

Breast cancer surgery in older women: outcomes of the Bridging Age Gap in Breast Cancer study

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Background: Breast cancer surgery in older women is variable and sometimes non-standard owing to concerns about morbidity. Bridging the Age Gap in Breast Cancer is a prospective multicentre cohort study aiming to determine factors influencing treatment selection and outcomes from surgery for older patients with breast cancer.

Methods: Women aged at least 70 years with operable breast cancer were recruited from 57 UK breast units between 2013 and 2018. Associations between patient and tumour characteristics and type of surgery in the breast and axilla were evaluated using univariable and multivariable analyses. Oncological outcomes, adverse events and quality-of-life (QoL) outcomes were monitored for 2 years.

Results: Among 3375 women recruited, surgery was performed in 2816 patients, of whom 24 with inadequate data were excluded. Sixty-two women had bilateral tumours, giving a total of 2854 surgical events. Median age was 76 (range 70–95) years. Breast surgery comprised mastectomy in 1138 and breast-conserving surgery in 1716 procedures. Axillary surgery comprised axillary lymph node dissection in 575 and sentinel node biopsy in 2203; 76 had no axillary surgery. Age, frailty, dementia and co-morbidities were predictors of mastectomy (multivariable odds ratio (OR) for age 1.06, 95 per cent c.i. 1.05 to 1.08). Age, frailty and co-morbidity were significant predictors of no axillary surgery (OR for age 0.91, 0.87 to 0.96). The rate of adverse events was moderate (551 of 2854, 19.3 per cent), with no 30-day mortality. Long-term QoL and functional independence were adversely affected by surgery.

Conclusion: Breast cancer surgery is safe in women aged 70 years or more, with serious adverse events being rare and no mortality. Age, ill health and frailty all influence surgical decision-making. Surgery has a negative impact on QoL and independence, which must be considered when counselling patients about choices.

*Bridging the Age Gap Trial Management Group members are co-authors of this study and can be found under the heading Collaborators

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Introduction

The age of the population in the UK is rising, and average life expectancy among women has risen from 80.5 years in 2003 to 82.9 years in 2016¹. In 2015, 54 741 women were diagnosed with breast cancer, of whom over one-third were aged over 70 years². Although overall survival outcomes are

predictably inferior in older than younger women owing to competing causes of death, breast cancer-specific survival (BCSS) rates are also lower³. This deficit is due to stage variation, compounded by treatment variance because of concerns about the morbidity of certain therapies.

Older women present with more advanced disease⁴, larger median tumour size^{5–7}, higher rates of node



positivity, and higher rates of locally advanced⁸ and metastatic⁹ disease. This is likely to have an adverse impact on BCSS, and is largely the result of lack of routine screening in this age group combined with reduced breast awareness¹⁰.

The UK National Audit of Breast Cancer in Older Patients (NABCOP) has shown significant variation in rates of surgery in older women between centres in the UK¹¹. Similar variation in surgery rates has been noted between European countries, with a recent audit¹² showing low rates in the UK compared with Poland, the Netherlands, Belgium and Ireland. Rates of surgery are also much higher in the USA¹³.

For the frailest older patients, surgery may have minimal benefit in terms of BCSS and cause harm, as reported in frail nursing home residents¹⁴. Surgery for breast cancer is, however, low risk and safe for the majority of older women. Previous published series^{9,15} have shown that modern breast cancer surgery and anaesthesia has a very low mortality rate; only 0.2 per cent died during admission. Morbidity should not be underestimated, with risk of seroma, wound complications and, in the longer term, arm morbidity such as lymphoedema and impairment of shoulder movement following axillary surgery. In addition, there may be a long-term and permanent adverse impact on quality of life (QoL) and a loss of functional reserve in this age group. These factors have received limited attention, but may be of significant importance to older women^{16,17}.

The National Institute for Health and Care Excellence (NICE) guidance¹⁸ for the management of early breast cancer published in 2009 recommends that the primary breast cancer should be removed and appropriate axillary management provided for all patients with breast cancer. Surgical management options for the breast are either mastectomy or breast-conserving surgery (BCS), and those for the axilla are sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND) or axillary radiotherapy for patients with axillary nodal metastases. The guidance does not make age-specific recommendations for treatment. Treatment algorithms have become more complex in recent years for the management of the axilla, permitting some flexibility in low-risk axillary disease to avoid ALND, following publication of the Z1¹⁹ and AMAROS²⁰ trials. The UK has, however, been slow to adopt these protocols, with NICE guidelines only recently being revised in light of these new data²¹. During the present trial interval, NICE guideline concordant care mandated ALND for all women with macrometastatic axillary disease and SLNB for all N0 disease, with no age or fitness stratification unless the woman was clearly unfit for anaesthesia.

The Bridging the Age Gap in Breast Cancer study²² is a National Institute for Health Research (NIHR)-funded programme (ISRCTN46099296) examining various aspects of the management of older patients with breast cancer. This study focused on surgical outcomes in the larger Age Gap study, and aimed to examine the characteristics and outcomes (survival, QoL and adverse events) of women aged at least 70 years in the UK undergoing surgery for breast cancer.

Methods

This was a prospective, multicentre observational cohort study. Patients could participate at three levels: full participation, partial (no requirement to complete QoL assessments) or proxy (simple third-party data collection for women with cognitive impairment). Patients were recruited from 57 UK breast units in England and Wales (*Appendix S1*, supporting information).

Ethics approval and research governance approval was obtained (IRAS: 12 LO 1808). All patients gave written informed consent, or consent was given by a proxy if the patient was cognitively impaired.

Inclusion and exclusion criteria

The study included women aged at least 70 years at the time of breast cancer diagnosis with primary operable invasive breast cancer (T1–4N0–2M0). Those with multifocal and bilateral cancers were eligible. Exclusion criteria were: disease unsuitable for surgery and previous breast cancer within 5 years. Patients without cognitive capacity were eligible if a relative or friend was willing to sign proxy consent.

Baseline data collection

A baseline comprehensive geriatric assessment was carried out using a range of validated tools, with data collected on: age; co-morbidities assessed using the Charlson Co-morbidity Index (CCI) score²³; frailty, evaluated by activities of daily living (ADL)²⁴ and instrumental activities of daily living (IADL)²⁵; cognitive function, assessed using the Mini Mental State Examination (MMSE)²⁶, with cognitive impairment defined as a MMSE score below 27, proxy consent or identification of dementia on the CCI; and nutritional status, evaluated using the abridged patient-generated subjective global assessment²⁷. Baseline tumour characteristics, including tumour size, biological subtype, grade and nodal status (both clinical, imaging and pathological status) were registered.

Breast surgery was categorized based on the maximum procedure the patient underwent as: BCS, which included wide local excision with or without wire guidance, therapeutic mastopexy and segmentectomy; or mastectomy, with or without reconstruction. As an example, a patient who initially had BCS followed by mastectomy because of involved margins was included in the mastectomy group as the patient was clearly deemed fit enough for the procedure and because the final surgery affects the risk of adverse events. Axillary surgery was classified as no axillary surgery, SLNB (axillary sampling, internal mammary node biopsy) or ALND.

Surgery was grouped into major (mastectomy and/or ALND) and minor (BCS with or without SLNB). For patients who had a bilateral procedure for invasive breast cancer, this was assessed as two unilateral procedures.

Outcomes

Mortality related to surgery was defined as death within 30 days of surgery or surgery being documented as contributing to cause of death. Death from breast cancer was assessed by death certification and expert review of all causes of death. Causes of death were grouped into breast cancer-related or other causes.

Complications, obtained by follow-up to 2 years, were categorized using the Common Terminology Criteria for Adverse Events (CTCAE)²⁸, and grouped into systemic (atelectasis, stroke, infarction, deep vein thrombosis (DVT)/embolism, arrhythmia, allergic reaction and somnolence) and local (lymphoedema, neuropathy, functional difference, wound pain, wound, necrosis, infection, haematoma, seroma and haemorrhage). Seroma was excluded from some analyses.

QoL data were compared at baseline (before starting treatment), 6 weeks and 6 months, and then at 6-month intervals up to 2 years after treatment using validated tools: the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 (generic)²⁹, QLQ-BR23 (breast cancer-related)³⁰ and ELD14 (elderly-specific)³¹, and the EuroQol Five Dimensions (EQ-5DTM; EuroQol Group, Rotterdam, the Netherlands). QoL was assessed only in patients who consented to full participation.

Statistical analysis

This article reports a planned subanalysis of the larger Age Gap study; because surgical outcomes were not the primary outcome measures, the sample size was not calculated to serve this analysis.

The significance of type of breast surgery and axillary surgery in relation to co-morbidity, dementia, IADL,

ADL and complications was analysed using χ^2 and Fisher's exact test.

Multivariable analyses were performed in the statistical package R 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria). A binary logistic regression model was developed to predict the odds of a patient receiving a mastectomy, whereas multinomial logistic regression was used to predict the odds of a woman receiving SLNB *versus* no axillary surgery or ALND *versus* no axillary surgery. In both analyses, univariable models were first built using the following variables: age, tumour size, preoperative nodal status, tumour grade, CCI score, MMSE, ADL, IADL and BMI. The model Akaike information criterion (AIC) values were used to determine which variables had most predictive importance. Multivariable models were then built by adding variables in order of importance until the model AIC value ceased to improve. Further tests with addition and removal of individual co-variables and comparison of AIC led to a preferred model, which explained but did not overfit the data. To account for missing data (approximately 15 per cent of total relevant fields), 25 complete data sets were formed using multiple imputation. Separate models, using the identified co-variables, were estimated using each of these complete data sets and the results combined to produce the final models. The R package mice 3.4.0³² was used for multiple imputation and the statistical package nnet 7.3.12³³ for logistic regression modelling.

For the QoL analysis, where relevant, the scores were converted to a 0–100 scale, as described in the EORTC scoring manual³⁴, and mean values compared using the independent *t* test.

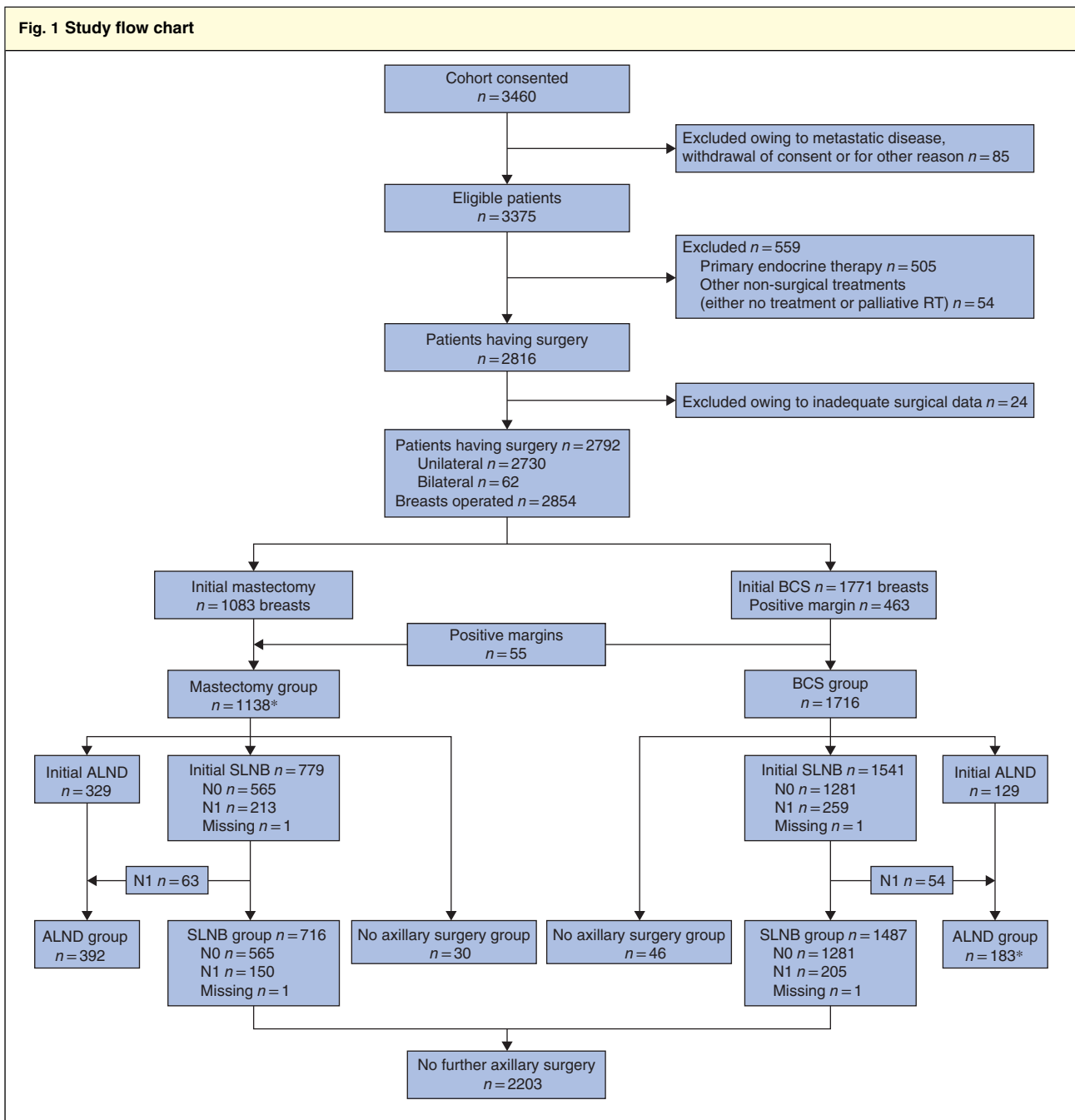
$P < 0.050$ was considered significant and SPSS[®] version 25 (IBM, Armonk, New York, USA) was used for statistical analysis, unless indicated otherwise.

Results

A total of 3375 women with primary operable breast cancer were recruited to the parent Bridging the Age Gap study between February 2013 and June 2018. Of these, 2816 (83.4 per cent) had surgical treatment, and these are the focus of the present article. The population recruited and procedures undertaken in the surgical population are shown in *Fig. 1*. The median age of surgical patients was 76 (range 70–95) years. Baseline patient and tumour characteristics are shown in *Tables 1* and *2* respectively.

Adequate data for analysis were available for 2792 of 2816 surgically treated patients. Most of the initial 3375 patients who did not have surgery received primary endocrine therapy (*Fig. 1*). Sixty-two bilateral tumours had operative treatment, giving a total of 2854 surgical events for analysis.

Fig. 1 Study flow chart



*Classed as major surgery. RT, radiotherapy; BCS, breast-conserving surgery; ALND, axillary lymph node dissection; SLNB, sentinel lymph node biopsy.

Among the surgical patients, 2445 of 2792 (87.6 per cent) had oestrogen receptor-positive tumours, of whom 2331 (95.3 per cent) received adjuvant endocrine therapy. Some 343 patients were recorded as having human epidermal growth factor receptor 2-positive disease and 168 (49.0 per cent) of these received adjuvant trastuzumab. In all, 1756 of 2792 patients received adjuvant radiotherapy

(62.9 per cent) and 134 (4.8 per cent) had adjuvant chemotherapy.

BCS was undertaken as the initial surgery in 1771 breast procedures, with therapeutic mammoplasty in 67 (3.8 per cent). Tumour margins were positive in 463 of these procedures; however, further surgery was undertaken in only 134 (28.9 per cent), with one or more re-excisions in 79

Table 1 Baseline patient characteristics of surgical population

	Breast surgery type		<i>P</i> *	Axillary surgery type			<i>P</i> *
	BCS (<i>n</i> = 1716)	Mastectomy (<i>n</i> = 1138)		SLNB (<i>n</i> = 2203)	ALND (<i>n</i> = 575)	No axillary surgery (<i>n</i> = 76)	
Age (years)			< 0.001				< 0.001
70–74	828 (70.1)	353 (29.9)		968 (82.0)	196 (16.6)	17 (1.4)	
75–79	541 (59.1)	374 (40.9)		706 (77.2)	195 (21.3)	14 (1.5)	
80–84	252 (47.9)	274 (52.1)		372 (70.7)	129 (24.5)	25 (4.8)	
≥ 85	95 (40.9)	137 (59.1)		157 (67.7)	55 (23.7)	20 (8.6)	
CCI score			< 0.001				< 0.001
3	681 (65.6)	357 (34.4)		837 (80.6)	191 (18.4)	10 (1.0)	
4	361 (55.4)	291 (44.6)		505 (77.5)	138 (21.2)	9 (1.4)	
5	337 (59.5)	229 (40.5)		438 (77.4)	111 (19.6)	17 (3.0)	
> 5	273 (55.3)	221 (44.7)		347 (70.2)	110 (22.3)	37 (7.5)	
Missing	64 (61.5)	40 (38.5)		76 (73.1)	25 (24.0)	3 (2.9)	
Dementia			0.025				0.314
Normal (MMSE ≥ 27)	1050 (62.4)	633 (37.6)		1306 (77.6)	331 (19.7)	46 (2.7)	
Impaired (MMSE < 27, consultee participant, known dementia)	159 (55.4)	128 (44.6)		212 (73.9)	64 (22.3)	11 (3.8)	
Missing	507 (57.4)	377 (42.6)		685 (77.4)	180 (20.4)	19 (2.1)	
ADL			0.032				0.103
Independent	1218 (61.2)	772 (38.8)		1559 (78.3)	384 (19.3)	47 (2.4)	
Dependent in ≥ 1	332 (56.3)	258 (43.7)		441 (74.7)	128 (21.7)	21 (3.6)	
Missing	166 (60.6)	108 (39.4)		203 (74.1)	63 (23.0)	8 (2.9)	
IADL			< 0.001				< 0.001
Independent	1258 (61.8)	776 (38.2)		1615 (79.4)	380 (18.7)	39 (1.9)	
Dependent in ≥ 1	270 (52.7)	242 (47.3)		357 (69.7)	121 (23.6)	34 (6.6)	
Missing	188 (61.0)	120 (39.0)		231 (75.0)	74 (24.0)	3 (1.0)	
BMI (kg/m²)			0.354				0.001
< 18.5	12 (52)	11 (48)		15 (65)	6 (26)	2 (9)	
18.5–24.9	441 (57.7)	323 (42.3)		590 (77.2)	146 (19.1)	28 (3.7)	
25.0–29.9	570 (62.3)	345 (37.7)		732 (80.0)	165 (18.0)	18 (2.0)	
30.0–34.9	276 (61.6)	172 (38.4)		344 (76.8)	94 (21.0)	10 (2.2)	
35.0–39.9	111 (59.0)	77 (41.0)		137 (72.9)	44 (23.4)	7 (3.7)	
> 40.0	47 (64)	27 (36)		48 (65)	26 (35)	0 (0)	
Missing	259 (58.6)	183 (41.4)		337 (76.2)	94 (21.3)	11 (2.5)	

Values in parentheses are percentages. BCS, breast-conserving surgery; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; CCI, Charlson Co-morbidity Index; MMSE, Mini Mental State Examination; ADL, activities of daily living; IADL, instrumental activities of daily living. * χ^2 test for trend.

and ultimately completion mastectomy in 55. Of the 463 procedures resulting in positive margins, the surgical margin was recorded as 0 mm in 143 (30.9 per cent), 1 mm in 259 (55.9 per cent), and more than 1 mm or no distance recorded in the remaining 61 (13.2 per cent). BCS was the main procedure in 1716 breasts, with adjuvant radiotherapy administered to 1432 (80.9 per cent).

Of 2854 breast operations, 1138 (39.9 per cent) were mastectomies, with reconstruction in 32 (2.8 per cent). Adjuvant therapy was administered after 363 of 1138 (31.9 per cent). Median tumour size was larger in the mastectomy group (30 *versus* 18 mm; $P < 0.001$).

In terms of axillary surgery, ALND was undertaken in 575 of 2854 axillary procedures (20.1 per cent), SLNB in 2203 (77.2 per cent) and no axillary surgery was performed in 76 (2.7 per cent). In the ALND group, positive lymph nodes were documented 560 of 575 (97.4 per cent) or the patient proceeded straight to ALND owing to clinically positive nodes; a positive SLNB was followed by ALND in 117 cases. Of 2320 SLNBs documented as the first axillary procedure, positive lymph nodes were recorded in 472 (20.3 per cent) and no lymph node involvement in 1846 (79.4 per cent); data were missing for the remaining two procedures. Completion ALND

Table 2 Baseline tumour characteristics of surgical population

	Breast surgery type		Axillary surgery type			Total (n = 2855)
	BCS (n = 1716)	Mastectomy (n = 1138)	SLNB (n = 2203)	ALND (n = 575)	No axillary surgery (n = 76)	
Tumour size (mm)*						
0–9	214	56	241	18	11	270
10–19	709	217	807	103	16	926
20–29	526	293	631	159	29	819
30–39	163	230	263	123	7	393
≥ 40	88	335	242	168	13	423
Missing	16	7	19	4	0	23
Median (range)	18 (0–100)	29 (0–210)	20 (0–155)	30 (0–210)	22 (0–120)	
Tumour grade						
1	312	81	359	26	8	393
2	952	595	1246	263	38	1547
3	431	441	569	279	24	872
Missing	21	21	29	7	6	42
Oestrogen receptor status						
Positive	1535	910	1924	460	61	2445
Negative	167	210	254	110	13	377
Missing	14	18	25	5	2	32
HER2 status						
Positive	149	194	225	111	7	343
Negative	1470	892	1870	433	59	2362
Missing	97	52	108	31	10	149
Focality						
Unifocal	1520	834	1849	442	63	2354
Multifocal	58	207	179	79	7	265
Missing	138	97	175	54	6	235
Axillary node stage						
N0	1331	594	1846	14	65	1925
≥ N1	383	536	355	560	4	919
Missing	2	8	2	1	7	10

BCS, breast-conserving surgery; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; HER2, human epidermal growth factor receptor 2. * $P < 0.001$, BCS *versus* mastectomy (χ^2 test).

was undertaken after only 117 of 472 positive SLNBs (24.8 per cent). Postoperative radiotherapy was administered after 257 of the remaining 355 (72.4 per cent). Thus, SLNB was the only axillary procedure for 2203 breast cancers.

Impact of age, co-morbidity, frailty and dementia on type of surgery

Univariable analysis was initially performed to identify associations between type of surgery and patient factors. Age was a significant predictor of mastectomy, with the youngest age group having a rate of only 29.9 per cent compared with 59.1 per cent in the oldest group ($P < 0.001$) (Table 1). Age was also a significant predictor of having no axillary surgery, with a rate of 1.4 per cent in the youngest

age group compared with 8.6 per cent in the oldest group ($P < 0.001$).

Increasing co-morbidity scores were associated with increasing mastectomy rates; the rate was 34.4 per cent in the group a CCI score of 3, compared with 44.7 per cent in the group with a CCI of above 5 ($P < 0.001$). Rates of no axillary surgery rose steadily as the co-morbidity burden increased (1.0 per cent for CCI score 3 *versus* 7.5 per cent for score above 5; $P < 0.001$).

Impaired cognitive function was associated with higher rates of mastectomy (37.6 *versus* 44.6 per cent in groups with normal *versus* impaired cognitive function; $P = 0.025$). There was a slightly higher rate of no axillary surgery in the dementia group, but this was not statistically significant (2.9 per cent *versus* 3.8 per cent in those with impaired cognitive function; $P = 0.314$).

Frailty, as measured by the ADL, showed an association with mastectomy; the rate was 38.8 per cent in the group of patients who were independent in all ADLs compared with 43.7 per cent when the patients were dependent in one or more ADL domain ($P = 0.032$). Moreover, a higher rate of no axillary surgery was observed in the frailer group, although this did not reach statistical significance (2.4 *versus* 3.6 per cent; $P = 0.103$). For IADL, there was an association between frailty and mastectomy rate (38.2 *versus* 47.3 per cent in groups that were independent *versus* not independent in all domains of IADL; $P < 0.001$). The group that was independent in all domains of IADL also had a lower rate of no axillary surgery (1.9 *versus* 6.6 per cent; $P < 0.001$).

In multivariable analysis, co-variables identified for the mastectomy model were age, preoperative tumour size and preoperative nodal status. Tumour size was the strongest predictor of whether a patient underwent mastectomy or BCS. Age was also a significant independent predictor, as was preoperative nodal status, which may reflect the close association between tumour size and nodal status (Table 3). Co-variables identified for the axillary surgery model were age, preoperative tumour size, preoperative nodal status, CCI score, IADL and BMI. Preoperative nodal status and tumour size were significant predictive factors for undergoing ALND. Increasing age, co-morbidity burden and frailty (as determined by IADL) were all associated with higher rates of no axillary surgery (Table 3).

Complications and mortality

Surgical complications were classified by type and severity using the CTCAE system²⁷, and further categorized as systemic or local wound complications. For analysis of complication rates, patients who underwent mastectomy and/or ALND were classified as having major surgery (1321 procedures); the remaining patients who had BCS with either SLNB or no axillary surgery were classified as having minor surgery (1533 procedures) (Fig. 1).

In total, 551 of 2854 operations (19.3 per cent) resulted in complications; some patients had more than one adverse event. The total number of complications, excluding seromas, was 761 (Table S1, supporting information). The overall rate of systemic complications, including cardiorespiratory problems, stroke, DVT or pulmonary embolism, was 59 of 2854 (2.1 per cent). As expected, major surgery had significantly higher rates of complications than minor surgery, but the rate was very low overall (2.9 *versus* 1.4 per cent; 95 per cent c.i. for difference in rates 0.5 to 2.6 per cent; $P = 0.005$). There was no clear association between systemic complications and age, co-morbidity, frailty or cognitive capacity.

Table 3 Multivariable analysis of type of surgery

	Odds ratio	P
Type of breast surgery (n = 2854) (mastectomy <i>versus</i> BCS*)		
Node-positive before surgery	2.30 (1.82, 2.91)	< 0.001
Tumour size (mm)	1.07 (1.06, 1.09)	< 0.001
Age (years)	1.06 (1.05, 1.08)	< 0.001
Type of axillary surgery (n = 2854)		
SLNB <i>versus</i> no surgery*		
Node-positive before surgery	1.02 (0.35, 2.97)	0.970
Tumour size (mm)	1.02 (0.99, 1.04)	0.231
Age (years)	0.91 (0.87, 0.96)	< 0.001
CCI score	0.72 (0.62, 0.84)	< 0.001
IADL	1.26 (1.06, 1.49)	0.008
BMI (kg/m ²)	1.02 (0.98, 1.06)	0.406
ALND <i>versus</i> no surgery*		
Node-positive before surgery	23.05 (7.87, 67.56)	< 0.001
Tumour size (mm)	1.05 (1.02, 1.08)	< 0.001
Age (years)	0.92 (0.87, 0.97)	< 0.001
CCI score	0.75 (0.63, 0.88)	< 0.001
IADL	1.17 (0.96, 1.42)	0.127
BMI (kg/m ²)	1.04 (1.00, 1.09)	0.062

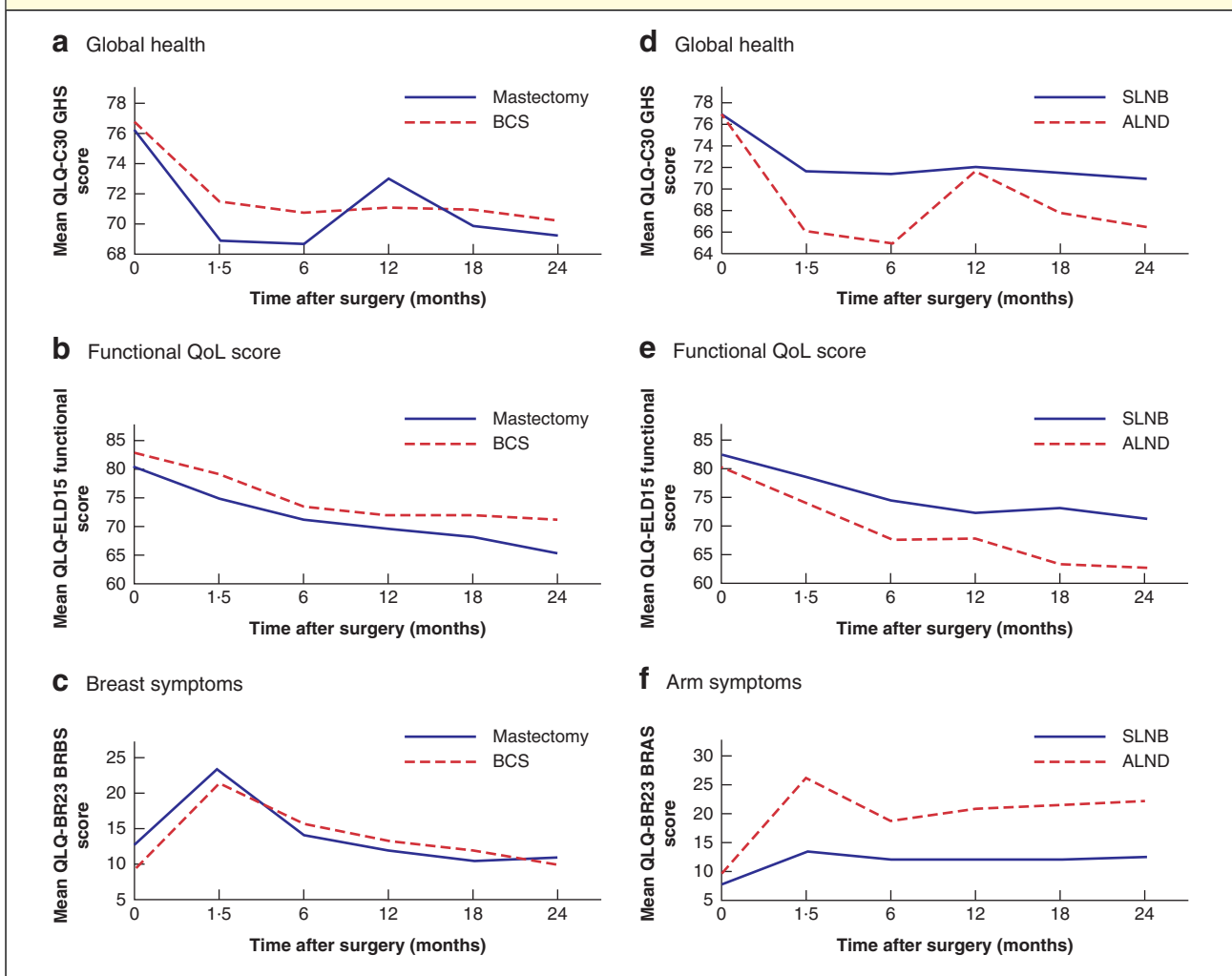
Values in parentheses are 95 per cent confidence intervals. *Reference group. BCS, breast-conserving surgery; SLNB, sentinel lymph node biopsy; CCI, Charlson Co-morbidity Index; IADL, instrumental activities of daily living; ALND, axillary lymph node dissection.

Local wound complications included haematoma, infection and wound dehiscence. Seroma was excluded from this analysis as it is an expected consequence of breast surgery and causes minimal harm (Table S1, supporting information). The seroma rate in the present cohort was 25.4 per cent. In total 525 operations (18.4 per cent) resulted in local wound complications. These were more common with major than minor surgery (22.7 *versus* 14.7 per cent; 95 per cent c.i. for difference 5.2 to 10.9 per cent; $P < 0.001$). There was no correlation with age, co-morbidity or cognitive status, but a positive association with frailty (ADL) on univariable analysis (22.7 *versus* 17.7 per cent in frail *versus* non-frail groups; 95 per cent c.i. for difference 1.4 to 8.6 per cent; $P = 0.006$). In terms of return to the operating theatre for local complications, there were five haematoma evacuations, one wound debridement and closure, and two patients had drainage and excision of a chronic seroma cavity.

There were no deaths reported within 30 days of surgery or attributable to surgery in this large prospective series.

Influence of surgery on quality of life

Patients who had mastectomy had a significant drop in scores on the global health status domains of the QLQ-C30

Fig. 2 Change in mean quality-of-life scores over time by type of surgery

a Global health, **b** functional quality-of-life (QoL) and **c** breast symptom scores after mastectomy and breast-conserving surgery (BCS); and **d** global health, **e** functional QoL and **f** arm symptom scores after sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND). Higher scores denote better QoL on global health status domains (**a,b**), better function (**c,d**) and worse symptoms (**e,f**).

questionnaire at 6 weeks compared with those who had BCS (mean 68.9 *versus* 71.44; 95 per cent c.i. for difference 0.74 to 4.32; $P = 0.006$), although there was no difference by 6 months (Fig. 2a). Scores on the functional domain of the QLQ-ELD15 questionnaire decreased in both groups after surgery, but patients who underwent mastectomy had significantly lower scores and this difference persisted; scores continued to deteriorate in both groups to the 2-year mark (65.58 *versus* 71.13; 95 per cent c.i. for difference 2.34 to 8.75; $P = 0.001$) (Fig. 2b).

Women who had ALND showed a significant drop in QLQ-C30 global health status scores at 6 weeks compared with those who had SLNB, and this difference persisted at

2 years after operation (66.43 *versus* 70.80; 95 per cent c.i. for difference 1.38 to 7.36; $P = 0.004$) (Fig. 2d). Similarly, there was a continual decline throughout the study interval in scores on the functional domains of the QLQ-ELD15 questionnaire in both ALND and SLNB groups, although scores were significantly lower after ALND (62.50 *versus* 71.10 at 2 years; 95 per cent c.i. for difference 4.72 to 12.48; $P < 0.001$) (Fig. 2e).

Body image scores (QLQ-BR23 BRBI) were significantly lower in the mastectomy group than the BCS group at all time points, especially immediately after surgery (82.54 *versus* 92.15; 95 per cent c.i. for difference 7.90 to 11.32; $P < 0.001$), although a difference was already present at

baseline (91.8 *versus* 94.5; 95 per cent c.i. for difference 1.43 to 4.03; $P < 0.001$).

Patients who underwent mastectomy initially had significantly poorer QoL scores in the breast symptoms domain of the QLQ-BR23 compared with those who had BCS (23.52 *versus* 21.43 at 6 weeks; 95 per cent c.i. for difference 0.32 to 3.85; $P = 0.021$) (Fig. 2c). However, this had changed by 6 months after treatment, with the BCS group having worse scores (14.09 *versus* 15.61 for mastectomy *versus* BCS; 95 per cent c.i. for difference in scores 0.01 to 3.05; $P = 0.048$). By 2 years, there was no difference in scores (10.87 *versus* 9.86; 95 per cent c.i. for difference 0.62 to 2.63; $P = 0.223$). Patients who had ALND had significantly poorer QoL scores in the arm symptoms domain of the QLQ-BR23 than those who underwent SLNB, and this difference persisted at 2 years (22.22 *versus* 12.71; 95 per cent c.i. for difference 6.52 to 12.50; $P < 0.001$) (Fig. 2f).

Discussion

In this large, prospective, multicentre cohort study of women aged at least 70 years with operable breast cancer treated between 2013 and 2018, 83.4 per cent had surgery as primary treatment. Limitations of the study include its non-randomized nature, meaning that there may be some inherent bias. Additionally, there were issues with completeness of data, and data were imputed when deemed appropriate³¹.

BCS was the most common operation (60.1 per cent). The rate of mastectomy varied according to tumour size, multifocality, and patient age and fitness. The overall mastectomy rate (39.9 per cent) is similar to that reported in the recent NABCOP audit¹¹. After BCS procedures with positive margins, further operation, as recommended in UK guidelines¹⁸ extant at the time of the study, was not undertaken in 71.1 per cent of breasts. However, it is worth noting that global and European guidelines^{35,36} during this interval accepted 'no tumour at the inked margin' rather than 'margin more than 1 mm' as the definition of a clear margin, and this may have begun to influence practice in the UK. Similarly, contrary to recommended practice during the study interval, ALND was not carried out after 75.2 per cent of 472 positive SLNBs, although no distinction was made between macrometastases and micrometastases, which may explain why some patients did not proceed to ALND. During the study period there was a trend towards a de-escalation of axillary surgery after the publication of, among others, the Z11¹⁹ and AMAROS²⁰ trials, which demonstrated that omitting further axillary surgery and/or axillary radiotherapy provides adequate regional control in women with one to two positive

sentinel nodes; some 20 per cent had no axillary surgery at all. For some of these patients, this reflects concerns about frailty and co-morbidity, but there is also increasing recognition that the axilla may be being overtreated in clinically node-negative diseases³⁷.

Reconstruction after mastectomy was rare, occurring after only 2.8 per cent of procedures, which is much lower than the national average of over 20 per cent for patients of all ages. The rate of reconstruction is known to fall after a threshold of approximately 70 years of age, and a woman's age has previously been shown to be the single most important factor in predicting whether they are offered reconstruction¹⁵. This may reflect the reluctance of surgeons to undertake major surgery in the older population with an increased rate of co-morbidities and frailty, or a lack of willingness of patients to undergo this type of procedure¹⁵. Similarly, the rate of therapeutic mastoplasticity was low at only 3.8 per cent, likely reflecting the same concerns about surgical morbidity, the risk of fat and nipple necrosis in patients with predominantly fatty breasts, and a higher risk of vascular insufficiency.

Analysis of treatment allocation showed that age was a significant determinant of both types of breast and axillary surgery, with rates of mastectomy doubling between the youngest and oldest age groups. It is important to note that some patients in the youngest age group will have undergone breast screening mammography, so there may have been a higher proportion of small, screen-detected tumours in this group, but also older patients have been shown to be less breast aware and thus present with larger tumours^{5,10}. Rates of ALND increased with age in line with higher rates of nodal involvement in older cohorts⁸, and rates of no axillary surgery increased sixfold between the youngest and oldest groups, potentially reflecting a trend towards less aggressive management in clinically negative axillas in light of recent trials¹⁹, particularly where SLNB is not expected to influence staging or further treatment choices. Rates of mastectomy also rose with increasing levels of co-morbidity, dementia and frailty in univariable analysis, possibly reflecting a desire to avoid radiotherapy in frailer, less fit women. Higher rates of omission of axillary surgery were also seen in patients with increased levels of co-morbidity and frailty, which again is likely to reflect treatment decisions being related to the shorter life expectancy in these patients.

The rate of systemic complications was low at 2.1 per cent, and there were no surgery-related deaths in the cohort, reaffirming that surgery for breast cancer in the older population is safe. This study included a selected subgroup of patients deemed suitable for surgery. Although rates of local complications were higher at 18.4 per cent,

only 0.3 per cent required a return to theatre. As expected, rates of lymphoedema were higher in the major surgery group and occurred more commonly after ALND than SLNB³⁸, although the rate in this series was very low overall (26 of 2854, 0.9 per cent). This may reflect the relatively short follow-up of only 2 years, and that only symptomatic lymphoedema as reported by the patients was captured, indicating a degree of under-reporting. QoL scores in the arm symptoms domain were significantly worse in patients undergoing ALND compared with SLNB, suggesting that even in the absence of overt lymphoedema, these patients have symptoms following axillary clearance. This was further supported by the significantly lower scores on the global health status domains of the QLQ-C30 questionnaire after ALND compared with SLNB.

Scores on the breast symptoms domain of the QLQ-BR23 indicated that symptoms were worse immediately after surgery in those undergoing mastectomy, but by 6 months patients in the BCS groups had more symptoms overall, which may be due to the addition of radiotherapy in this period. Patients who underwent mastectomy also had significantly lower QLQ-C30 global health status scores at 6 weeks than those who had BCS, although there was no difference at 6 months. As expected, body image was worse in patients who had mastectomy than those who underwent BCS. These differences were already present at the baseline assessment, which could be a result of patients anticipating the surgery, or may reflect that patients opting for mastectomy already had lower body image scores contributing to their decision. Further work is needed in this area. It is worth noting that some of the differences in mean scores were small when taken in context of the 0–100 scale, so may be of little clinical or practical importance. For example, for EORTC QLQ-C30 global health status, it has been suggested that a difference of 8 points or more is important³⁹.

Breast and axillary surgery are low risk in selected patients in the elderly breast cancer population, although not without complications or impact on QoL, and this should be taken into account. Age remains an independent predictor of the type of treatment an older women with breast cancer receives.

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.