer version	Survivors >60 had a better QoL than younger women
Ashing-Giwa (1999) [10]	12	117 African-American 161 white	Mean = 63.6 (range 32–90)	Mean = 7 (range 6–8)	Comparison	Unselected	Rand-SF-36 CARES Ladder of life	Survivors report a good health-related QoL, no ethnical differences
Ganz (2002) [16]	13	763 survivors	Mean = 55.6	Mean = 6.3 (range 5.0–9.5)	Follow-up study	Unselected	Rand-SF-36 CARES Ladder of life	High levels of functioning and QoL, systemic adjuvant treatment = lower functioning
Tomich and Helgeson (2002) [11]	10	164 survivors 164 controls	Mean = 54.4 (range 33–81)	5.5	Comparison	Selected	MOS-SF-36	QoL of survivors and controls was largely the same
Amir and Ramati (2002) [12]	14	39 survivors 39 controls	Mean = 50.42 (range 37–60)	>5	Comparison	Unselected	WHOQOL-Bref	Survivors exhibited a lower QoL than controls
Cimprich (2002) [13]	13	105 survivors	Mean = 65.5	Mean = 11.5	Cross-sectional study	Unselected	QoL-CS	Age at diagnosis and years of survival are predictors of QOL
Kornblith (2003) [14]	10	153 survivors	Mean = 65 (range 41–87)	Mean = 18 (range 15–23)	Cross-sectional study	Selected	EORTC-QLQ-C30	Impact on survivor QoL was minimal 20 years after treatment
Bloom (2004) [15]	11	185 survivors	Median 50 at follow-up	5	Follow-up study	Unselected	MOS-SF-36	QoL after 5 years was better than QoL at diagnosis

^a The second column represents 'study quality'. Each item of a selected study, which met our criteria, was assigned one point. If an item did not meet our criteria, was described insufficiently, or not at all, zero points were assigned. The highest possible score was thus 14. Studies scoring 75% or more of the maximum attainable score (*i.e.* ≥ 10 points) were arbitrarily considered to be of 'high quality'. Studies scoring between 50% and 75% were rated as moderate quality. Studies scoring lower than 50% were considered as low quality.

healthy controls; these depression scores predict a lower quality of life in all areas except family functioning. Cancer had negative effects on other domains of life as well. Survivors reported arm problems [7] and 51% of survivors still experienced pain [8]. Several studies revealed that sexual functioning was problematic [7,9,12–15]. Hormonal changes and menopausal symptoms, such as hot flashes and vaginal dryness, are the main causes of these problems in sexual functioning. One study stated that 29% of breast cancer survivors in their study had reported sexual problems [13]. Another study reported that 69% of women with partners were sexually active, but many of these women reported sexual problems, including lack of desire (56%), difficulty with arousal (46%), less enjoyment (35%), or no orgasm (38%) [14].

3.4. Predictors of quality of life

The predictive value of the socio-demographic variables as well as disease and treatment characteristics for quality of life was determined. More specifically, demographic (age, education, ethnicity, income, employment), social (social support, marital status, children living at home), psychological (stress, anxiety, belief that the world is controllable, purpose) and disease variables (general health, stage of disease, years since diagnosis, health perceptions, chemotherapy and medical condition) were investigated. Some factors were examined in several studies, others in just one. The levels of evidence are described in Table 2. The predictors of quality of life, described below in order of level of evidence, are listed in Table 3.

3.4.1. Strong evidence

Strong evidence was found for the predictive value of chemotherapy, medical condition, social support and income for quality of life. Past chemotherapy is a statistically significant predictor of a poor current quality of life [15]. Women who received chemotherapy are also at risk for a post-traumatic stress syndrome and thus a lower quality of life experience [11]. In contrast, a greater increase in physical quality of life since treatment was associated with chemotherapy [14]. Medical condition (*i.e.* co-morbidity) at the time of the examination also appeared to be a strong predictor of quality of life. A patient who suffers from other medical conditions in addition to cancer experiences a lower quality of life [9,14,15].

A third important predictor of quality of life is social support, defined as the number of social contacts and the amount of social involvement with friends and family [15]. A greater increase in quality of life in the years after diagnosis was associated with a smaller decrease in emotional support from family and friends in those years [14]. Finally, income emerged as a predictor in

two American studies, a higher income being associated with a better quality of life [9,15].

3.4.2. Weak evidence

Weak evidence was found for the predictive value of employment status, no children under age 18 living at home, ethnicity (Euro-American, African-American, Latino, Asian or other), trait anxiety, state anxiety, health perceptions, life stress, the ‘belief that the world is controllable’ and ‘purpose’. These variables were investigated only once in the selected studies, implying that at best only weak evidence was available. At least part-time employment and having no children under age 18 living at home predicted a greater increase in physical quality of life [14]. Ethnicity was not a predictor of quality of life [9]. Trait anxiety, which represents a long-standing personality feature, was the most consistent predictor of quality of life in one study [6] in contrast to state anxiety. Breast cancer survivors with better health perceptions and survivors who experience less life stress reported a better quality of life [9]. The ‘belief that the world is controllable’ predicted physical functioning scores and ‘purpose’ predicted mental functioning scores on the SF-36 [10].

3.4.3. Inconclusive evidence

Inconclusive evidence was found for age at diagnosis, current marital status, time since diagnosis and stage of disease. Four population-based studies identified age as a predictor of quality of life [8,12,14,15], one study found no relation between age and quality of life [9]. Age was a predictor of scores on the general health scale of the Rand SF-36 [15]. Young women who survived breast cancer without recurrence and without the development of other forms of cancer improved in both their physical and mental well-being compared to their well-being at diagnosis [14]. Women who were diagnosed at a higher age (>65) reported a lower quality of life outcome in the physical domain [12], whereas in another study women over age 60 reported a better physical well-being than younger women [8]. A fifth study found that age was not a predictor of quality of life [9].

Evidence about education is also inconclusive. A higher quality of life seems to prevail among survivors with a higher educational achievement [9], but educational level was inversely correlated with total quality of life scores in another study [12]. In addition, a third study revealed that educational level did not influence ratings of quality of life among breast cancer survivors [15].

Current marital status is another inconclusive predictor of quality of life. It was found to be associated with better physical well-being [12] and survivors who had a partner and a shared living situation (not living alone) reported a better quality of life [9], but a third study

failed to find any association between quality of life and marital status [15].

Inconclusive evidence also applies with respect to time since diagnosis. Time since diagnosis did not influence quality of life in two studies [9,15], but a third study showed that the number of survival years was significant as a predictor of quality of life [12]. Women with more years of survival after diagnosis of breast cancer reported better overall quality of life and better psychological and social well-being than women with fewer years of survival [12].

The predictive value of stage of disease was investigated twice in the selected studies. One study found that stage of disease was predictive of quality of life in the health/functioning domain. Stage III survivors appeared to have a lower quality of life than other survivors [6]. This result can be explained by the fact that these patients are in an advanced stage of disease and thus experience more symptoms. Moreover, it is well known that stage is associated with chemotherapy and past chemotherapy was a statistically significant predictor of a poor current quality of life [15]. In contrast, a second study found that women with a low stage of disease were significantly more likely to suffer from a post-traumatic stress syndrome, which by definition is associated with more distress and a lower quality of life [11].

4. Discussion

This systematic review summarises the results of 10 studies on the quality of life of long-term survivors of breast cancer (*i.e.* >5 years). Most studies reported that long-term survivors of breast cancer experienced good overall quality of life. In general, it can be concluded that survivors with a high quality of life are probably those who did not need chemotherapy; who have no comorbid diseases; who received sufficient emotional support from family and friends; and who had a relatively high income. If the survivor is also employed at least part-time; has no children under 18 living at home; enjoys a feeling of good health; experiences little life stress; believes that the world is controllable; and that she has a purpose in life, then the chance that she experiences good quality of life gets even better. The role of other variables is less clear. Age, education, marital status, years since diagnosis and stage of disease, for example, predict quality of life in some studies but not in others.

In spite of the fact that the quality of life for long-term survivors is relatively good, there is no doubt that many survivors still experience substantial complaints as a result of the cancer or its treatment. Most frequently mentioned are sexual problems and a painful/swollen arm. These complaints can be caused by many factors, some of which are known, others are not yet uncovered

or are based on weak evidence. With the implementation of new or adjusted treatments, new problematic side-effects can arise [20]. Since the group of breast cancer survivors will only continue to increase over the next few decades due to the demographic age-shift, with populations living longer and many new developments being made in breast cancer therapy [21], it will be necessary to monitor survivors in order to identify possible negative long-term effects.

If we chose to perform more research in this area, it is important that high demands be made on the quality of the new studies. The inclusion of a reference group of equally aged individuals without cancer drawn from the general population is very important. Furthermore, the selection of an appropriate quality of life questionnaire is essential. In addition there is the question about the difference between ‘real’ quality of life measures, (such as the WHO-QOL), which stress the contentment of the patient with several aspects of her life, and instruments (like the RAND SF-36) which merely focus on functional health status. Moreover, there are both advantages and disadvantages in applying generic measures *versus* disease specific instruments. Standardisation of the use of assessments might be essential for adequate evaluation and mutual comparison of studies. Data on demographical factors and information about health status of survivors should also be collected in order to establish their predictive value. These recommendations seem to be logical but in daily practice it appears that these obvious recommendations for good research are still not always applied.

The results described in this review were partially inconclusive, even though all studies included in this review were of high quality. By the implementation of additional qualitatively good studies, more clarity with respect to the quality of life of breast cancer survivors could possibly be achieved. In the mean time, we can implement new strategies with the knowledge we have already gained. We know that medical condition (*i.e.* co-morbidity), chemotherapy, social support and income are important predictors of quality of life. Extra attention is, therefore, warranted for women with a poor medical condition. As far as chemotherapy is concerned this finding might imply that we need to be more reluctant about broadening the indications for this aggressive systemic therapy [20] because of the possible negative side-effects that can last for years. Offering better social support to women with breast cancer can possibly change social support. Psychosocial intervention projects [22] resulted in both short and long-term good results for breast cancer patients. This not only improved quality of life but also reduces health care billings by 24% compared with women who did not attend psychosocial intervention projects. A low income cannot be influenced easily. Generally, solutions should be found in broad health care insurance and better access

to health care, of course, only in countries where this is a real problem, as in the US.

If anything, this review shows that focusing on the long-term effects of breast cancer is important when evaluating the full extent of cancer treatment.

Conflict of interest statement

None declared.

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