

BMJ Open Quality of life in patients with breast cancer with neoadjuvant chemotherapy: a systematic review

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ABSTRACT

Objectives The aims of this systematic review were to assess the impact of neoadjuvant chemotherapy (NAC) on breast cancer (BC) patients' quality of life (QOL), to compare the different regimens of NAC on BC patients' QOL, to compare NAC versus adjuvant chemotherapy on BC patients' QOL and to identify predictors of QOL on patients with BC receiving NAC.

Design The design used Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Data sources Cinahl, Embase, Pubmed, Scopus, Web of Science, Cochrane library and PsycINFO were searched through 27 December 2021.

Eligibility criteria for selecting studies The inclusion criteria were included: patients with BC receiving NAC, outcome measures related to QOL and published in English. The exclusion criteria were included: duplicates or overlapping participants, not original research, data or full text not available and qualitative study.

Data extraction and synthesis Two independent reviewers used standardised methods to search, screen and code included studies. The risk of bias in individual studies was evaluated with Cochrane collaboration's tool for assessing risk bias, Newcastle Ottawa Score or Joanna Briggs Institute Critical Appraisal tool. This systematic review performs narrative synthesis based on several different themes.

Results The initial search resulted in 2994 studies; 12 of these studies fulfilled inclusion criteria. There was no significant difference in the QOL of BC before and after NAC, but patients experienced adverse reactions and depression during chemotherapy. Different regimens of NAC have different effects on patients' QOL. Patients with NAC had more severe physical discomfort than those with adjuvant chemotherapy. However, BC patients' QOL can be improved by intervening on social or family support, and these predictors, including chronotype, QOL before NAC and depression.

Conclusions More original research is needed in future to understand the profile and predictors of QOL in patients with BC on NAC, which will help clinicians and patients make decisions and deal with NAC-related issues.

INTRODUCTION

Breast cancer (BC) is the most common disease in women worldwide, with the prevalence now surpassing lung cancer as the leading global cancer incidence in women in

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This systematic review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.
- ⇒ Our information sources were 7 research databases from inception through 27 December 2021.
- ⇒ This review included studies published in the English language only.

2020, with 11.7% of all new cases (2.3 million); and it is the fifth leading cause of cancer deaths worldwide, accounting for 6.9%.¹ Treatment of BC usually consists of two parts: local surgical treatment and systemic treatment; systemic treatment can precede surgical treatment (neoadjuvant) or follow it (adjuvant).² Neoadjuvant chemotherapy (NAC) is used in patients with locally advanced BC or inoperable BC to improve the likelihood of breast-conserving surgery by reducing the size of the tumour in the past. Current studies have shown that NAC can also be used in the treatment of patients with early-stage operable BC to improve cosmetic outcomes and reduce postoperative complications, such as lymphoedema and prolong survival.^{3–5} NAC is associated with improved survival compared with adjuvant chemotherapy in patients with triple-negative BC only after complete pathologic response,⁶ and the same effect has been observed in other cancers like bladder cancer and colon cancer.^{7,8} NAC is widely used, while more and more scholars are studying the survival outcomes of patients after NAC, such as pathologic complete response, disease-free survival and overall survival.^{4,9}

However, the goals of cancer treatment should include not only survival outcomes but also quality of life (QOL), which is an important outcome measure in clinical investigations and survival studies in BC.^{10–12} Now, the treatment regimens of BC are numerous and effective, but the side effects associated with different treatment modalities and the impact on QOL are different. So, optimal



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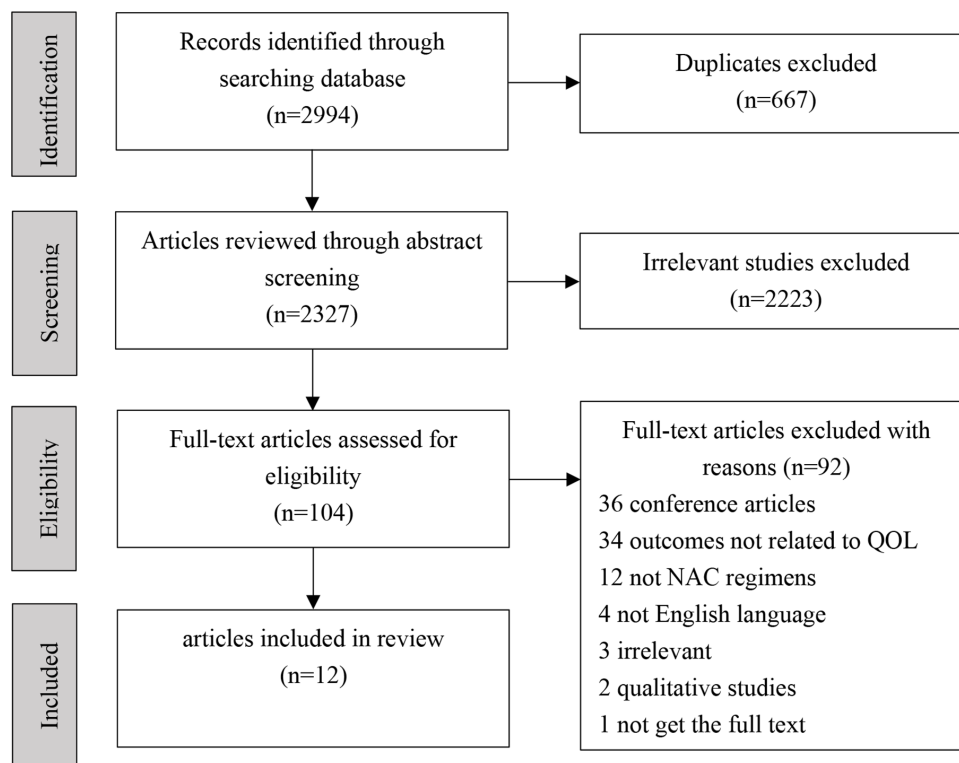


Figure 1 Flow chart for systematic review methodology as per PRISMA guidelines. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

stratification and ranking of treatment strategies should focus on individual risk profiles as well as QOL.¹³ Meanwhile, QOL is a major factor in treatment decisions for advanced or metastatic disease.¹⁴ It is worthwhile to consider the choice of an effective, least toxic anticancer treatment before implementing definitive therapy. Therefore, studying the QOL of NAC patients and comparing it to other treatments can help patients and clinicians make decisions.

The aims of this systematic review were (1) to assess the impact of NAC on BC patients' QOL, (2) to compare the different regimens of NAC on BC patients' QOL, (3) to compare NAC vs adjuvant chemotherapy on BC patients' QOL and (4) to identify predictors of QOL on patients with BC receiving NAC.

METHODS

We primarily followed the Joanna Briggs Institute guidelines¹⁵ on systematic reviews and we used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement¹⁶ (figure 1).

Search strategy

A systematic search of the following databases was performed: CINAHL, Embase, Pubmed, Scopus, Web of Science, Cochrane library and PsycINFO. The final search was in December 2021. Three categories of terms were searched: (1) BC, (2) NAC and (3) QOL. In PubMed and Cochrane library, medical subject headings were used (breast neoplasms, neoadjuvant therapy, QOL, sexuality,

anxiety, depression and social support). In Embase, Emtree terms were exploded (breast tumour, NAC, QOL, sexuality, anxiety, depression and social support). In Scopus, Web of Science, CINAHL and PsycINFO, only keywords were used (online supplemental material 1).

Data analysis

The inclusion criteria were as follows: (1) adult patients (18 years older); (2) patients with BC receiving NAC; (3) outcome measures related to QOL, including QOL, psychological impact, support from various sources and so on and (4) published in the English language. The exclusion criteria were as follows: (1) data could not be extracted; (2) duplicates or overlapping participants; (3) not original research, such as commentaries, editorials or reviews; (4) full text not available and (5) qualitative study. Two independent researchers (YZ and XZ) screened for potentially relevant studies by reviewing abstracts. The full texts were then screened further according to the inclusion and exclusion criteria. Any uncertainty was solved by a third researcher (YS). Two researchers (YZ and XZ) independently extracted and recorded the following information from the enrolled studies: author, published year, country, study design, sample size, age, regimens of NAC, timing of assessment, instrument and outcomes. The risk of bias in individual studies was evaluated by two independent researchers (YZ and LC) in accordance with Cochrane collaboration's tool for assessing risk bias,¹⁷ or Newcastle Ottawa Score (NOS)¹⁸ or Joanna Briggs Institute Critical

Appraisal tool.¹⁹ Any disagreement was resolved by a third researcher (YS).

Patient and public involvement

Patients or the public were not involved in the conceptualisation or carrying out of this research.

RESULTS

Flow of included studies

An initial search identified a total of 2994 studies (PubMed: 98, Scopus: 1191, Embase: 281, Web of Science: 1011, CINAHL:1 89, Cochrane library: 35 and PsycINFO: 189). After removing the duplicates, the total number of studies left was 2327 and all of these were screened. On screening, 2223 studies failed to meet our inclusion criteria and were removed from the analysis. The full text was obtained for 104 studies. Out of these 104 studies, an additional 92 were excluded and 12 met our inclusion criteria as defined above (figure 1).

Risk of bias in the included studies

The quality of cohort studies was assessed by NOS, randomised controlled trials (RCTs) by Cochrane collaboration's tool and cross-sectional study by Joanna Briggs Institute Critical Appraisal tool (online supplemental tables S1–S3).

Characteristics of included studies

Seven studies were designed as prospective cohort studies,^{20–25} three were RCTs,^{26–28} one was a retrospective cohort study²⁹ and one was a cross-sectional study.³⁰ Two studies were each from Brazil^{25 27} and Korea,^{21 31} and one each from China,²⁰ Japan,²⁹ India,²² UK,²⁶ Germany,²³ Indonesia,³⁰ Iran²⁴ and the USA.²⁸ One study compared QOL in BC patients with NAC and adjuvant therapy,²⁵ and three studies compared QOL in patients with different regimens of NAC.^{22 24 26} Two studies were in the same clinical trial registration with different included subjects.^{21 31} The QOL-related instruments used were: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30, the Quality of Life Questionnaire-Breast Cancer Module, the Hospital Anxiety and Depression Scale, Pittsburgh Sleep Quality Index, Multinational Association of Supportive Care in Cancer Antiemesis Tool, Quality of Life Questionnaire for Cancer Patients Treated with Anti-Cancer Drugs-Breast, Functional Assessment of Cancer Therapy of Breast, Functional Assessment of Cancer Therapy-Taxane, 36-Item Short Form Health Survey Questionnaire, Body Image Scale, Rotterdam Symptom Checklist, Mood Rating Scale, Global Distress Scale, Treatment Side-Effects Questionnaire, Fragebogen erlebter Defizite der Aufmerksamkeit, Rosenberg Self Esteem Scale, Brief Fatigue Inventory and Centre for Epidemiologic Studies-Depression Scale (table 1).

Quality of life

Physical symptoms

Ten studies evaluated patients' physical aspects with NAC. NAC affects all aspects of a patient's body and 80%

of the patients had adverse physical symptoms (table 2; figure 2). Three studies evaluated dyspnoea^{20 24 25} and pain,^{26 27 29} respectively, two evaluated nausea/vomit,^{21 27} fatigue^{20 24} and cognitive function,^{23 24} respectively, one evaluated body image²⁸ and five evaluated other symptoms.^{22 24 25 27 29} Lee *et al*²¹ found that 48.5% of patients undergoing NAC experienced chemotherapy-induced nausea and vomiting (CINV), with delayed CINV (prevalence 42.5%) being more common than acute CINV (prevalence 39.6%). Ding *et al*²⁰ reported patients experienced increased dyspnoea and fatigue after chemotherapy. Takada *et al*²⁹ found that before NAC, the low QOL group had significantly lower scores on the subscale of Physical symptoms and pain, and the subscale of Dress, sexual aspect, other categories than the high QOL groups (both $p < 0.001$). However, there was no significant difference between the two groups of these subscales after NAC. Hermelink *et al*²³ reported during NAC that cognitive function remained stable in most patients with BC, but cognitive decline predominated in 27% of patients. It is caused by anxiety and depression from chemotherapy.

Different regimens of NAC

Three studies investigated the changes in physical symptoms with different treatment regimens of NAC. Chellappan²² showed that there was no difference in physical problems between the weekly regimen of paclitaxel and the 3-weekly regimen of paclitaxel. Rezapour *et al*²⁴ reported that QOL declined in both doxorubicin and cyclophosphamide (AC) and paclitaxel and gemcitabine (PG) groups, but the two were reflected in different symptoms. The AC group had a significantly better situation in fatigue, pain, cognitive functioning and constipation compared with the PG group. Nausea and vomiting, dyspnoea, insomnia and diarrhoea were better in the PG group. There was no statistically significant difference in physical performance and physical capability between the two groups. Walker *et al*²⁶ reported patients had severe pain in the 3-weekly group compared with the weekly docetaxel group ($p = 0.034$).

Neoadjuvant versus adjuvant chemotherapy

Only one study compared the effects of neoadjuvant and adjuvant chemotherapy on physical symptoms. Coelho *et al*²⁵ observed that QOL was altered with the greater loss for getting NAC compared with adjuvant. Physical function and dyspnoea symptoms had a greater impact in the neoadjuvant group compared with the adjuvant group. It is attributed to late diagnoses that provide aggressive treatments.

Intervention in NAC

Two of these studies intervened in BC patients on NAC. Souza *et al*²⁷ showed that nutritional interventions improved patients' grip strength, positively affected the occurrence of nausea/vomiting and loss of appetite, and reduced the frequency of leucopenia and abdominal pain during NAC. Basen-Engquist *et al*²⁸ reported that

Table 1 Characteristics of included studies

Author	Year	Country	Study design	Sample size (n)	Age	Regimens of NAC	Timing of assessment	QOL-related instrument
Ding <i>et al.</i> ²⁰	2019	China	Prospective cohort study	29	46±8	CEF regimen	Before and after NAC	EORTC QLQ-C30
Lee <i>et al.</i> ²¹	2017	Korea	Prospective cohort study	134	44.48±7.48	Anthracycline-based regimens along with standard doses of antiemetics	Before and after the first cycle of NAC	PSQI, HADS, MAT
Takada <i>et al.</i> ²⁸	2018	Japan	Retrospective cohort study	300	55 (27–90)	FEC+paclitaxel (HER2-positive + trastuzumab)	Before and after NAC	QOL-ACD-B
Chellappan ²²	2018	India	Prospective cohort study	50 (weekly) vs 50 (3-weekly)	Weekly: ≤50 years accounted for 58%, ≥50 years accounted for 42% 3-weekly: ≤50 years accounted for 56%, ≥50 years accounted for 44%	0 patients: paclitaxel and doxorubicin (4 course) every 3 weeks Other 50: paclitaxel weekly (10 course) along with doxorubicin (4 course) every 3 weeks	Weekly (total 10 weeks)	HAM-D, FACT-B, FACT-Taxane
Walker <i>et al.</i> ²⁶	2011	UK	RCT	41 (weekly) vs 41 (3-weekly)	Weekly: 50.1 (27–68); 3-weekly: 48.3 (32–70)	Weekly: AC+weekly docetaxel 3-weekly: AC+3-weekly docetaxel	Before randomisation, every 3 weeks during docetaxel, and 3 weeks after completion of chemotherapy	FACT-B, RSCL, HADS, MRS, GDS, TSEQ
Hermelink <i>et al.</i> ²³	2007	Germany	Prospective cohort study	101	48.6±9.7	Standard chemotherapy or dose-intensified therapy	Before and toward the end of NAC	FEDA, Cognitive Function Scale of EORTC QLQ-C30; HADS
Aprilianto <i>et al.</i> ³⁰	2021	Indonesia	Cross-sectional study	56	Almost half (33.9%) of respondents were between the ages of 41–50 years old.	–	–	A self-made family social support questionnaire, RSES
Rezapour <i>et al.</i> ²⁴	2018	Iran	Prospective cohort study	50 vs 50	28–70	AC vs PG regimens	At the beginning and end of chemotherapy	EORTC QLQ-C30
Coelho <i>et al.</i> ²⁵	2017	Brazil	Prospective cohort study	53 (NAC) vs 14 (adjuvant chemotherapy)	51.3 (30–77)	NAC: anthracyclines and taxanes Adjuvant chemotherapy	T1: on the day the treatment was started T2: from 40 days to 50 days after the first, when the adverse effects began T3: from 40 days to 50 days after the second, when the women were already adapted to treatment or the effects were being handled by the team	EORTC QLQ-C30, QLQ-BR23
Souza <i>et al.</i> ²⁷	2021	Brazil	RCT	19 (IG) vs 15 (CG)	44.3±9.2 (IG) vs 45.5±8.6 (CG)	AC regimen	T0: before the beginning of the first cycle T1: during the second cycles T2: during the third cycles T3: until the end of the third one	EORTC QLQ-C30, HGS
Basen-Engquist <i>et al.</i> ²⁸	2020	USA	RCT	19 (IG) vs 18 (CG)	49.6±13.3 (IG) vs 49.2±9.2 (CG)	–	T0: at baseline T1: mid-chemotherapy (3 months) T2: post-chemotherapy (6 months)	SF-36, BIS
Lee <i>et al.</i> ³¹	2021	Korea	Prospective cohort study	193	44.89±7.913	Four sessions of anthracycline and cyclophosphamide, followed by 4 sessions of docetaxel	T1: before the first session of chemotherapy T2: 6 months after the end of chemotherapy	HADS, FACT-B

–, not reported; AC, doxorubicin and cyclophosphamide; BFI, Brief Fatigue Inventory; BIS, Body Image Scale; CEF, cyclophosphamide, epirubicin, and 5-fluorouracil; CES-D, Center for Epidemiologic Studies-Depression Scale; CG, control group; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; FACT-B, Functional Assessment of Cancer Therapy-Breast; FACT-Taxane, Functional Assessment of Cancer Therapy-Taxane; FEC, fluorouracil injection, epirubicin, and cyclophosphamide; FEDA, Fragebogen erlebter Defizite der Aufmerksamkeits (Questionnaire of Experienced Attention Deficits); GDS, Global Distress Scale; HADS, the Hospital Anxiety and Depression Scale; HAM-D, Hamilton Rating Scale for Depression; HGS, handgrip strength; IG, intervention group; MAT, Multinational Association of Supportive Care in Cancer Antiemesis Tool; MRS, Mood Rating Scale; NAC, neoadjuvant chemotherapy; NAST, neoadjuvant systemic therapy; PG, paclitaxel and gemcitabine; PSQI, Pittsburgh Sleep Quality Index; QLQ-BR23, the Quality of Life Questionnaire-Breast Cancer Module; QOL-ACD-B, Quality of Life Questionnaire for Cancer Patients Treated with Anti-Cancer Drugs-Breast; RSES, Rosenberg Self Esteem Scale; SF-36, 36-Item Short Form Health Survey Questionnaire; TSEQ, Rotterdam Symptom Checklist; RSES, Rotterdam Symptom Checklist; RSCL, randomised controlled trial; RSCL, Rotterdam Symptom Checklist; RSES, Rosenberg Self Esteem Scale; SF-36, 36-Item Short Form Health Survey Questionnaire; TSEQ, Treatment Side-Effects Questionnaire.

Table 2 QOL of patients with BC

Subjects	Themes	Study (n)	Author	Outcomes
Physical symptoms	Body image	1	Basen-Engquist <i>et al.</i> ²⁸	The difference in body image was not significant between IG and CG.
			Lee <i>et al.</i> ²¹	48.5% of patients undergoing NAC experienced CINV.
	Nausea/vomit	2	Souza <i>et al.</i> ²⁷	Nutritional interventions during NAC positively affected the occurrence of nausea/vomiting and loss of appetite.
			Ding <i>et al.</i> ²⁰	Patients experienced increased fatigue after NAC.
	Fatigue	2	Rezapour <i>et al.</i> ²⁴	The PG group had increased fatigue than the AC group.
			Hermelink <i>et al.</i> ²³	During NAC, cognitive function remained stable in most patients, but cognitive decline predominated in 27% of patients.
	Cognitive function	2	Rezapour <i>et al.</i> ²⁴	The PG group had impaired cognitive function than the AC group.
			Ding <i>et al.</i> ²⁰	Patients experienced increased dyspnoea after NAC.
	Dyspnoea	3	Coelho <i>et al.</i> ²⁵	Patients who received NAC had increased dyspnoea compared with adjuvant chemotherapy.
			Rezapour <i>et al.</i> ²⁴	The AC group had increased dyspnoea than the PG group.
			Takada <i>et al.</i> ²⁹	Before NAC, the low QOL group had significantly lower scores on the subscale of Physical symptoms and pain than the high QOL groups(p<0.001). However, there was no significant difference between the two groups after NAC.
	Pain	3	Souza <i>et al.</i> ²⁷	Nutritional interventions reduced the frequency of abdominal pain during NAC.
			Walker <i>et al.</i> ²⁶	The pain was significantly greater in the 3-weekly group compared with the weekly group(p=0.034).
			Chellappan <i>et al.</i> ²²	There was no difference in physical problems between the weekly regimen of paclitaxel and the 3-weekly regimen of paclitaxel.
	Other symptoms	5	Takada <i>et al.</i> ²⁹	Before NAC, the low QOL group had significantly lower scores on the subscale of Dress, sexual aspect, other categories than the high QOL groups(p<0.001). However, there was no significant difference between the two groups after NAC.
Rezapour <i>et al.</i> ²⁴			The AC group had a significantly better situation in constipation compared with the PG group. Insomnia and diarrhoea were better in the PG group.	
Coelho <i>et al.</i> ²⁵			The physical function had a greater impact in the neoadjuvant group compared with the adjuvant group.	
Souza <i>et al.</i> ²⁷			Nutritional interventions improved patients' grip strength, positively affected the loss of appetite and reduced the frequency of leucopenia during NAC.	
Rezapour <i>et al.</i> ²⁴			The AC group had a better role function compared with the PG group.	
Psychological effects	Role function	2	Souza <i>et al.</i> ²⁷	Nutritional interventions were able to improve the role function.
			Lee S <i>et al.</i> ³¹	The depression in BC patients was most severe during NAC compared with before and after NAC. Anxiety was most severe before NAC but gradually improved throughout the treatment session.
	Anxiety/depression	3	Lee KM <i>et al.</i> ²¹	40 patients were anxious and 49 were depressed. In the univariate analyses, overall CINV was significantly associated with anxiety (p=0.036).
			Walker <i>et al.</i> ²⁶	Anxiety and depression were not statistically significant between the weekly group and the 3-weekly group.
			Chellappan <i>et al.</i> ²²	Three weekly patients had more problems regarding emotional well-being than weekly patients. But the observed difference in scores of depression among the two groups was not statistically significant.
	Emotional function	4	Rezapour <i>et al.</i> ²⁴	The PG group had better emotional functioning compared with the AC group.
			Coelho <i>et al.</i> ²⁵	The emotional function was significantly affected in adjuvant chemotherapy and NAC, but there was no difference in the effects of the two treatments.
			Basen-Engquist <i>et al.</i> ²⁸	Differences in role emotional were not significant between IG and CG.
			Aprilianto <i>et al.</i> ³⁰	36 respondents (64.3%) were in a good category of family social support. The self-esteem of almost half of the BC patients (27 respondents or 48.2%) was in a moderate level category.
Support	Family support	1	Chellappan <i>et al.</i> ²²	Weekly group had a high level of social well-being than 3-weekly group.
			Walker <i>et al.</i> ²⁶	There was no significant difference in the social dimension between weekly group and 3-weekly group.
			Basen-Engquist <i>et al.</i> ²⁸	Differences in social function of IG and CG groups were not significant.
			Rezapour <i>et al.</i> ²⁴	The AC group had better social function compared with the PG group.

AC, doxorubicin and cyclophosphamide; BC, breast cancer; CG, control group; CINV, chemotherapy-induced nausea and vomiting; IG, intervention group; NAC, neoadjuvant chemotherapy; PG, paclitaxel and gemcitabine; QOL, quality of life.

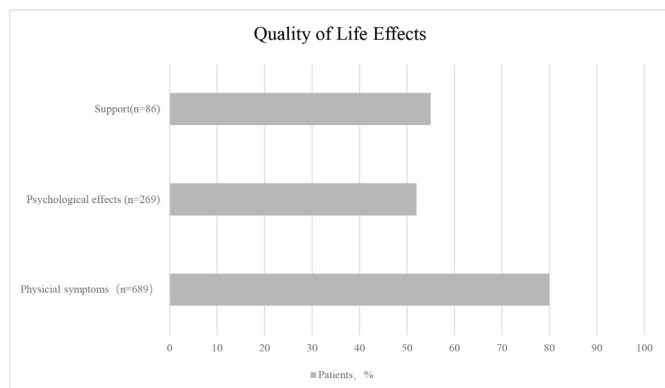


Figure 2 Summary results of the proportion of each negative impact on QOL. QOL, quality of life.

weight gain prevention intervention reduced more in waist circumference ($p=0.03$) and greater improvements in self-reported vitality scores ($p=0.03$) compared with the control group. The majority of participants reported being satisfied with the intervention during chemotherapy (88%).

Psychological effects

Eight studies evaluated psychological effects during NAC and 52% of patients get negative effects on psychological aspects (table 2; figure 2). Four studies evaluated emotional function,^{22 24 25 28} three studies evaluated anxiety/depression^{21 26 31} and two evaluated role function.^{24 27} Lee *et al*³¹ reported that the depression in BC patients was most severe during NAC compared with before and after NAC. Anxiety was most severe before NAC but gradually improved throughout the treatment session. Lee *et al*²¹ reported that overall CINV was significantly associated with anxiety.

Different regimens of NAC

Three studies investigated the changes in psychological effects with different regimens of NAC. Chellappan *et al*²² studied NAC with different regimens and showed that patients who were treated once a week had a high level of emotional well-being than those who were treated three times a week. But depression among the two groups was not statistically significant. Meanwhile, Walker *et al*²⁶ found anxiety and depression were not statistically significant between the weekly group and the 3-weekly group. Rezapour *et al*²⁴ reported that the AC group had a high level of role functioning than the PG group. The emotional functioning was better in the PG group compared with the AC group.

Neoadjuvant vs adjuvant chemotherapy

One study investigated the psychological effects between NAC and adjuvant chemotherapy. Coelho *et al*²⁵ reported that emotional function was significantly affected in adjuvant chemotherapy and NAC, but there was no difference in the effects of the two treatments.

Intervention in NAC

Two studies intervened in BC patients on NAC. Souza *et al*²⁷ reported that nutritional interventions were able to improve the role function. Basen-Engquist *et al*²⁸ reported that weight gain prevention intervention did not change mental health or role emotion.

Support

Five studies evaluated support from society or family and 55% of patients did not receive adequate support (table 2; figure 2). Aprilianto *et al*³⁰ reported that 64.3% of the respondents reported that social support for the patient's family was mostly in the good category, and 48.2% of the patients with BC had a moderate level of self-esteem. There was a strong positive correlation between family social support and patient self-esteem.

Different regimens of NAC

Three studies evaluated support between different regimens of NAC. Chellappan *et al*²² reported that weekly group had a high level of social well-being than 3-weekly group ($p=0.007$). Rezapour *et al*²⁴ reported that the AC group had significantly better social function compared with the PG group. Walker *et al*²⁶ showed that the weekly group and the 3-weekly group had no significant difference in the social dimension.

Intervention in NAC

Basen-Engquist *et al*²⁸ reported that weight gain prevention intervention couldn't change social function of patients.

QOL-related predictors

Three studies have extrapolated QOL-related predictors of BC patients during NAC: chronotype, QOL before NAC, and depression.^{21 29 31} Lee KM *et al*²¹ suggest late chronotype may be a predictor of CINV. Patients with BC with late chronotype have an increased risk of CINV during NAC. In another study, Lee *et al*³¹ indicated that depression during NAC was a mediator in the relationship between resilience and health-related QOL in patients with BC, and QOL after NAC can be improved by screening and intervening for depression during NAC in patients with BC. Meanwhile, Takada *et al*²⁹ reported that high QOL before chemotherapy was an independent factor in overall survival (table 3).

DISCUSSION

In recent years, NAC has been widely used in the treatment of BC, and its efficiency in early-stage BC is as high as 70%~90% and has improved the success rate of breast-conserving surgery and the long-term prognosis of patients in complete pathological remission.^{32 33} However, it also has significant side effects on various organs of patients. Patients with BC after NAC require further surgical treatment. Chemotherapy-related symptoms and poor QOL inevitably affect the patient's surgical tolerance and it may delay the patient's surgical treatment in severe cases.

Table 3 QOL-related predictors

Study	Sample size(n)	Study design	Instrument	Predictors
Lee <i>et al.</i> ²¹	134	Prospective cohort study	PSQI, HADS, MAT	Late chronotype may be a predictor of CINV.
Takada <i>et al.</i> ²⁹	300	Retrospective cohort study	QOL-ACD-B	The level of QOL before chemotherapy was an independent factor in overall survival.
Lee <i>et al.</i> ³¹	193	Prospective cohort study	HADS, FACT-B	Depression was a mediator in the relationship between resilience and health-related QOL.

CINV, chemotherapy-induced nausea and vomiting; FACT-B, Functional Assessment of Cancer Therapy of Breast; HADS, the Hospital Anxiety and Depression Scale; MAT, Multinational Association of Supportive Care in Cancer Antiemesis Tool; PSQI, Pittsburgh Sleep Quality Index; QOL, quality of life; QOL-ACD-B, Quality of Life Questionnaire for Cancer Patients Treated with Anti-Cancer Drugs-Breast.

The initial stages of treatment and the months following the end of treatment can be difficult times for patients, both physically and emotionally, and patients with BC are vulnerable to maladjustment and decreased QOL during these periods.³⁴ Therefore, information about expected QOL will play an important role in the decision-making process of patients and clinicians considering NAC, so this study was conducted to systematically evaluate the QOL of NAC patients.

The results of this systematic review showed no significant change in overall QOL before and after NAC in patients with BC. However, during chemotherapy, patients' QOL decreased, patients experienced increased pain, nausea and vomiting, dyspnoea and fatigue,^{20 21 24 25 29} and nausea remained unimproved despite the use of an antiemetic regimen that relieved vomiting.²¹ Patients' QOL decreases during chemotherapy due to the toxic effects of chemotherapy drugs, and after chemotherapy, some of the toxic effects diminish and patients' QOL improves. Emotional problems, such as anxiety and depression, are also aggravated during chemotherapy, but they all resolve at the end of chemotherapy.^{25 31} Emotional problems during NAC showed a significant association with resilience before NAC. These findings are largely consistent with previous studies on QOL during NAC for other cancers, such as oesophageal cancer,³⁵ rectal cancer,³⁶ pancreatic cancer³⁷ and muscle-invasive bladder cancer.³⁸ A transient increase in physical symptoms and a decrease in QOL were seen after neoadjuvant therapy, and in those patients who underwent surgery, most domains returned back by several months.^{35–38} Different regimens of NAC have different aspects of impact on patients' QOL. The regimen of doxorubicin, cyclophosphamide and docetaxel weekly had less distressing side effects compared with the 3-weekly group,²⁶ and another regimen of paclitaxel and doxorubicin had fewer social well-being compared with weekly group.²² Comparisons of AC and PG regimens showed that PG had fewer physical adverse effects and AC had better psychological effects.²⁴ Only one study of included studies compared the impact of NAC to adjuvant chemotherapy on BC patients' QOL,²⁵ both regimens could affect patients' emotions. However,

NAC was more damaging in the terms of physical, cognitive and personal performance due to more toxicity of the drugs in NAC. QOL can be improved in various ways, including appropriate interventions and enhanced social or family support. Past studies reported that women who are malnourished have a serious negative impact on QOL,³⁴ and nutritional intervention can improve the symptoms of nausea, vomiting, and loss of appetite in patients with BC, and exercise can reduce fatigue and improve the physical quality of patients with BC.^{27 39 40} Good nutritional status enables patients to better cope with intensive cancer treatment regimens.⁴¹ Patients with BC with high levels of social support have lower severity of chemotherapy-related symptoms.⁴² In addition, interventions can be based on QOL predictors of BC, such as chronotype, the level of QOL before chemotherapy and depression.

The limitations of this study are mainly in the low inclusion of literature on some subtopics and insufficient evidence, especially the contrast between NAC and adjuvant chemotherapy. This study suffered from publication bias and language bias and did not include some grey literature or unpublished, non-English language literature.

More original studies of high quality are needed. A potential area for further investigations provided by this systematic review is QOL in the perioperative and long-term postoperative periods after NAC. It is important to improve the long-term survival prognosis of NAC but also to focus on and improve QOL during and after NAC.

CONCLUSION

The results of this systematic review showed that BC patients' QOL was significantly lower during NAC. There was no significant change in overall QOL before and after NAC. And this review found that the influences are mainly reflected in physical symptoms (80%), psychological effects (52%) and support from society or family (55%). QOL could be improved with appropriate interventions. Factors that affect QOL include chronotype, QOL before NAC and depression can affect the QOL. More

original research is needed in the future to understand the profile and predictors of QOL in patients on neoadjuvant therapy, which will help clinicians and patients make better decisions and deal with NAC-related issues.

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REFERENCES

- Sung H, Ferlay J, Siegel RL, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209–49.
- Runowicz CD, Leach CR, Henry NL, *et al*. American cancer society/American society of clinical oncology breast cancer survivorship care guideline. *J Clin Oncol* 2016;34:611–35.
- Montemurro F, Nuzzolese I, Ponzzone R. Neoadjuvant or adjuvant chemotherapy in early breast cancer? *Expert Opin Pharmacother* 2020;21:1071–82.
- Asaoka M, Gandhi S, Ishikawa T, *et al*. Neoadjuvant chemotherapy for breast cancer: past, present, and future. *Breast Cancer* 2020;14:117822342098037.
- Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. *Lancet Oncol* 2018;19:27–39.
- Fisher CS, Ma CX, Gillanders WE, *et al*. Neoadjuvant chemotherapy is associated with improved survival compared with adjuvant chemotherapy in patients with triple-negative breast cancer only after complete pathologic response. *Ann Surg Oncol* 2012;19:253–8.
- Choi SY, Ha MS, Chi BH, *et al*. Neoadjuvant versus adjuvant chemotherapy in bladder cancer: a nationwide cohort study. *J Cancer Res Clin Oncol* 2022;148:3135–44.
- Dehal A, Graff-Baker AN, Vuong B, *et al*. Neoadjuvant chemotherapy improves survival in patients with clinical T4b colon cancer. *J Gastrointest Surg* 2018;22:242–9.
- Broglio KR, Quintana M, Foster M, *et al*. Association of pathologic complete response to neoadjuvant therapy in HER2-positive breast cancer with long-term outcomes: a meta-analysis. *JAMA Oncol* 2016;2:751–60.
- Mokhtari-Hessari P, Montazeri A. Health-related quality of life in breast cancer patients: review of reviews from 2008 to 2018. *Health Qual Life Outcomes* 2020;18:338.
- Lee Y, Jeon Y-W, Im E-O, *et al*. Causal attributions and quality of life of Korean breast cancer survivors. *Asian Nurs Res* 2021;15:53–9.
- Ho PJ, Gernaat SAM, Hartman M, *et al*. Health-related quality of life in Asian patients with breast cancer: a systematic review. *BMJ Open* 2018;8:e020512.
- Kretschmer A, Ploussard G, Heidegger I, *et al*. Health-related quality of life in patients with advanced prostate cancer: a systematic review. *Eur Urol Focus* 2021;7:742–51.
- Fukushi K, Narita T, Hatakeyama S, *et al*. Quality-of-life evaluation during platinum-based neoadjuvant chemotherapies for urothelial carcinoma. *Int J Clin Oncol* 2017;22:366–72.
- Aromataris E, Munn Z. *JBI manual for evidence synthesis*. JBI, 2020.
- Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
- Higgins JPT, Altman DG, Gøtzsche PC, *et al*. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
- Wells GA, Shea B, O'Connell D. *The Newcastle- Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses*. Ottawa: The Ottawa Hospital Research Institute, 2021. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
- Moola S, Munn Z, Tufanaru C. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z, eds. *JBI manual for evidence synthesis*. JBI, 2020. <https://synthesismanual.jbi.global>
- Ding L, Wang L, Yin J, *et al*. Effects of neoadjuvant chemotherapy on respiratory function in patients with breast cancer. *Chin J Cancer Res* 2020;32:36–42.
- Lee K-M, Jung D-Y, Hwang H, *et al*. Late phenotypes are associated with neoadjuvant chemotherapy-induced nausea and vomiting in women with breast cancer. *Chronobiol Int* 2017;34:480–91.
- Chellappan N. To assess the quality of life of paclitaxel based dose dense and conventional neoadjuvant chemotherapy in locally advanced female breast cancer patients. *J Evol Med Dent Sci* 2018;7:3496–501.
- Hermelink K, Untch M, Lux MP, *et al*. Cognitive function during neoadjuvant chemotherapy for breast cancer: results of a prospective, multicenter, longitudinal study. *Cancer* 2007;109:1905–13.
- Rezapour A, Javan-Noughabi J, Faramarzi A. Quality of life in breast cancer patients using neoadjuvant AC (doxorubicin and cyclophosphamide) in comparison with PG (paclitaxel and gemcitabine) therapy. *Middle East J Cancer* 2018;9:41–7.
- RCFP C, Panobianco MS, Guimarães PRB. Adjuvant and neo adjuvant chemotherapy and the implications in the quality of life women with breast cancer. *Nurs UFPE* 2017;11:4732–40.
- Walker LG, Eremin JM, Aloysius MM, *et al*. Effects on quality of life, anti-cancer responses, breast conserving surgery and survival with neoadjuvant docetaxel: a randomised study of sequential weekly versus three-weekly docetaxel following neoadjuvant doxorubicin and cyclophosphamide in women with primary breast cancer. *BMC Cancer* 2011;11:179.
- Souza APSde, Silva LCda, Fayh APT. Nutritional intervention contributes to the improvement of symptoms related to quality of life in breast cancer patients undergoing neoadjuvant chemotherapy: a randomized clinical trial. *Nutrients* 2021;13:589.
- Basen-Engquist KM, Raber M, Carmack CL, *et al*. Feasibility and efficacy of a weight gain prevention intervention for breast cancer patients receiving neoadjuvant chemotherapy: a randomized controlled pilot study. *Support Care Cancer* 2020;28:5821–32.
- Takada K, Kashiwagi S, Fukui Y, *et al*. Prognostic value of quality-of-life scores in patients with breast cancer undergoing preoperative chemotherapy. *BJS Open* 2019;3:38–47.
- Aprilianto E, Lumadi SA, Handian FI. Family social support and the self-esteem of breast cancer patients undergoing neoadjuvant chemotherapy. *J Public Health Res* 2021;10:2234.
- Lee S, Jung S, Jung S, *et al*. Psychiatric symptoms mediate the effect of resilience on health-related quality of life in patients with breast cancer: longitudinal examination. *Psychooncology* 2022;31:470–477.
- Earl H, Provenzano E, Abraham J, *et al*. Neoadjuvant trials in early breast cancer: pathological response at surgery and correlation to longer term outcomes - what does it all mean? *BMC Med* 2015;13:234.

- 33 Baulies S, Belin L, Mallon P, *et al*. Time-varying effect and long-term survival analysis in breast cancer patients treated with neoadjuvant chemotherapy. *Br J Cancer* 2015;113:30–6.
- 34 Rahman MM, Ahsan MA, Monalisa NN, *et al*. Influence of socioeconomic status and BMI on the quality of life after mastectomy in Bangladeshi breast cancer patients in a public hospital. *Jpn J Clin Oncol* 2014;44:1150–7.
- 35 Noordman BJ, Verdam MGE, Lagarde SM, *et al*. Effect of neoadjuvant chemoradiotherapy on health-related quality of life in esophageal or junctional cancer: results from the randomized cross trial. *J Clin Oncol* 2018;36:268–75.
- 36 Sciafani F, Peckitt C, Cunningham D, *et al*. Short- and long-term quality of life and bowel function in patients with MRI-defined, high-risk, locally advanced rectal cancer treated with an intensified neoadjuvant strategy in the randomized phase 2 EXPERT-C trial. *Int J Radiat Oncol Biol Phys* 2015;93:303–12.
- 37 Serrano PE, Herman JM, Griffith KA, *et al*. Quality of life in a prospective, multicenter phase 2 trial of neoadjuvant full-dose gemcitabine, oxaliplatin, and radiation in patients with resectable or borderline resectable pancreatic adenocarcinoma. *Int J Radiat Oncol Biol Phys* 2014;90:270–7.
- 38 Kitamura H, Hinotsu S, Tsukamoto T, *et al*. Effect of neoadjuvant chemotherapy on health-related quality of life in patients with muscle-invasive bladder cancer: results from JCOG0209, a randomized phase III study. *Jpn J Clin Oncol* 2020;50:1464–9.
- 39 Furmaniak AC, Menig M, Markes MH. Exercise for women receiving adjuvant therapy for breast cancer. *Cochrane Database Syst Rev* 2016;9:CD005001.
- 40 Tsuji K, Ochi E, Okubo R, *et al*. Effect of home-based high-intensity interval training and behavioural modification using information and communication technology on cardiorespiratory fitness and exercise habits among sedentary breast cancer survivors: habit-B study protocol for a randomised controlled trial. *BMJ Open* 2019;9:e030911.
- 41 Fayh APT, Bezerra ADdeL, Friedman R. Appetite hormones in children and adolescents with cancer: a systematic review of observational studies. *Nutr Hosp* 2018;35:201–10.
- 42 Oh GH, Yeom C-W, Shim E-J, *et al*. The effect of perceived social support on chemotherapy-related symptoms in patients with breast cancer: a prospective observational study. *J Psychosom Res* 2020;130:109911.