Review article

Title: The impact of breast cancer surgery on functional status in older women – A systematic review of the literature

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Abstract

Primary endocrine therapy as treatment of breast cancer is only recommended in older women with limited life expectancy. However, many older women opt for endocrine therapy due to concerns regarding frailty and potential decline in function after surgery. A decline in functional status after surgery is documented in some cancer types, such as colorectal, however, the full impact of breast cancer surgery is less understood. A systematic review was performed to examine the evidence for impact of breast cancer surgery on functional status in older women. PubMed and Embase databases were searched. Studies were eligible if performed within the last 10 years; included patients over the age of 65 years undergoing breast cancer surgery; included stratification of results by age; measured functional status pre-operatively and at least six months following surgery. A total of 11 studies including 12 030 women were appraised. Two studies represented level-II and nine level-IV evidence. Overall, physical activity level was negatively impacted by breast cancer surgery and this was compounded by the extent of surgery. Evidence for impact of breast cancer surgery on quality of life, fatigue and cognition, was conflicting. The possibility of decline in functional status after breast cancer surgery should be discussed in all older women considering surgery. A structured exercise program may improve the negative effects of surgery on physical activity. Further work is required in the areas of quality of life, fatigability and cognition.

Keywords: older women, breast cancer, functional status, physical activity, activities of daily living

Introduction

Breast cancer is the most common female malignancy worldwide[1]. Incidence increases with age; over a quarter of all new diagnoses made in the UK every year are in women aged over 75 years[2]. With an ageing population, the burden of breast cancer care will continue to rise. Improved survival rates and management of co-existing conditions means that patients who are older at the time of cancer diagnosis can still expect an extended period of survival. In 2018, it was observed that while the rate of breast cancer surgery decreases with age, 75% of women over 65 with breast cancer underwent surgery as their primary intervention in England and Wales[3]. While surgery has better outcomes in terms of local recurrence, endocrine therapy may be offered as the primary treatment in frailer women[4.] Decision making regarding primary treatment in older women is not influenced by chronological age alone. Co-morbidities and frailty can impact the decision for surgery[5]. Additionally, preservation of functional status and quality of life (QOL) may hold more importance than curative treatment and extended life[6].

Functional status can be defined as the ability of an individual to carry out their daily activities, fulfill their usual roles; both socially and occupationally and maintain their overall health and wellbeing[7]. Many domains are considered when defining functional status, including fatigability, cognition, psychological functioning, physical activity, social activity and sleep quality[8]. An individual's functional status will be influenced by any physical impairment, the presence of symptoms, their mood and perceptions of health[9]. Risk factors for poor functional recovery after surgery include functional disability, frailty at baseline, malnutrition and cognitive impairment[9]. Older women are more likely to have co-morbidities

and a lower baseline functional status than younger women, suggesting that the impact of surgery of any kind, on functional status may be greater[10].

Many studies have been performed examining the importance of functional status in visceral surgeries, such as colorectal surgery. A cohort study by Ronning et al[11] showed that older patients had significant decline in activities of daily living (ADL) and instrumental activities of daily living (IADL) scores following surgery for colorectal cancer, without intervention. While Bailey et al[12] found that older patients had more impairment in self-care capacity and physical activity following colorectal cancer surgery, compared to a younger cohort.

Comparatively, little is known about the impact of breast cancer surgery on functional status[13]. It could be hypothesised that, as it is more superficial surgery, breast cancer surgery will impact functional status to a lesser degree than colorectal and other visceral surgeries, but there is insufficient supportive evidence of this. Factors other than the invasiveness of surgery should also be considered, such as the impact of anaesthesia, prolonged drug effects and reduced mobility following surgery[14].

This systematic review of the literature has been conducted to assess the impact of breast cancer surgery on the functional status of women over the age of 65 years. The aim of the review was to identify whether breast cancer surgery impacts functional status and if so, whether the type of surgery makes a difference. In better understanding the relationship between surgery and functional status in this population, health-care practitioners will be able to better inform the decision-making process when comparing surgery with alternative treatments for breast cancer and optimise peri-operative management.

Methods

This systematic review was conducted in adherence with the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement[15].

Search strategy and study selection

The search was carried out on PubMed and Embase (which also includes published extracts presented at important biomedical, drug and medical device conferences dating back to 2009) on the 18th of February 2021. The search was limited to studies carried out in the last 10 years, published in the English language and with available full text. A 10-year cut off was implemented, due to use of sentinel lymph node biopsy becoming incorporating into routine practice[16] and increase in the expertise of oncoplastic techniques over this time period. Studies have found no evidence of systemic bias in the context of language restriction within systematic reviews[17].

An age cut-off of greater than or equal to 65 years was used, as this is most commonly used in medical literature to define older women[18]. The following terms were used to search for titles and abstracts: (older OR elderly) AND (functional status OR physical activity OR activities of daily living OR ADLs) AND (after OR following) AND breast cancer AND surgery. Duplicate publications were excluded from the search. Articles were screened by two independent researchers in two stages. First titles and abstracts were screened, then relevant full-text articles were retrieved and screened. Any discrepancies over inclusion of studies were resolved by discussion.

Inclusion criteria were as follows: female participants, studies carried out in women greater than or equal to 65 years of age, or including women of multiple age groups with clear

representation of women greater than or equal to 65, studies carried out in participants who have undergone breast cancer surgery or including multiple cancer sites with a defined subgroup of patients who had undergone breast surgery, must have data from at least two points in time with one time point before surgery and one at least six months after surgery. Studies were excluded if: there was failure to fulfil inclusion criteria or breast cancer surgery not discussed, restricted access, review article, editorial or case report.

Data extraction

All data was extracted directly from the study text. No statistical analysis was carried out where data was not presented. Where available, the following variables were extracted from the included studies: lead author, year of publication, country, study design, definition of older women, number of women >65 years in study, aim of study, type of surgery, other types of treatment, duration of follow up, tool used to assess functional status, measurement of functional status before and after surgery. The methodology and context of the included studies was extremely variable and therefore meta-analysis was not performed.

Critical appraisal

To assess the studies that were identified by the search, a system proposed by Harbour and Miller[19] was used. The quality of the studies was assessed using the PRISMA statement[20]. The level of evidence was assessed as level-I through level-VII using the guide derived by Ackley et al[21]. Level-I evidence is obtained from systematic reviews or meta-analysis, level-II from randomised controlled trials, level-III from controlled trials without randomisation, level-IV from cohort studies, level-V from systematic reviews of descriptive studies, level-VI from single qualitative studies and level-VII from expert opinion[20]. Risk of bias was assessed using the Cochrane risk-of-bias assessment tool[22] and was done at a study and outcome level.

Results

Summary

In total, 11 studies met the inclusion criteria and were included in the review (Figure 1). Of these, nine were full papers[23-32] and one a published abstract presented at a conference[33]. These studies included a total of 12 030 women over the age of 65 who had undergone breast cancer surgery.

General characteristics

Characteristics of the included 11 studies are presented in Table 1. A total of seven of the studies were conducted in Europe[23,25,27, 30-33] and four in the USA[24,26,28,29]. The group consisted of various study designs: two of the studies were surveys[23,26], two randomised trials[24,31], two longitudinal studies[25,30], three cohort studies[25,30,33], one population based study[28] and one observational study[29]. The number of eligible participants in each study varied from 18[24] to 5969[29]. In five studies, the definition of older women was 65 years of age[23,24,26,28,30] and five studies used 70 as a cut off[25,27,31,32,33]. One study used 67 as the definition of older women[29].

Level of evidence

Two included studies represented level-II evidence[24,32] and nine represented level-IV[23,25-31,32,33].

Risk of bias assessment

A summary of the risk of bias assessment for the included studies is given in Table 3 and expanded on in supplementary File 1.

For the remainder of the article, the included 11 studies are referred to as numbered in Table 1 (Study #1-11).

Findings

The aims and findings of the studies included in the review varied. They can broadly be categorised into two main areas: the effects of breast cancer surgery on functional status in older women (Table 1), and the effects of different types of breast surgical procedures on functional status in older women (Table 2). The areas of functional status can be divided into: physical activity and functioning, QOL, fatigue and cognition. These domains were assessed using a range of validated tools, which will be discussed below.

Effect of breast cancer surgery on functional status

Physical activity

Physical activity was measured by five studies[23,24,26,27,31] using the following: Metabolic equivalent hours per week (MET hrs/week)[23,27], six-minute walk test (6MW)[24], physical component score (PCS) derived from 36-item short form survey (SF-36)[27], short physical performance battery (SPPB)[31] and physical health score, derived from Duke health score[26].

Study#2[31] defined a significant functional decline as an SPPB score greater than one. At 12 months after treatment, it was found that SPPB score remained unchanged or increased in 74.1% of older patients and decreased by greater than one point in 25.9%. After 24 months, 54.8% remained unchanged or increased and 45.2% decreased by greater than one point. Physical activity was found to be improved by intervention of strength, balance, proprioceptive, flexibility and aerobic exercise.

Study#10[24] found that the regression score for the 65-75 age group for change in 6MW after exercise intervention was not significant (p=0.086). However, over the 18-month study assessment period, women receiving an exercise intervention had increased physical function and showed improvement relative to controls. Study#2 and study#10, were both randomised control trials, offering the highest level of evidence in our study. This adds weight to the conclusion that exercise intervention improves physical functioning post-breast cancer surgery.

Overall, physical functioning decreased after breast cancer to a higher extent in older patients when compared to younger patients. In support of this, study #11[23] showed physical activity decreased by an average of 4.0 MET hrs/week one year after surgery in patients undergoing lumpectomy and mastectomy and decrease was inversely associated with age. Study #7[27], found physical functioning score (measured as a mean value between 0-100) decreased by 2.59 between one and two years post-operatively, in older patients. Comparatively, patients under 60 years old showed an increase in physical functioning of 1.86 points. Study #8[26] found that the physical health score, was significantly lower in women over the age of 65 after surgery.

When specifically looking at the older age group and changes over time, study #6[28], found that predictors of poor PCS included advanced age, having greater than two comorbidities and an inability to perform more than two out of six ADLs. An association between decline in physical functioning post-surgery and ability to carry out ADLs was also found by study #5[29]. In their study, 55-60% of older patients were found to have a significant functional decline after surgery. Decline in ADLs and cognition prior to surgery were associated with increased risk of functional decline after one year.

Quality of life

Quality of life was measured in five studies[24,26,20,32,33]. Three of the studies assessed QOL using the questionnaire QLQ C-30 and the breast cancer specific QLQ BR-23[30,32,33], one study each used the functional assessment of cancer therapy-breast (FACT-B)[24] and the BREAST-Q tool of patient reported measures[26].

QOL scores were found to remain high three years after surgery in most areas (>70/100), with only moderate limitations in sexual functioning and enjoyment, in study #3[30]. Compared with baseline assessment, four QOL areas improved during follow-up: pain, nausea and vomiting, financial impact and breast symptoms. Conversely, study#4[32] found that the QOL for older women decreased at 6 weeks from a score of 71 (out of 100) to 66 and did not recover over 2 years of follow up. Long-term impact on breast and arm symptoms were reported as well as pain. This was supported by the findings of study#1[33], which found that QOL decreased from a score of 77.1 (out of 100) to 70.3 24 months after breast cancer surgery.

Study #8[26] showed older women had similar mean BREAST-Q scores compared to younger women, a median of four years following treatment. Study #10[24] found change in FACT-B after exercise intervention was not significant (p=0.825) in women over 65.

Fatigue

Fatigue was assessed by one study, with the functional assessment of chronic illness therapy-fatigue tool (FACIT-F) in study #9[25] and revealed that age <60 years and having anxiety symptoms were significantly associated with experiencing high fatigue at 8 months after surgery.

Cognition

Cognitive function was assessed in study #6 by the mental component score (MCS) derived from SF-36 tool[28]. The median MCS in older women two years after breast cancer surgery was 50.6 and 27.1% of patients presented with a poor score. A poor score was defined as a component score 10 or more points below the median score. Predictors of a poor score included: income below $30,000 per year, greater than two comorbidities and inability to perform greater than two of six ADLs. Age itself was not a predictor for low MCS[28].

Effect of different surgical procedures on functional status

Five of the included studies further divided findings by the type of surgical procedure that was carried out[26,28-30,33]. Study #8[26] and study #6[28] compared women who had undergone different forms of mastectomy (partial, simple or radical). Study #5[29] compared lumpectomy or mastectomy +/- axillary lymph node dissection (ALND). Study #3[30] compared functional status outcomes in patients undergoing ALND and sentinel lymph node biopsy (SLNB). Study#1[33] compared the effect mastectomy and BCS on QOL, as well as ALND with SLNB. Study #6[28] showed that health related QOL in older women was not significantly impacted two years after surgery, regardless of whether they had undergone partial, simple or radical mastectomy. Study #8[26] found that older women were less likely to undergo bilateral mastectomy than younger women. There was no significant difference in general health, physical health, pain health and disability health scores between unilateral and bilateral mastectomy in women aged over 65.

Comparatively, study #5[29] found that MDS-ADL score worsened by 4.6 points after ALND, compared to 4.1 points after mastectomy and 2.8 points after lumpectomy. Study #3[30] showed that patients undergoing ALND had a worse ‘future perspective’ score and higher

occurrence of diarrhoea and appetite loss than those undergoing SLNB. Study#1[33] found that patients who underwent mastectomy had significantly lower QOL scores than those who underwent BCS, at 6 weeks, although this difference did not persist past 6 months. Initially QOL scores in the breast symptoms domain of the QLQ-BR23 were significantly poorer in patients who underwent mastectomy, but by 2 years there was no significant difference between the two groups. Women who had ALND had significantly lower QOL scores compared to the SLNB group 2 years after surgery.

Discussion

Most included studies were level of evidence 4, which is low. Only two studies were level of evidence 2, which were randomised controlled trials. Although there was a lack of high levels of evidence included in the study, considering the demographic of the study population and aim of this present review to examine functional status, randomised controlled trials may not be the most suitable method of assessment. The two randomised controlled trials assessed the impact of an intervention on functional status, however cohort studies are sufficient to examine change in functional status over time, without intervention.

There appears to be a decrease in some areas of functional status in older women after breast cancer surgery, however, there is conflicting evidence in other areas. While surgery can be viewed as necessary and curative in the treatment of breast cancer, the risks of surgery itself may outweigh the benefit in a frail population, with already limited life expectancy. These findings could be critical in deciding on treatment in this group.

Effect of breast cancer surgery on functional status

Physical functioning

There is good evidence from this review to suggest that physical function declines to a greater extent after surgery in older women compared to younger women. There is a higher burden of disease and frailty in the older population, which could lead to them being less likely to return to their preoperative level of physical activity[34]. Furthermore, there is evidence that prescribed physical activity, both pre- and post- operatively, could lead to improved outcomes in functional status and potentially survival. This is found by studies #2 and #10 which have the highest level of evidence of the included studies at level-II.

In a study carried out by De Glas et al[35] it was found that women with high levels of physical activity before undergoing breast cancer surgery had better survival compared to those who were not physically active. This effect was noted to be more apparent in women over the age of 65 when compared to younger age groups. Physical activity improves body composition, physical function and quality of life in breast cancer patients[36], as well as improving fitness and strength[37]. Other studies have shown the association between a low hand grip strength and functional status in older patients[38]. A recent meta-analysis showed that 'up and go' time in older adults was improved when aerobic exercise and resistance training were used as an intervention. The frailest participants were found to have the greatest benefit[39].

A rapid decline in physical function is often seen when older adults are admitted to hospital, with mobilising often discouraged for fear of falls[40]. Interventional exercise could be utilised to prevent significant functional decline in older surgical patients. Supporting older adults to carry out physical activity pre- and post- surgery could help to maintain independence and decrease the burden of social care requirements. More opportunities for individuals to be

active should be made available by both national and local organisations, incorporating guidelines into home life, transport and social activities.

Performance of ADLs leads to improved QOL and interventions to enable this in older patients facing surgical therapy should be considered. In a study carried out by Van Abbema et al[41] it was found that pre-surgical decline in ADLs lead to worsening of post-surgical functional status decline in women undergoing surgery for breast or colorectal cancer[41]. Adaptations to assist older adults carry out their ADLs at home should be provided to ensure a good level of QOL post-operatively. In addition, relatives and health care professionals should encourage individuals to carry out tasks for themselves. When functional status declines, an individual may need to move into a residential care home, costing on average £32 600 a year[40]. Ensuring that older people maintain their ADLs could help to reduce demand for social care and have financial implications for the NHS. Increase in level of ability could be the difference between living comfortably at home or being dependent on residential care.

Quality of life

There were conflicting findings regarding QOL. While study#4 and #1 found that QOL decreased at six weeks post-operatively in older women and never recovered to pre-surgical levels, study #3 and study #8 found that QOL remained high in older women after breast cancer surgery when compared to younger women.

These findings are supported by a study by Avis et al[42] who found that younger women had worse QOL scores for years after breast cancer diagnosis compared to older women. This was attributed to greater impact on sexual functioning, relationships and body image QOL

domains in younger women. In another study, older age was associated with more efficient adjustment after surgery[43]. This could be attributed to younger women receiving more aggressive adjuvant therapy or more emotional maturity and financial stability seen in older age. In a study by Xia et al[44], financial difficulty was one of the biggest predictors of poor QOL in women who had undergone surgery for breast cancer[44]. Poor socioeconomic status has been shown to negatively impact functional status in females with breast cancer[45] and this may be further exacerbated by surgical treatment and its required recovery. Differences in QOL between studies could also relate to differences in how it was measured. The conflicting results found by this review suggests that further research, using a fixed measure of QOL, in a large cohort of older women who have undergone breast cancer surgery is required.

Fatigue

Interestingly, the older age groups were found to be at decreased risk for experiencing high levels of fatigue after treatment, however there was only one study, study #9 to support this. This may be explained by younger women more likely to be offered chemotherapy or more intensive chemotherapy as an adjuvant therapy, leading to greater fatigue[46]. However, after 8 months, when adjuvant therapy would normally be completed, fatigue remained high in those in the 'high fatigue' group. There must therefore be other factors at play.

Cognition

While advancing age itself was not found to be a predictor for low MCS, declining cognition pre-surgery in the older age group, was found to increase risk of functional decline in study #6. While women with dementia are less likely to undergo surgical treatment for breast cancer[47], studies have demonstrated a higher rate of postoperative complications when they do, including long term cognitive decline[48]. Additionally, post-operative delirium, very

common in the older population, has been found to be a strong independent predictor of functional status decline and dependency in ADLs[49].

Effect of different surgical procedures on functional status

It was found by study#8 and study#1 that older women who underwent more invasive and potentially impairing procedures, such as an axillary lymph node dissection, were less able to care for themselves and had worse functional status and QOL[26,33]. ALND was also found to lead to a worse perspective when thinking of the future and future health. This could be due to the impact of breast cancer surgery on functional status[28].

Lumpectomy was found to have less impact on decline in ADLs and functional status compared to mastectomy in study #7[29]. These findings are supported by those examining the effects of abdominal surgeries on functional status. Laparoscopic surgery has been found to have better QOL outcomes when compared to more invasive open surgery for cholecystectomy and splenectomy[50]. Laparoscopic surgery also leads to shorter postoperative lengths of stay[51]. Treatment for breast cancer should be individualised, with consideration for the least invasive surgery possible to give the desired oncological outcome, specific to age. Further research is required into the effects of different surgical procedures on functional status in older women with breast cancer.

Potential for intervention

An Enhanced Recovery after Surgery (ERAS) pathway for total mastectomy has been shown to reduce use of analgesia and antiemetics following surgery and promote successful early recovery[52]. One of the main features of ERAS is preoperative counselling to reduce anxiety[53]. When consenting and counselling patients for surgical intervention, the potential effect on

functional status should be effectively conveyed. At this stage, pre-surgical physical activity levels and ability to carry out ADLs can also be assessed, and appropriate interventions employed. A preoperative Geriatric Assessment (GA) is often used by other surgical specialties, such as Orthopaedics, and includes assessment of comorbidities, medication, nutritional status, physical functioning, mental state and environmental factors[54]. This tool could be more routinely incorporated into preoperative assessment in breast cancer surgery to identify women who would most benefit from intervention. If women choose to opt for surgery, those identified as at high risk of functional decline could be offered rehabilitation programmes or exercise intervention. Improving preoperative walking functional capacity in older patients undergoing colorectal surgery, through exercise and counselling, means individuals are more likely to return to walking capacity baseline postoperatively[55]. However, it must be considered that extending the preoperative period in oncological patients may not be appropriate. Interventions put in place after discharge, including physical therapy and nursing care, lead to better functional status in postoperative vascular patients[56].

Alternatively, with the understanding that older adults may value QOL and functional independence over extended life span, choosing not to operate and subject individuals to functional decline, may be the most suitable and patient-centered option in some cases. In a study carried out by Van der Kluit et al[57] it was found that older patients in hospital had diverse goals of treatment, including reaching a diagnosis, controlling disease, extending life, improving symptoms and functioning, resumption work or hobbies and maintenance of autonomy[57]. Discussing goals with older adults is not currently routinely practiced and should be encouraged. For patients who wish to opt for surgery after the appropriate discussions, risks should be acknowledged and minimised wherever possible.

Strengths and limitations of the present study

This present study is a novel review of the literature on effect of breast cancer surgery on functional status in older women. Although there is a lack of high level of evidence in this review, it does give new information for older women with primary breast cancer; although breast cancer surgery may be less invasive than surgery for other types of cancer, functional status may be reduced. This should be an impetus towards high level further research in this field.

Defining 'functional status' is difficult as it encompasses many themes. This was considered in our search and we included papers looking at activities of daily living, pain, quality of life, physical activity and fatigue. However, it is a limitation of the paper that we may have missed relevant studies due to the broad nature of 'functional status' and being unable to incorporate all aspects.

All the studies presented a degree of bias. All studies exhibited some form of reporting bias. The next most common type of bias was selection bias, reported by six studies, followed by detection bias, reported by five studies.

Older adults are a cohort generally underrepresented in the literature. There is often a lack of older adults recruited to clinical trials, leading to a lack of evidence-based knowledge in how to treat these patients. A prospective randomised trial to investigate functional status further is not necessarily feasible in this population. Therefore, future work should involve review of good-quality 'real-world' data sets such as national databases and cohort studies investigating breast cancer in older women.

Conclusions

Overall, this present study shows that there is a paucity of high-level data about functional outcomes of breast cancer in older women. The evidence available suggests that physical activity does decline after breast cancer surgery to a measurable degree, supported by two high-level studies and this appears to be associated with extent of surgery. This is also supported by the included studies with level-IV evidence. Therefore, we must take this into consideration when consenting breast cancer patients for surgery and consider methods to optimise function pre-and postoperatively, including exercise intervention. On the other hand, there is limited evidence to support a decline in associated QOL, fatigability and cognition. These are important areas in the holistic treatment of the older person with cancer and should be explored further. Evidence-based information about functional outcomes is needed to make informed consent and anticipatory guidance for those that decide to undergo breast cancer surgery.

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Declarations of interest

None

Author contributions

Conceptualization	All
Methodology	All
Validation	CH and RP
Investigation	CH and RP
Data Curation	CH and RP
Writing – Original Draft	CH and RP
Writing – Review and Editing	All
Supervision	KLC

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Figure 1. Flow chart demonstrating database search and study selection

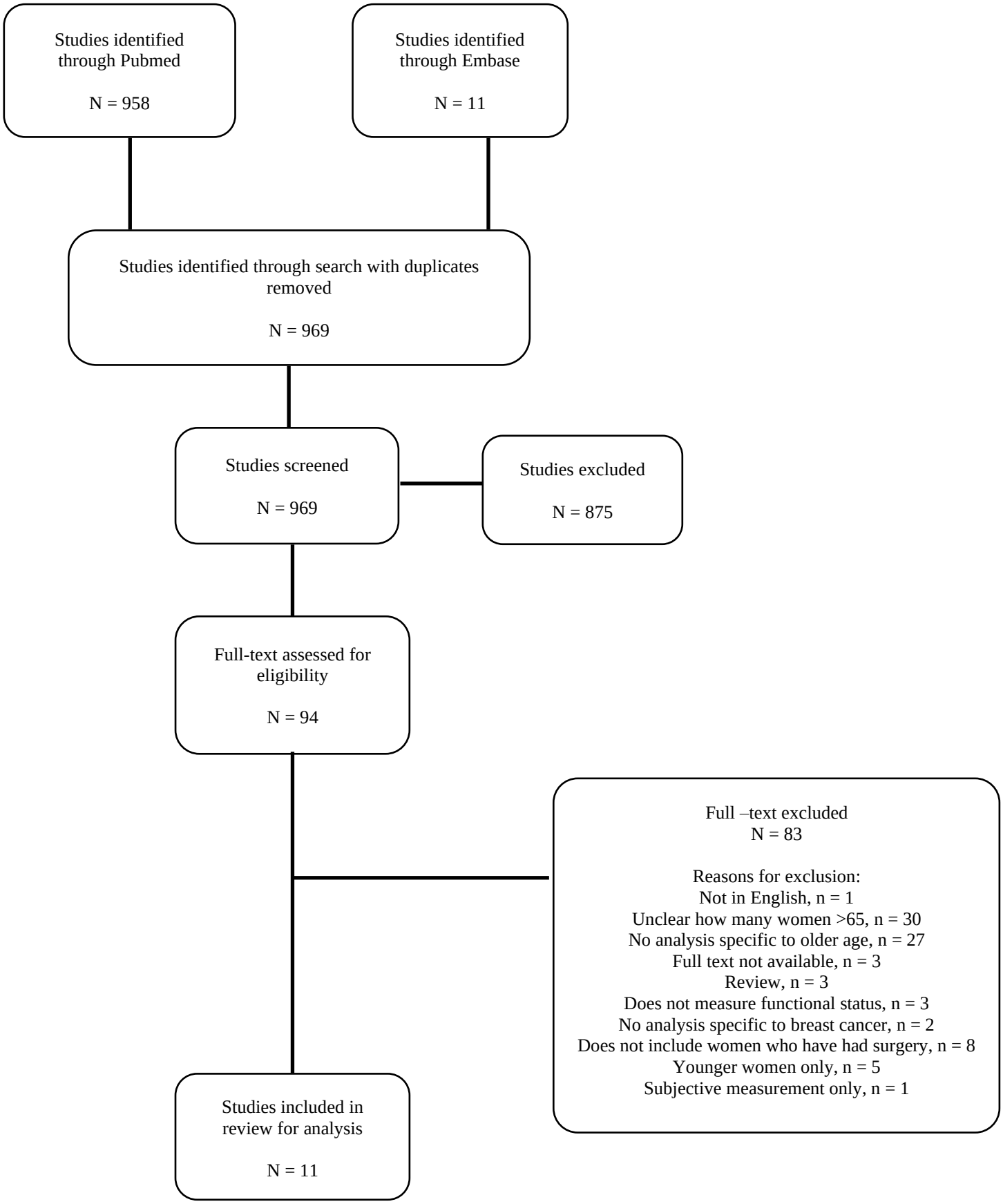

Table 1: Characteristics and findings of ten included studies examining effect of breast cancer surgery on functional status in older women

Study number	First author	Country of study	Study design	Evidence level	Age in years	N	Aims of study	Surgical procedure	Other Rx received	Follow-up duration	Tool used to measure functional status	Baseline result	Follow-up result	*p*-value of change	Conclusion
1	Morgan JL[33] 2020	UK	Cohort study	4	≥70	3416	To identify whether PET is appropriate for less fit, older women	Mx BCS ALND SLNB	CT RT ET	I: 12 months II: 18 months III: 2 years	QLQ C30 (0-100)	77.1	I: 75.6 II: 72.1 III: 70.3	<0.05	Global QOL decreased significantly after surgery
2	Arrieta H[31] 2019	Spain	Randomised clinical trial	2	≥70	180	Assess effect of exercise on PA in geriatric oncology patients	Any	-	I: 12 months II: 2 years	SPPB decline > 1 point	-	I: 25.9% II: 45.2%	I: 0.119 II: 0.006	PA improved FS

3	Arraras JI[30] 2019	Spain	Longitudinal study	4	≥65	173	To assess QOL in elderly patients following surgery	Mx ALND SLNB	RT	3 years	QLC-BR23 (0-100)	72.4	75.7	0.053	QOL remains high after follow-up
4	Shrestcha A[32] 2018	UK	Cohort study	4	≥70	1652	Compare QOL in older women after surgery and ET	Any	-	2 years	QLC-BR23 (0-100)	71	66	0.0067	Surgery has a negative effect on QOL
5	Tang V[29] 2018	USA	Observational study	4	≥67	5969	Assess FS in care home residents after surgery	I: Mx II: BCS III: ALND	-	12 months	MDS-ADL (0-28)	-	I: +2.8 II: +4.1 III: +4.6	I: <0.001 II: <0.001 III: <0.001	Functional decline after surgery associated with pre-surgery ADLs

6	Mogal HD[28] 2017	USA	Population based study	4	≥65	373	Assess QOL of African Americans following surgery	Mx Partial Mx Radical Mx	RT	2 years	I: MCS II: PCS (0-100)	-	I: OR = 1.1 I: OR = 1.0	II: 0.02 II: 0.272	Poor HRQOL associated with ADL impairment
7	Derks MG[27] 2016	Netherlands	Cohort study	4	≥70	100	Assess difference in physical functioning after surgery in advanced age	Mx ALND SLNB	CT RT ET	2 years	PF score (0-100)	--	-2.59 points	0.008	Older age associated with decline in function
8	Johnson DB[26] 2016	USA	Survey	4	≥65	108	Assess the effects of outcomes of mastectomy by age	Mx	-	4 years	I: BREAST-Q (0-100) II: Duke health score (PF)	-	I: 81.2 II: 52.6	I: >0.05 II: <0.05	Older women have similar wellbeing to younger women

											(0-100)				after surgery
9	Bodtcher H[25] 2015	Denmark	Longitudinal study	4	≥70	41	Identify specific groups of fatigue trajectory following surgery	MX BCS	CT RT ET	8 months	FACIT-F (0-52)	-	OR=1.27 (correlation between old age and score <40)	-	Age >70 not significantly associated with having high fatigue after surgery
10	Anderson RT[24] 2012	USA	Randomised trial	2	≥65	18	To assess effect of exercise on wellbeing and function after surgery	Mx BCS ALND SLNB	-	18 months	I: 6MW II: FACT-B	-	I: Regression = 61.7 II: Regression = 1.21	I: 0.086 II: 0.825	Exercise improved physical functioning

11	Huy C[23] 2011	Germany	Survey	4	≥65	400	Identify factors associated with change in PA post-operatively	Mx BCS ALND	CT RT ET	12 months	MET hrs/week	-	-4 hrs	0.003	PA decreased significantly after surgery

Abbreviations: 6MW = six-minute walk; ADL = activities of daily living; ALND = axillary lymph node dissection; BCS = breast conserving surgery; CT = chemotherapy; ET = endocrine therapy; FACT-B = functional assessment of cancer therapy – breast cancer; FS = functional status; HRQOL = health related quality of life; MCS = mental component score; MET = metabolic equivalent; Mx = mastectomy; PA = physical activity; PCS = physical component score; PF = physical functioning; QOL = quality of life; RT = radiotherapy; Rx = treatment; SLNB = sentinel lymph node biopsy; SPPB = short physical performance battery

Table 2: Impact of different breast cancer surgical procedures on functional status in older women

Study number	Author	Measurement tool (scale)	Type of surgery	Measurement	*p*-value	Findings
1	Morgan JL[33]	I: QLC-BR23 (0-23) II: QLQ-C30 (0-100)	I: Mx I: BCS II: ALND II: SLNB	10.87 9.86 66.43 70.80	I: 0.223 II: 0.04	ALND worse for QOL outcomes than SLNB. No significant difference in QOL after 2 years between BCS and Mx
3	Arraras JI[30]	QLC-BR23 (0-23)	ALND SLNB	+1.9 +3.0	0.221	ALND worse than SLNB for future perspective and diarrhoea.
5	Tang V[29]	MDS-ADL (0-28)	BCS Mx ALND	+2.8 +4.1 +4.6	<0.001 <0.001 <0.001	Higher dependence following ALND compared to mastectomy and lumpectomy
6	Mogal HD[28]	MCS and PCS score (0-100)	Simple Mx Partial Mx Radical Mx	Reference OR=1.5 OR=2.4	- 0.936 0.256	HRQOL not impacted by type of surgery
8	Johnson DB[26]	Mean BREAST-Q (0-100) Duke health score (PF) (0-100)	Unilateral Mx Bilateral Mx Unilateral Mx Bilateral Mx	81.2 77.3 52.6 50.0	>0.05 >0.05	Older women less likely to undergo bilateral mastectomy. Upper body morbidity scores similar in bilateral and unilateral.

Abbreviations: ADL = activities of daily living; ALND = axillary lymph node dissection; BCS = breast conserving surgery; HRQOL = health related quality of life; MCS = mental component score; MDS = minimum data set activities; Mx = mastectomy; OR = odds ratio; PCS = physical component score; PF = physical functioning; QOL = quality of life; SLNB = sentinel lymph node biopsy

Table 3: Summary of risk of bias assessment

Study number	Author	Selection bias	Performance bias	Attrition bias	Detection bias	Reporting bias	Recall bias
1	Morgan JL[33]	+	-	-	+	+	-
2	Arrieta H[31]	+	+	+	+	+	-
3	Arraras JI[30]	-	-	+	+	+	-
4	Shrestcha A[32]	-	-	-	-	+	-
5	Tang V[29]	+	-	-	-	+	-
6	Mogal HD[28]	+	-	-	+	+	-
7	Derks MG[27]	+	-	+	-	+	+
8	Johnson DB[26]	+	-	-	+	+	+
9	Bødtcher H[25]	-	-	-	+	+	-
10	Anderson RT[24]	+	+	-	-	+	-
11	Huy C[23]	-	-	+	-	+	+

\+ High risk of bias
\- Low or unclear risk of bias