

Outcomes of complex oncoplastic breast surgery in older women. Analysis of data from the Age Gap cohort study

Ratul Quddus^{a,1}, Jessica Banks^{a,1}, Jenna L. Morgan^a, Charlene Martin^a, Malcolm WR. Reed^b, Stephen Walters^c, Kwok Leung Cheung^d, Annaliza Todd^a, Riccardo Audisio^e, Tracy Green^f, Deirdre Revell^f, Jacqui Gath^f, Kieran Horgan^g, Chris Holcombe^h, Rishi Parmeshwarⁱ, Alastair Thompson^j, L. Wyld^{a,*}

^a Department of Oncology and Metabolism, University of Sheffield Medical School, Beech Hill Road, Sheffield, S10 2RX, UK

^b Brighton and Sussex Medical School, Falmer, Brighton, UK

^c Clinical Trials Research Unit, School for Health and Related Research, University of Sheffield, UK

^d University of Nottingham, Royal Derby Hospital, Uttoxeter Road, Derby, DE22 3DT, UK

^e University of Gothenberg, Sahlgrenska Universitetssjukhuset, 41345, Göteborg, Sweden

^f Yorkshire and Humber Consumer Research Panel, UK

^g Dept of Breast Surgery, Bexley Cancer Centre, St James's University Hospital, Leeds, LS9 7TF, UK

^h Liverpool University Hospitals Foundation Trust, Prescott Street, Liverpool, L7 8 XP, UK

ⁱ University Hospitals of Morecambe Bay, Royal Lancashire Infirmary Ashton Road, Lancaster, Lancashire, LA1 4RP, UK

^j Department of Surgery, Baylor College of Medicine, One Baylor Plaza, Houston, TX, USA

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1. Introduction

Modern breast cancer surgery aims to achieve optimal cancer excision whilst maintaining the aesthetic of the breast. Oncoplastic surgery aims to optimise breast aesthetics without compromising oncology outcomes using a range of complex surgical techniques. Women who require a mastectomy are offered post mastectomy breast reconstruction (PMBR) and those who require breast conservation surgery (BCS) may be offered a range of therapeutic mammoplasty (ThM) techniques to achieve a better aesthetic outcome and/or facilitate removal of a larger tumour volume. These more complex surgeries have a higher rate of adverse events, take longer to perform and may not be desired by all women [1]. They are rarely performed in older women due to concerns about increased adverse event rates and clinician perception that older women may value breast aesthetics less than younger women [2]. In addition older women themselves may regard aesthetic issues as less of a priority [3] and be more reticent to undergo more complex and potentially morbid surgery.

There is little specific data available about the prevalence, selection criteria and outcomes for these surgeries in older women. The prevalence of complex oncoplastic surgery (COS, PMBR/ThM) in women over

70 is lower than in younger women, with only 4–14% of women >70 having COS, compared to 42% in those <70 [4]. Few studies specific to this age group have been published and studies with wider age ranges rarely present data about the older age group specifically. There is therefore little available data regarding outcomes of COS for women >70. The outcomes for these techniques are well documented in younger women and demonstrate that they are well tolerated and result in substantial improvements in QoL when compared to mastectomy alone [5,6] although data on the QoL benefits of ThM compared to BCS are less easy to interpret [7].

Data show that older women are more likely to undergo COS if the option is discussed with the surgeon at length and any fears or questions are communicated [8]. It is possible that due to the lack of convincing data and potentially preconceived bias by physicians [9], older women are offered COS less frequently. Those that do undergo COS are a highly selected subgroup of fitter women at the lower end of the over 70 age range [10]. There is very little data about the QoL impacts of COS in older women.

This study aimed to determine the characteristics of older women having COS and their surgical outcomes (adverse events and QoL) in a large, prospectively collected cohort of older women with early breast

* Corresponding author. Department of Oncology and Metabolism, University of Sheffield, Sheffield, S10 2RX, UK.

E-mail address: l.wyld@sheffield.ac.uk (L. Wyld).

¹ Denotes joint first authorship.

cancer [11].

2. Methods

2.1. Study design

The Age Gap study was a multicentre, prospective, observational study which recruited women over age 70 with early breast cancer from breast units in England and Wales between 2013 and 2018 [12]. This study represents an unplanned secondary analysis of the pre-existing dataset. An abbreviated summary of the main study method is presented below and is reported in detail elsewhere [13].

2.2. Ethics and research governance approvals

Ethics approval (12/LO/1808) and research governance approvals were obtained. All patients gave written informed consent (or their proxies in cases of women with cognitive impairment).

2.3. Recruitment

The study recruited women age 70 or over with operable, invasive breast cancer (Tumour Node Metastasis (TMN) staging: T1-3 (and some limited T4 if operable) N0-2 M⁰). Women were followed up for 2 years. The study recruited across 56 sites in England and Wales.

2.4. Inclusion and exclusion criteria (abridged)

Inclusion: Age over 70, operable breast cancer.

Exclusion: Previous breast cancer within 5 years, cognitive impairment and no available proxy available to give consent.

2.5. Baseline data collection and outcomes

Data were collected on a range of measures at baseline and at 6 weeks, 6, 12, 18 and 24 months. These included measures of fitness, tumour characteristics, treatments, adverse events, and QoL. Measures are summarised below.

At diagnosis, tumour characteristics (size, grade, nodal status, staging and subtype) were recorded. A comprehensive geriatric assessment was performed including: age; activities of daily living (ADL) [14], instrumental activities of daily living (IADL) [15]; comorbidities (Charlson Co-morbidity Index, CCI) score [16]; cognition (Mini-Mental State Examination, MMSE) [17]; functional status, assessed via the Eastern Cooperative Oncology Group (ECOG PS) Performance Status [18] and deprivation status, assessed using the Index of Multiple Deprivation (IMD) score [19].

The surgical procedure was categorised as mastectomy with or without reconstruction (Mx or post mastectomy breast reconstruction (PMBR), simple breast conservation surgery (sBCS) or therapeutic mammoplasty (ThM). Surgical groups were categorised as simple surgery (Mx/BCS) and complex oncoplastic surgery (COS, PMBR/ThM). Patients who underwent bilateral surgery were documented as two individual procedures. Axillary surgery was also recorded and divided into no axillary surgery, sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND). Data collection about surgery technique was categorical allowing for breast conservation surgery or therapeutic mammoplasty or mastectomy with or without reconstruction. Second and subsequent surgeries were also reported to allow us to collect data about delayed reconstructions, re-excisions of margins and mastectomy for margins. Data on the precise technique of reconstruction was requested but not the precise technique of therapeutic mammoplasty.

Quality-of-life was evaluated preoperatively and at the follow-up intervals listed above. Three different tools were used: the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaires (EORTC-QLQ) generic cancer QoL instrument (the C30

[20]), the breast cancer specific module (EORTC-QLQ-BR23 tool [21]) and a non-cancer specific generic QoL instrument the EuroQoL five dimension, five level, tool (EQ-5D-5L) [22].

Adverse events were documented at each scheduled follow up visit and classified using the Common Terminology Criteria for Adverse Events (CTCAE) system. They were categorised as systemic (atelectasis, myocardial infarction, deep vein thrombosis (DVT)/pulmonary embolism (PE), stroke, allergic reaction, arrhythmia and somnolence) or local wound complications (neuropathy, haematoma, functional impairment, lymphedema, haemorrhage, wound pain, non-infectious wound complications, skin necrosis, infection, and seroma).

2.6. Statistical analysis

Descriptive statistics are presented as means plus standard errors if normally distributed data or medians plus ranges if non-normally distributed.

Categorical data were compared using Chi squared. Continuous data were compared using t tests for normally distributed data or Mann Whitney U test if non-Normally distributed. P values were accepted as significant if less than 0.05. Statistical analyses were performed using Microsoft Excel (version 16.17, United Kingdom) and IBM SPSS 26.0.

Baseline geriatric assessment domains and their difference in relation to surgical group were analysed using χ^2 and the Mann-Whitney U test. Adverse event frequency in each group was collated and the difference between both groups was analysed using χ^2 . These adverse events were categorised into systemic and local complications and the difference in frequency of both groups was compared using the same method. Quality of life was analysed according to the scoring manual for each tool [23]. Analysis was performed on the subsequent mean values using the independent t-test. Analysis was performed on the whole cohort comparing sBCS/Mx to COS. Further analysis was performed comparing patients who underwent sBCS versus ThM and Mx versus PMBR, in a 2 to 1 matched analysis. Patients were manually matched for age, comorbidities (using the Charlson comorbidity score), level of physical function (using ADL and IADL scores) and axillary surgery.

3. Results

The study recruited 3460 women, of whom 665 were excluded (non-surgical treatment, metastatic disease at diagnosis or missing data)

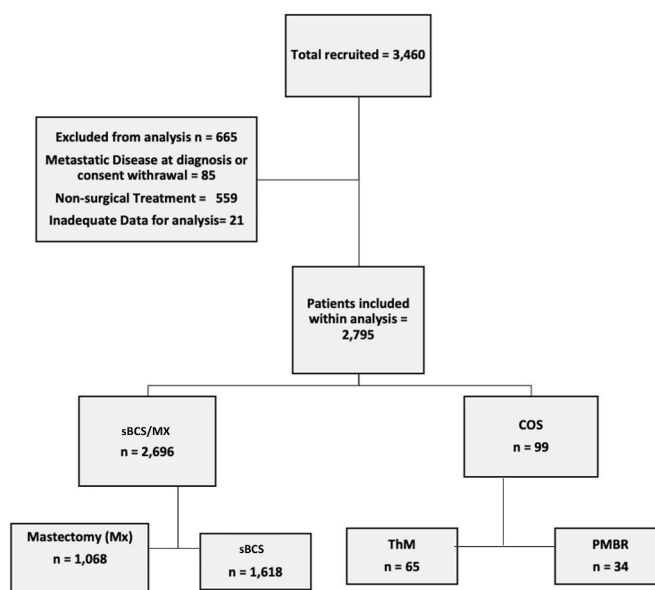


Fig. 1. STROBE (strengthening the reporting of observational studies in epidemiology) diagram, showing patient dispositions within the study.

(Fig. 1) leaving 2795 women in this analysis. Of these, 2696 (96.5%) patients underwent simple surgery (sBCS or Mx) while the remaining 99 (3.5%) patients had complex oncoplastic surgery (ThM or PMBR). Of the 2696 patients in the simple surgery group, 1068/2696 (39.6%) had mastectomy and 1618/2696 (54.5%) had sBCS. Of those having COS, 65/99 (65.7%) patients had ThM while 34/99 (34.3%) had PMBR. The majority of the PMBR surgeries were implant based (31/34 (91.2%)) with the remainder being largely DIEP flap (autologous) reconstructions. The present analysis excluded patients who did not undergo any form of surgery, (Fig. 1).

The characteristics of the patients, according to whether they had SS or COS are displayed in Table 1. Women in the simple surgery (sBCS/Mx) group were older than those who had COS (median age: sBCS/MX:

Table 1
Patient baseline characteristics according to type of surgery received. Scores compared using Chi squared or Mann-Whitney U test.

Variable	Simple Surgery (BCS/Mx)	Complex Oncoplastic Surgery (ThM/PMBR)	Total	Statistical analysis
No. Of patients (%)	2696 (96.6)	99 (3.5)	2795 (100.0)	
Age (Years) ^a	76 (70–95)	73 (70–87)		P < 0.001
BMI ^a	27.1 [24–30]	27.2 (23.9–30.1)		P = 0.106
Mini mental state examination score category MMSE (%)				P = 0.856
Normal	1753 (94.2)	67 (93.1)	1820 (94.2)	
Mild	79 (4.2)	3 (4.2)	82 (4.2)	
Moderate	28 (1.5)	2 (2.8)	30 (1.6)	
Severe	1 (0.1)	0 (0.0)	1 (0.1)	
Activities of Daily Living ADL (%)				P=0.020
Independent	1882 (77.2)	78 (87.6)	1960 (77.6)	
Dependent in ≥1 activity	556 (22.8)	11 (12.4)	567 (22.4)	
Instrumental Activities of Daily Living ADL (%)				P=0.001
Independent	1917 (79.7)	81 (94.2)	1998 (80.2)	
Dependent in ≥1 activity	489 (20.3)	5 (5.8)	494 (19.8)	
Age-Adjusted Charlson Comorbidity Index (%)				P = 0.081
0	1259 (48.5)	53 (57.0)	1312 (48.8)	
1	479 (18.4)	11 (11.8)	490 (18.2)	
2	539 (20.8)	23 (24.7)	562 (20.9)	
3	320 (12.3)	6 (6.5)	326 (12.1)	
ECOG performance status (%)				P=0.006
Fully Active	1857 (72.5)	77 (85.6)	1934 (72.9)	
Other	705 (27.5)	13 (14.4)	718 (27.1)	
Radiotherapy to the breast or chest wall (%)				P = 0.947
Yes	1694 (62.8)	60 (62.5)	1754 (62.8)	
No	1002 (37.2)	36 (27.5)	1038 (37.2)	

^a Median (range).

76 years (range 70–95), COS: 73 (range 70–87), (P < 0.001)), more likely to be functionally independent in basic activities (activities of daily living (ADL) score ≥1: sBCS/Mx: 1882/2,696, 77.6%; COS: 78/99, 87.6%, P = 0.020) and higher level functions (instrumental activities of daily living (IADL) score ≥1: sBCS/Mx: 1917/2,696, 79.7%; COS: 81/99, 94.2%, P = 0.001). Performance status was also better in the COS group (ECOG performance status sBCS/Mx: 72.5%; COS: 85.6%, P = 0.006). The simple surgery group also had a higher burden of comorbidities (non-age adjusted CCI score of ≥6: sBCS/Mx: 468/2,600, 18.0% versus COS:8/93, 8.6%; P = 0.022, age adjusted CCI score of >3: sBCS/MX: 320/2,593, 12.3% versus COS: 6/93, 6.5%; P = 0.081). No differences were found in BMI, cognition score, or deprivation levels between the two groups.

3.1. Patient characteristics

3.2. Adverse events

Complications were recorded using the CTCAE classification system according to type and degree of severity. They were also categorised as local wound complications and systemic complications. The overall rate of all complications monitored over the two-year follow-up period were very similar between the two groups.

Adverse events by type are summarised in Table 2 below. Whilst there was no overall difference according to broad local or systemic groups, when individual adverse events were examined, some significant differences were seen. Several specific complications were more frequent after COS including wound pain (COS: 6/99, 6.1% versus sBCS/Mx: 69/2,755, 2.5%, P = 0.030), infection (COS: 11/99, 11.1% versus sBCS/Mx: 165/2,755, 6.0%, P = 0.037) and functional difficulties (COS: 5/99, 5.1% versus sBCS/Mx: 41/2,755, 1.5%, P = 0.006).

A matched analysis was also performed to compare complications between ThM vs sBCS and Mx vs PMBR (Table 3). Patients were manually matched on a two-to-one basis for age, comorbidities, functional status and axillary surgery. Some significant differences in adverse events remained for the matched analysis. For the ThM vs sBCS

Table 2
Specific adverse events experienced in each group for all patients. These data show specific complications and their frequency in each group compared using Chi squared.

ADVERSE EVENT	ALL PATIENTS		
	Simple Surgery (sBCS/Mx) (2696) % (n)	Complex Oncoplastic surgery (ThM/PMBR) (99) % (n)	P Value
ATELECTASIS	0% (1/2696)	0% (0/99)	0.850
STROKE	0.1% (2/2696)	0% (0/99)	0.789
MYOCARDIAL INFARCTION	0.1% (4/2696)	0% (0/99)	0.704
DVT/PE	0.1% (3/2696)	0% (0/99)	0.743
ARRHYTHMIA	0.8% (22/2696)	1% (1/99)	0.817
ALLERGIC	0.1% (3/2696)	0% (0/99)	0.743
SOMNOLENCE	1.1% (30/2696)	1% (1/99)	0.941
LYMPHEDEMA	0.9% (24/2696)	2% (2/99)	0.237
NEUROPATHY	1.5% (41/2696)	1% (1/99)	0.698
FUNCTIONAL DIFFICULTIES	1.5% (41/2696)	5% (5/99)	0.006
WOUND PAIN	2.5% (69/2696)	6% (6/99)	0.030
NON-INFECTIOUS WOUND COMPLICATIONS	1.6% (45/2696)	2% (2/99)	0.766
SKIN NECROSIS	0.5% (14/2696)	3% (3/99)	0.001
INFECTION	6.0% (165/2696)	11% (11/99)	0.037
HAEMORRHAGE	1.1% (30/2696)	2% (2/99)	0.387
HAEMATOMA	6.9% (189/2696)	4% (4/99)	0.272

Table 3

Specific adverse events experienced in each group for matched patients. These data show specific complications and their frequency in each group compared using Chi squared.

MATCHED PATIENTS						
ADVERSE EVENT	Breast Conserving surgery (128) % (n)	Therapeutic Mammoplasty (64) % (n)	P Value	Mastectomy (66) % (n)	Mastectomy Reconstruction [33] % (n)	P Value
ATELECTASIS	0% (0/128)	0% (0/64)	1.00	0% (0/66)	0% (0/33)	1.00
STROKE	0% (0/128)	0% (0/64)	1.00	0% (0/66)	0% (0/33)	1.00
MYOCARDIAL INFARCTION	0% (0/128)	0% (0/64)	1.00	0% (0/66)	0% (0/33)	1.00
DVT/PE	0% (0/128)	0% (0/64)	1.00	0% (0/66)	0% (0/33)	1.00
ARRHYTHMIA	0.8% (1/128)	1.5% (1/64)	1.00	1 (1.5)	0% (0/33)	1.00
ALLERGIC	0% (0/128)	0% (0/64)	1.00	0% (0/66)	0% (0/33)	1.00
SOMNOLENCE	0% (0/128)	1.5% (1/64)	0.33	0% (0/66)	0% (0/33)	1.00
LYMPHEDEMA	1.6% (2/128)	1.5% (1/64)	0.75	0% (0/66)	3% (1/33)	0.34
NEUROPATHY	1.6% (2/128)	0% (0/64)	0.55	0% (0/66)	0% (0/33)	1.00
FUNCTIONAL DIFFICULTIES	0.8% (1/128)	10.1% (7/64)	0.002	0% (0/66)	3% (1/33)	0.34
WOUND PAIN	0% (0/128)	8.8% (6/64)	0.001	1.5% (1/66)	6% (2/33)	0.257
NON-INFECTIOUS WOUND COMPLICATIONS	3.2% (4/128)	3% (2/64)	0.98	1.5% (1/66)	3% (1/33)	1.00
SKIN NECROSIS	0% (0/128)	0% (0/64)	1.00	0% (0/66)	9% (3/33)	0.035
INFECTION	6.4% (8/128)	8.8% (6/64)	0.56	1.5% (1/66)	15% (5/33)	0.015
HAEMORRHAGE	0% (0/128)	3% (2/64)	0.11	1.5% (1/66)	0% (0/33)	1.00
HAEMATOMA	5.6% (7/128)	1.5% (1/64)	0.272	9% (6/66)	6% (2/33)	0.37

group this included wound pain (sBCS 0/128, 0% versus ThM 6/64, 8.8%, $p = 0.001$) and functional difficulties (sBCS 1/128, 0.8% versus ThM 7/64, 5.1%, $p = 0.002$). For the Mx vs PMBR analysis, wound necrosis (Mx 0/66, 0% versus PMBR 3/33, 9%, $p = 0.035$) and infections (Mx 1/66, 1.5% versus PMBR 5/33, 15%, $P = 0.015$) were significantly higher in the PMBR group.

3.3. Quality of life outcomes

QOL outcomes were compared between sBCS versus ThM and Mx versus PMBR following patient matching as previously described. Three key domains were assessed in the EORTC-QLQ-BR23 questionnaire; the first of those being Arm Function. Mean scores for patients who underwent mastectomy alone compared to PMBR and scores of those who had sBCS compared to those who had ThM were not significantly different at any point. Mean patient scores followed a similar trend for Pain Scores. For all four groups pain scores increased at 6 weeks and then gradually declined over the following 24 months. For the Mx versus PMBR group, the PMBR group had significantly higher pain scores at 6 weeks (Mx 6.18 ± 21.3 Vs PMBR 17.3 ± 16.7 , diff 11.12, 95% CI -19.8, 2.44), which correlates to a moderate clinical difference in pain. However, from 6 months onwards there was no difference in pain scores between these two groups. There was no difference in pain scores between the ThM versus sBCS group at any point. A higher score was regarded as a better outcome in the Body Image domain The QLQ-BR23 does not specifically ask about cosmetic outcomes, however questions focus on feeling less attractive or less feminine as a results of the disease or treatment. There was no statistically significant difference in body image scores between sBCS versus ThM or Mx versus PMBR groups throughout the 24-month follow-up period. Body Image scores slightly declined across all groups over the 24 months.

The mean Global Health and Burden of Health domains of the EORTC-QLQ-C30 questionnaire were similar at 24 months between sBCS versus ThM or Mx versus PMBR groups. At 6 weeks the global health score was significantly worse in the PMBR group compared to Mx (Mx -7.78 ± 17.23 vs PMBR -16.38 ± 17.23 , mean difference 8.6 95% CI -0.023, 17.14), this correlates to a mild clinical difference, but this difference did not persist beyond 6 months. Global Health scores showed a constant trend in decline (worsening global health) throughout the entirety of the follow up period across all surgical groups.

Mean EQ-5D-QL scores from patients who underwent sBCS versus ThM or Mx versus PMBR were not significantly different, and the outcomes worsened throughout the follow up period for both groups. No

significant differences in mean scores were noted by specific surgery type.

Quality of life outcomes are shown in Figs. 2 and 3. Supplementary tables for mean QOL score in each domain at baseline, 6 weeks, 6, 12 and 24 months are included in the appendix.

4. Discussion

Older women (>70 years) have a much lower rate of complex oncoplastic surgery than rates reported in younger cohorts, with only 3.5% of this large multicentre cohort of women undergoing more complex surgery. This compares with the UK National GIRFT audit where a reconstruction rate of 27% in the overall population was noted, which dropped to <10% in patients over 70 years. The UK NABCOP audit found a similar rate of 5% of women having PMBR in their population of UK women over age 70. This study demonstrates that older women who are offered COS are at the lower end of the over 70 age range, have lower rates of co morbidities and better physical function than those who have sBCS/Mx. These findings are aligned with other recent studies [24] and are hypothesised to be due to both patient preference and the reluctance of doctors to offer COS to older patients, due to concerns regarding increased comorbidities in older patients, and the belief that older patients may not desire the potentially improved cosmetic outcomes of COS [4,25–28].

Rates of adverse events overall were similar between the two groups which likely reflects the selected nature of the women who had this more complex surgery. In this selected group, rates of adverse events are similar to rates in younger women and should be included in discussions regarding treatment options for women who are fit for this type of surgery. Decisions around cancer treatment should be a shared process between patient and surgeon and although some studies have highlighted older women may be more passive in their decision making [29] shared decision making is still valued by this group and older women who are involved in decision around their care report high levels of satisfaction with their choices and low decision regret [30].

Throughout the two-year follow up period the overall complication rate in the sBCS/Mx group was 39.2% (1079/2755) and in the COS group was 34.3% (34/99). It is difficult to compare these rates with those found in the current literature as these surgical techniques have not been grouped in other studies. Despite the large sample size and multicentre nature of this study, it is solely UK based and consequently due to differences in treatment approach and baseline patient populations globally, the generalisability of the results may be limited. The

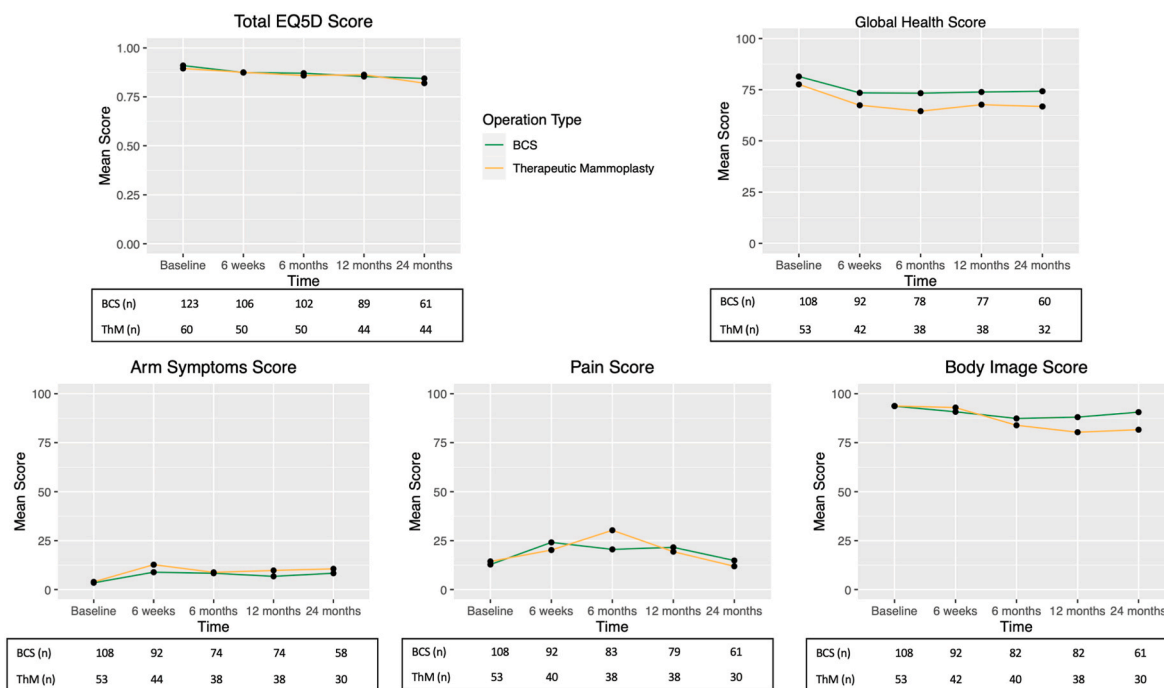


Fig. 2. Profile of QOL outcomes for ThM versus sBCS, mean score reported at 6 weeks, 6, 12 and 24 months for matched patients, number of patients at specific time point for each QOL outcome reported below the corresponding graph.

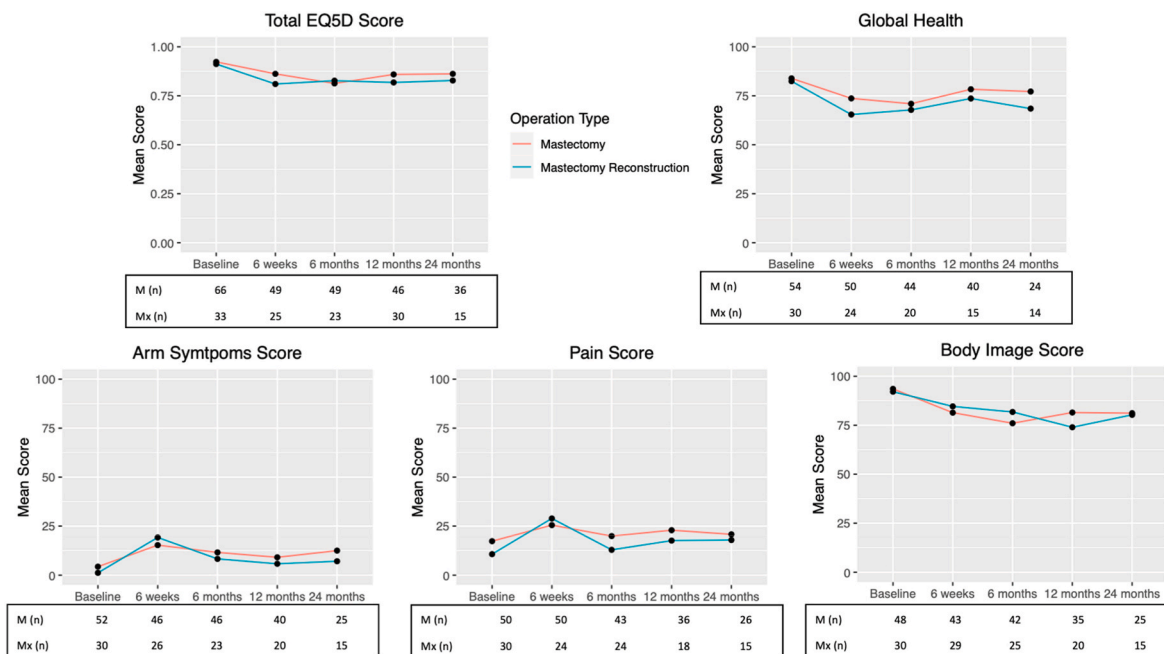


Fig. 3. Profile of QOL outcomes for Mx versus PMBR, mean score reported at 6 weeks, 6, 12 and 24 months for matched patients, number of patients at specific time point for each QOL outcome reported below the corresponding graph.

similarity in the rate of adverse events between the groups is supported by a recent study which explored complication rates in older BR patients against older non-BR patients and found there to be no difference between the two [24]. In the same study, which compared complication rates in women over 60 with PMBR against those without, a significantly higher rate of skin flap necrosis was observed in the breast reconstruction group, similar to this study [24]. The increase in rates of infection, wound pain and functional difficulties noted in our cohort is consistent with the existing literature [10]. Complication rates are generally higher

following complex surgery, and both the increased duration and more invasive nature of these procedures have previously been associated with increased rates of post-operative infection and pain [31].

QOL outcomes varied by time and surgery type but in general did not differ by surgical group. The trend for both patient groups in all of the domains reported showed a sharp deterioration in outcomes 6 weeks postoperatively, the EORTC-QLQ-BR23 domains showed improvements in mean score following this however the majority of the other domains did not. The lack of significant difference in overall QOL and overall

body image scores was unexpected as this is dissimilar to the findings in other literature. A significant factor behind the development of COS techniques is for the purpose of improved cosmesis and body image, which is noted in studies demonstrating superior body image outcomes in BR patients compared to non-BR patients [32,33]. A study which compared the QOL outcomes of BR against non-BR in older women concluded that BR patients are more satisfied with their outcomes [8]. The contrasting observations from this study may be the result of the low proportion of patients who underwent COS. Another explanation for this finding may be due to differences in measuring QOL outcomes between studies. A recent systematic review on the impact of breast surgery on functional status in older women also found conflicting results with QOL outcomes [34], highlighting that further research with a larger cohort of older women using a fixed measure for QOL outcomes is required.

5. Limitations

Precise details about the therapeutic mastoplasty technique were not collected and the magnitude of this surgery may vary greatly between a minor batwing or vertical scar uplift to a major reduction using a wise pattern technique.

6. Conclusion

Oncoplastic surgery for breast cancer is uncommon in older women with a significant selection bias towards younger, fitter women. Within this highly selected population of older women, oncoplastic surgery is tolerated well with broadly similar rates of adverse events overall and similar quality of life after surgery. There are slightly higher rates of local wound complications. Impacts on aesthetic outcomes were not superior, although this may reflect the fact that the comparator group (simple surgery) for therapeutic mastoplasty includes large numbers of women having small volume breast conservation resections where aesthetic impacts are minimal and a more detailed matched analysis for tumour size would be needed to explore these issues in more detail.

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CRediT authorship contribution statement

Ratul Quddus: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Jessica Banks:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Jenna L. Morgan:** Conceptualization, Data curation,

Investigation, Methodology, Writing – original draft, Writing – review & editing. **Charlene Martin:** Investigation, Project administration, Software, Writing – original draft. **Malcolm WR. Reed:** Conceptualization, Funding acquisition, Investigation, Supervision, Writing – original draft. **Stephen Walters:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Kwok Leung Cheung:** Investigation, Writing – original draft. **Annaliza Todd:** Data curation, Investigation, Writing – original draft. **Riccardo Audisio:** Funding acquisition, Investigation, Writing – original draft. **Tracy Green:** Investigation, Writing – original draft. **Deirdre Revell:** Writing – original draft. **Jacqui Gath:** Funding acquisition, Writing – original draft. **Kieran Horgan:** Investigation, Writing – original draft. **Chris Holcombe:** Investigation, Writing – original draft. **Rishi Parmeshwar:** Investigation, Writing – original draft. **Alastair Thompson:** Investigation, Project administration, Software, Writing – original draft. **L. Wyld:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Supervision, Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2023.107075>.

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