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Review

Factors influencing cosmetic outcome of breast-conserving treatment in breast cancer: a narrative review

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Background: A deformed breast following Breast-Conserving Treatment (BCT) is influenced by an array of factors encompassing final cosmesis. This overview examines the factors that may influence cosmetic outcome for BCT patients. *Methods*: Literature search was performed using PubMed and EMBASE databases. Research articles published in English (1990–2018) pertaining to patients that had previously undergone unilateral BCT for breast cancer were included. *Results*: 42 articles were used for our final analysis that utilized subjective and objective tools to assess cosmetic outcome. Factors can be allocated as patient, tumor, surgery, radiotherapy or systemic therapy associated. Based on significance in both univariable as well as multivariable analysis and frequency of reporting, extensiveness of primary tumor resection, tumor size, tumor location, adjuvant radiotherapy and adjuvant chemotherapy, were the factors affecting cosmetic outcome the most. *Conclusions*: In this study, we reviewed and discussed several patient-, tumor- and treatment related factors affecting cosmetic outcome. Many different tools, either subjective or objective, are observed worldwide.

Keywords

Breast-conserving therapy; Breast cancer; Cosmetic outcome

1. Introduction

Breast cancer is the most common malignancy in women worldwide [1]. The surgical treatment of breast cancer may consist of a mastectomy or BCT. Daily practice shows that, based on tumor characteristics and personal decision making, the majority of women will chose to undergo BCT when possible. Meanwhile, BCT has established itself as a feasible option in the treatment of early breast cancer. Various articles have reported the equivalence of BCT compared with mastectomy in terms of disease-free and overall survival rates [2, 3]. The two important goals of BCT are to achieve an optimal local tumor control as compared to mastectomy and a good cosmetic outcome [4]. Various patient, tumor and treatment-related factors are known to influence the cosmetic outcome. In this study, we overviewed the methods of assessing cosmetic outcome and analyzed the factors that might affect this outcome.

2. Materials and methods

2.1 Statement of search strategies used and sources of information

We conducted a narrative review to analyze the practice of cosmetic outcome in breast-conserving treatment (BCT). Data for this review was selected by searching Pubmed and EMBASE, using the search terms 'breast neoplasms', 'breast cancer', 'breast tumor', 'mammary cancer', 'mammary neoplasm', 'breast carcinoma', 'ductal carcinoma *in situ*', 'DCIS', 'intraductal carcinoma', 'breast conservation', 'breast preservation', 'breast sparing', 'esthetic', 'cosmetic', 'cosmesis-factor', 'prediction'. Only articles published in English between February 1990 and July 2018 were used for this analysis. In addition to that, the selected articles included patients that had previously undergone unilateral BCT (without oncoplastic surgery) including external irradiation of the whole breast (with boost or no boost) for breast cancer. Fig. 1 shows the search strategy with the number of hits for individual databases Pubmed and EMBASE. More detailed search strategy is included in the addendum. The articles found were assessed by at least two authors for content and usability. Details of the publications and populations is depicted in Table 1.

2.2 Methods of cosmesis evaluation

In addition to patient factors, a change in breast appearance depends on various treatment modalities, such as type of surgery, systemic therapy (chemotherapy, hormonal therapy), radiotherapy or a combination of these. Most cosmetic changes take place within the first 3 years after BCT, after which the situation stabilizes [48–51]. During this period, the assessment of cosmesis is an important topic in daily clinical practice since "Patient Reported Outcome Measurements (PROMS)" are considered to be increasingly important. In literature, different methods of assessing cosmesis have been described. Most investigators used some form of subjective measurement, others used more objective ones or a combination of both to analyze breast cosmetic outcome. An often validated and the most frequently used subjective scoring system is 'The Harvard scale', categorizing patient's cosmesis into four categories of excellent, good, fair or poor [52]. Others used 4-point scales i.e., 'not at all different, slightly dif-

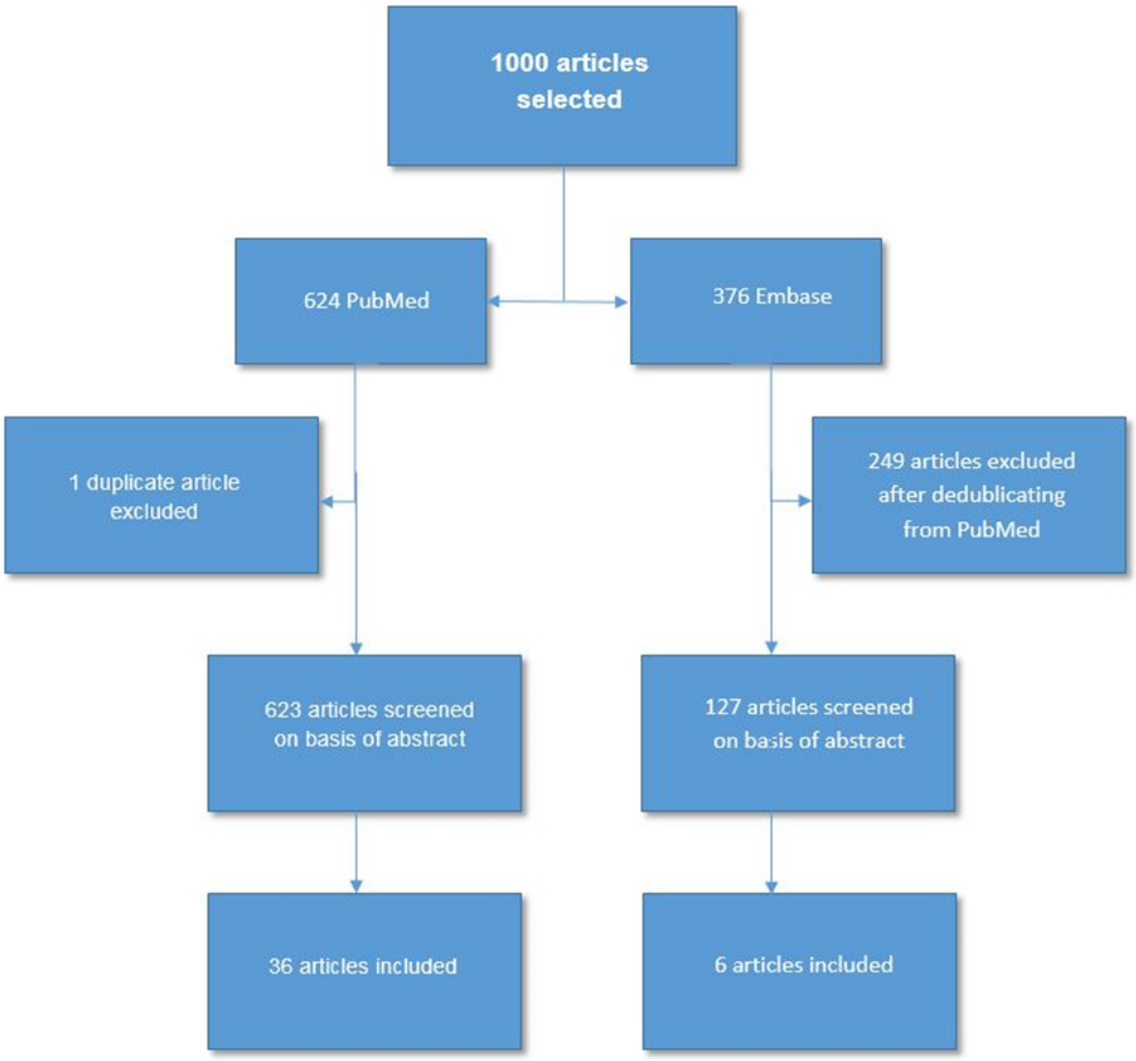

Fig. 1. Search strategy with the number of hits of the individual databases Pubmed and EMBASE.

ferent, moderately different, extremely different', 'very good, good, sufficient, insufficient', 'poor, fair, good, very good' and finally 'very satisfied, satisfied, moderately satisfied, not satisfied'. Objective scoring systems for example are, 'breast retraction assessment (BRA)', 'Breast Cancer Conservative Treatment.cosmetic results (BCCT.core software)', 'percentage breast retraction index (pBRA)' and symmetry measurements (for example BCE (Breast Compliance Evaluation)). The most commonly used subjective instrument for assessing the cosmetic consequences of breast-conserving treatment is some 4-point scale, whether or not mentioned under the Harvard scale [52]. BCCT.core software is the most commonly used objective tool.

3. Factors influencing cosmesis in breast cancer

Factors that influence cosmesis after BCT can be divided into three groups i.e., patient related, tumor related, or therapy related factors. In the studies that were reviewed, some factors arise from univariable analysis and others arise from multivariable analysis. Table 2 shows factors affecting cosmetic outcome that arose at least once from multivariable analysis ($P \leq 0.05$). However, in some reviewed studies, the same factors were only considered in univariable analysis. The factors in both univariable and multivariable analysis are discussed below. The outcome measures only included overall cosmetic outcome or (a)symmetry. Factors that have a significant association with another subarea related to the cosmetic outcome were considered (for example, only scar as an outcome, or only breast size).

3.1 Patient related factors

Univariable and multivariable analysis showed some significant factors, albeit not always consistent. A larger breast size appeared to be a unequivocal risk factor for poor cosmesis [7, 14, 15, 17, 20, 24, 33, 35]. Patients with larger breasts tend to have more breast retraction [33]. However, there was one study that found that small breasts affected cosmetic outcome negatively [37].

Table 1. Details of the publications and populations.

Study	Year	Treatment	Population (n)	Study design	Outcome assessment tool	Assessed by
Volders [5]	2018	RT, RTb	128	prospective	4-point scale (cosmesis and satisfaction)	pat
Brouwers [6]	2018	RT, RTb, CHT, HT	2421	prospective	BCCT.core, Harvard, Sneeuw	pro + pat
Negenborn [7]	2017	RT, RTb	109	unknown	7-item questionnaire (4-point scale)	pro
Hennigs [8]	2016	CHT, RT	21	prospective	BCTOS	pat
Ojala [9]	2016	RT, RTb	379	retrospective	BCTOS, questionnaire (5-point scale)	pat
Shiina [10]	2016	RT	250	unknown	Harvard, BCCT.core	pro
Yu [11]	2016	RT, RTb, CHT, HT	51	retrospective	BCCT.core, Harvard	pat
Dahlback [12]	2016	RT, RTb, CHT, HT	297	prospective	6-item questionnaire (4-point scale)	pat
Hennigs [13]	2015	RT	294	prospective	BCCT.core	pro
Olfatbakhsh [14]	2015	RT, CHT	103	retrospective	5-item questionnaire (0-10 rating scale)	pro
Ozmen [15]	2014	RT, CHT, HT	284	retrospective	Harvard	pro
Foersterling [16]	2014	RT	709	prospective	BCTOS	pat
Lyngholm [17]	2013	RT, RTb, CHT, HT	214	retrospective	4-point scale, BCCT.core	pro + pat
Medina-Franco [18]	2013	RT, CHT	133	unknown	BCTOS, photos (breast volume difference)	pro + pat
Kelemen [19]	2012	RT, RTb, CHT, HT	198	prospective	4-point scale	pro + pat
Barnett [20]	2011	RT, RTb, CHT, HT	1014	prospective	photos (3-point scale) + clinical assessment (3 or 4-point)	pro
Waljee [21]	2008	RT	714	retrospective	BCTOS	pat
Wang [22]	2008	RT	46	retrospective	4-point scale	pro + pat
Johansen [23]	2007	RT, RTb, CHT, HT	266	prospective	4-point scale	pro + pat
Cardoso [24]	2007	RT, CHT, HT	120	retrospective	Harvard scale	pro
Chie [25]	2007	RT, RTb, CHT, HT	424	retrospective	symmetry index, 4-point-scaleb	pro
Arenas [26]	2006	RT, RTb	145	retrospective	4-point scale	pro + pat
Fedorcik [27]	2006	RT, RTb	100	prospective	5-item questionnaire (0–10 score)	pro + pat
Pawlaczyk [28]	2005	RT, RTb, CHT, HT	67	prospective	4-point scale, photos (symmetry measurements)	pro
Fabry [29]	2005	RT, RTb, CHT, HT	40	retrospective	pBRA	pro
Yamamoto [30]	2003	RT	106	unknown	4-point scale	pro
Cochrane [31]	2003	RT	151	retrospective	3-point scale	pro + pat
Deutch [32]	2003	RT, RTb, CHT, HT	265	retrospective	4-point scale	pro
Johansen [33]	2002	RT, RTb, CHT, HT	266	prospective	4-point scale	pro + pat
Cetintas [34]	2002	RT, RTb, CHT, HT	96	retrospective	5-point scale	pro + pat
Vrieling [35]	2000	RT, RTb, CHT, HT	1141	prospective	pBRA, 6-item questionnaire (4-point scale)	pro
Fujishiro [36]	2000	RT, RTb, CHT, HT	206	retrospective	pBRA, Harvard	pro
Al-Ghazal [37]	1999	RT, CHT, HT	254	retrospective	pBRA, photos (4-point scale)	pro
Moro [38]	1997	RT, RTb, CHT	164	retrospective	3-point scale	pro
Mills [39]	1997	RT, RTb	90	retrospective	4-point scale	pro
Taylor [40]	1995	RT, RTb, CHT, HT	458	prospective	4-point scale	pro + pat
Amichetti [41]	1995	RT, RTb, CHT, HT	225	retrospective	4-point scale	pro + pat
Tsouskas [42]	1990	RT, CHT	151	prospective	BCE- measurement, 4-point scale, dichotomous scale	pro + pat
Hamilton [43]	1990	RT, RTb, CHT	120	unknown	11-item questionnaire (5 items on cosmesis, 4-point scale)	pat
Hallahan [44]	1989	RT, RTb, CHT, HT	207	retrospective	4-point scale	pro + pat
Pezner [45]	1985	RT, RTb, CHT	41	unknown	BRA	pro
Patterson [46]	1985	RT, RTb, CHT	32	retrospective	questionnaire (3-point scale)	pat

BCCT.core, Breast Cancer Conservation Treatment. cosmetic results software; Harvard, Harvard scale, a 4-point scale (Harris *et al.*, 1979) [9]; Sneeuw, Sneeuw questionnaire, 9-item questionnaire (Sneeuw *et al.*, 1992) [47]; BCTOS, Breast Cancer Treatment Outcome Scale; (p)BRA, (percentage) Breast Retraction Assessment index; BCE measurement, Breast Compliance Evaluation measurement.

pat, patients; pro, health professional.

Explored treatment characteristics: CHT, chemotherapy; RT, radiotherapy; RTb, radiotherapy-boost; HT, hormonal therapy.

Patients with higher BMI reported increasingly higher scores of breast asymmetry, and thus a poorer cosmetic result [14, 17, 18, 21, 24].

Age seems to influence the outcome but is not necessarily related to either young or old age group [5, 17, 21, 22, 24, 33, 40, 45]. In this context pBRA values increased positively with increasing age ($P < 0.02$), which means that more retraction of the treated breast was seen [45]. Another study showed that patients > 60 years demonstrated a lower proportion of excellent cosmetic scores [40]. Postmenopausal status was significantly associated with poor cosmesis after BCT ($P = 0.02$ and $P < 0.002$) [24, 34, 40]. However, other studies described a young age as a risk of an unacceptable outcome [5, 21, 22]. We conclude that increasing age can be seen as a negative factor effecting cosmetic outcome, albeit not unequivocal in various studies.

Smoking increases the risk of development of fibrosis [OR 2.4, CI (1,1; 4.9), $P = 0.002$] [17] and two studies also reported poor cosmesis related to black race [32, 40].

Table 2. Factors significantly affecting cosmetic outcome in multivariable analysis.

Factors	Study	Cosmesis assessment tool	*P*-value	Odds ratio (95% CI)[a]
Patient related				
Volumetric breast density				
< 13.8% vs ≥ 13.8%	Shiina [10]	Harvard scale	0.0005	4.55 (1.90–11.6)
Body Mass Index kg/m^2				
≥ 25 vs < 25	Lyngholm [17]	4-point	0.001	2.7 (1.5–4.8)
> 25 vs < 25	Olfatbakhsh [14]	0–10 rating scale	0.022	NR
≥ 35 vs < 25	Waljee [21]	BCTOS	0.007	NR
continuous	Cardoso [24]	Harvard	NR	1.24 (1.08–1.43)
Menopausal status	Cetintas [34]	5-point scale	0.0087	NR
Heat exposure (yes vs no)	Chie [25]	4-point scale	0.0152	NR
	Chie [25]	symmetry index	0.00355	NR
Breast size	Johansen [33]	4-point scale	0.05	1.33 (1.00–1.81)
Breast cup size				
EFG vs AB	Negenborn [7]	4-point scale	0.04	3.81 (1.07–13.62)
> D vs < D	Olfatbakhsh [14]	0–10 rating scale	0.04	NR
C and D vs A/B	Vrieling [35]	pBRA	< 0.001	1.17 (1.10–1.26)[c]
Age				
NR	Johansen [33]	4-point scale	0.04	0.97 (0.93–1.00)[b]
continuous	Lyngholm [17]	4-point scale	0.02	3.9 (1.3–11.8)
continuous	Pezner [45]	pBRA	< 0.02	NR
> 60 vs ≤ 60	Taylor [40]	4-point scale	0.007	NR
per 10 years	Volders [5]	4-point scale	0.027	2.1b
51–60 vs 61–70	Waljee [21]	BCTOS	0.04	NR
Smoking				
current vs non/ex	Lyngholm [17]	4-point scale	0.01	3.8 (1.4–10.3)
Race				
black vs white	Taylor [40]	4-point scale	0.002	NR
black vs white	Deutsch [32]	4-point scale	0.0056	NR
Tumor related				
Location (quadrants)				
inferior vs other	Vrieling [35]	4-point scale	< 0.001	0.21 (0.13–0.36)[b]
central/superior vs other	Vrieling [35]	pBRA	0.001	1.21 (1.06–1.37)[c]
lower vs upper/central	Moro [38]	3-point scale	0.015	NR
upper inner vs upper outer	Waljee [21]	BCTOS	0.006	NR
lower outer vs upper outer	Waljee [21]	BCTOS	0.022	NR
upper vs lower	Chie [25]	symmetry index	< 0.0001	NR
lower vs upper	Chie [25]	4-point scale	0.0026	NR
retro areolar	Foersterling [16]	BCTOS	0.003	8.10 (2.10–31.87)
Size				
T2 vs T1	Vrieling [35]	4-point scale	0.005	0.53 (0.34–0.82)[b]
11–20 and > 20 vs ≤ 10 mm	Vrieling [35]	pBRA	< 0.001	1.14 (1.06–1.23)[c]
T2 vs T1	Moro [38]	3-point scale	0.002	NR
continuous	Negenborn [7]	4-point scale	0.028	1.63 (1.06–2.52)
≥ 3 cm < 1 cm	Waljee [21]	BCTOS	0.015	NR
> 2 cm vs ≤ 2 cm	Chie [25]	4-point scale	0.0109	NR
> 2 cm vs ≤ 2 cm	Chie [25]	symmetry index	< 0.0001	NR
continuous	Fabry [29]	pBRA	0.05	NR
continuous	Fedorcik [27]	0–10 rating scale	0.023	NR
pT ≥ 3 vs pT1a/1b	Foersterling [16]	BCTOS	< 0.001	27.35 (4.99–149.83)

Table 2. Continued.

Factors	Study	Cosmesis assessment tool	*P*-value	Odds ratio (95% CI)[a]
Surgery related				
Extensiveness of primary tumor resection				
continuous				
> 100 vs ≤ 100 cm^3	Pezner [45]	pBRA	< 0.001	NR
> 50 vs ≤ 50 cm^3	Taylor [40]	4-point scale	0.0001	NR
51–200 and > 200 cm^3 vs ≤ 50 cm^3	Vrieling [35]	4-point scale	0.002	0.29 (0.12–0.90)[b]
quadrantectomy vs excisional biopsy/wide excision	Vrieling [35]	pBRA	< 0.001	1.19 (1.11–1.28)[c]
continuous	Taylor [40]	4-point scale	0.0001	NR
PBVE (%) < 10.1 vs ≥ 10.1				
continuous	Foersterling [16]	BCTOS	0.017	2.76 (1.20–6.33)
excision volume per 10 cc	Shiina [10]	Harvard scale	0.004	0.28 (0.10–0.68)
	Fedorcik [27]	0–10 rating scale	0.039	NR
	Volders [5]	4-point scale	0.002	0.64
Surgery of the axilla				
axillary clearance	Dahlbäck [12]	4-point scale	NR	2.87 (1.20–6.83)
axillary lymph node dissection vs sentinel node	Fabry [29]	pBRA	0.042	NR
axillary lymph node dissection vs sentinel node				
	Negenborn [7]	4-point scale	0.013	3.09 (1.27–7.52)
Re-excision	Dahlbäck [12]	4-point scale	NR	3.30 (1.19–9.14)
	Waljee [21]	BCTOS	0.013	NR
Scar length/visibility/type				
very visible vs not visible	Cardoso [24]	Harvard scale	NR	29.8 (5.72–155.36)
radial/en bloc/not evaluable vs concentric	Vrieling [35]	pBRA	0.008	0.93/0.94/0.71[c]
Institution where operation was performed	Cetintas [34]	5-point scale (dichotomized)	0.0015	NR
Baseline surgical cosmesis	Barnett [20]	3-point scale	< 0.0005	37.23 (21.5–64.3)
	Brouwers [6]	BCCT.core	< 0.0001	1.80 (1.40–2.33)
Breast complications				
present vs absent	Vrieling [35]	4-point scale	< 0.001	0.34 (0.19–0.61)[b]
Postoperative seroma	Waljee [21]	BCTOS	0.005	NR
Radiotherapy related				
Radiation therapy	Waljee [21]	BCTOS	0.008	NR
	Yu [11]	BCCT.core	0.047	1.697 (1.006–2.863)
	Chie [25]	symmetry index	0.0006	NR
Lymph node irradiation	Chie [25]	4-point scalea	0.0028	NR
	Lyngholm [17]	4-point scale	0.004	3.8 (1.5–9.5)
High boost dose	Brouwers [6]	BCCT.core	< 0.0001	1.83 (1.33–2.54)
Boost volume per 10 cc	Brouwers [6]	BCCT.core	< 0.0001	1.04 (1.02–1.05)
Boost technique: photon vs electron	Brouwers [6]	BCCT.core	< 0.0001	1.98 (1.31–3.01)
Boost vs no boost	Vrieling [35]	4-point scale	< 0.001	0.42 (0.27–0.65)[b]
Max. dose central plane (Gy)	Vrieling [35]	pBRA	0.002	1.10 (1.04–1.16)[c]
Electron radiotherapy	Johansen [33]	4-point scale	0.002	2.3 (1.4–4.1)
Number of elapsed days of radiation therapy over 50 days	Cetintas [34]	5-point scale	0.0090	NR
Systemic therapy related				
Concomitant adjuvant chemotherapy (CMF) and radiotherapy	Moro [38]	4-point scale	0.0024	NR
	Chie [25]	symmetry index	0.0136	NR
Adjuvant chemotherapy				
CMF	Johansen [23]	4-point scale	NR	2.2 (1.2–4.2)
NR	Brouwers [6]	BCCT.core	0.032	NR
NR	Johansen [33]	4-point scale	0.02	2.0 (1.1–3.7)

NR, not reported; BCCT.core, Breast Cancer Conservation Treatment. cosmetic results software; Harvard, Harvard scale, 4-point scale (Harris et al, 1979); BCTOS, Breast Cancer Treatment Outcome Scale; pBRA, percentage Breast Retraction Assessment index; CMF, Cyclophosphamide/Methotrexate/5-FU.

[a] Odds ratio represent probability of having a worse cosmetic outcome, unless indicated otherwise.

[b] Odds ratio represents 'probability of having an excellent/good result instead of having a worse cosmetic outcome'.

[c] Value represents ratio from linear regression model instead of odds ratio.

One study found high educational level to be associated with subjective breast asymmetry ($P = 0.02$) [18].

Furthermore, breast symmetry was worse in patients with heat exposure: immersion baths with water temperatures exceeding 40 °C or sauna visits [25].

3.2 Tumor related factors

In most studies, location, size and node positive stage were found to be critically related.

Larger tumors, either defined by T-stage or tumor diameter, obviously need larger excisions (for description of volumes, see below) of breast tissue which may lead to a poorer outcome [7, 9, 13, 15–17, 19, 21, 25, 27, 29, 30, 35, 36, 38].

Several studies reported the effect of the tumor location on cosmesis. In some studies, the inner quadrants appeared to be significantly worse in relation to cosmetic outcome [21, 22, 36, 37], which was followed by tumors in the 12 o' clock position [13, 16]. Others studies reported that tumors in respectively lower and lateral quadrants and retro-areolar gave a poorer cosmesis [15, 16, 21, 35, 37, 38].

Based on these results, we conclude that there is no obvious location that affects cosmesis negatively.

One study described a significantly negative effect ($P = 0.029$) of node positivity on cosmesis [9]. We hypothesize that this is probably related to treatment modalities applied in these patients (see below).

3.3 Surgery related factors

The most common and significant factor frequently described in literature was 'extensiveness of primary tumor resection' [5, 8–10, 13, 16, 24, 27, 28, 35–37, 40, 43–45]. Extensiveness of resection was the major factor associated with breast retraction [45]. Some investigators described the extensiveness of resection in cm^3 [5, 10, 27, 40, 44], while others describe it in weight [8, 9, 13, 16, 24, 37]. It is obvious that this surgical extensiveness is related to the above mentioned tumor related factor: size.

Scar related factors also effected cosmesis [8, 24, 35, 37, 40, 44, 46].

Scar orientation compliance with National Surgical Adjuvant Breast Bowel Project (NSABP) guidelines seems to be an important factor, with a 44% excellent cosmetic rating, compared to 27% for patients with noncompliant scar orientations [40]. Scar length of less than 8 cm directly correlated with better cosmetic results [37, 44, 46].

One study described the type of incision: circular incisions led to the best cosmesis, whereas radial or periareolar incision methods almost equivalently appeared to be worse [8]. Another study concluded that scar visibility was a significant factor for poor esthetic evaluations [24]. Axillary dissection, especially compared to sentinel lymph node biopsy, results in more breast retraction and thus negatively influences cosmetic outcome ($P = 0.042$) [29]. Other studies confirmed such a finding [7, 8, 12, 13, 19]. An axillary lymphadenectomy increased the risk of unfavorable cosmesis approximately by a factor four compared to no axillary surgery ($P = 0.004$) [13].

Reexcision to clear surgical margins also resulted in significantly worse cosmesis [12, 21, 37, 40].

Postoperative complications such as impaired wound healing and infection requiring antibiotics appeared significantly correlated with poor cosmesis [8, 20, 35]. The same was found for postoperative seroma formation ($P = 0.005$) [21] and puncture of seroma ($P = 0.001$) [8].

One study investigated the use of scalpel and scissor versus electrocautery influencing outcome. The use of scalpel plus scissors in BCT resulted in less tissue damage and better cosmetic results at 3-year follow up [30].

We conclude that the extensiveness of surgery either in breast and/or axilla, combined with scar orientation are the most critical factors influencing outcome.

3.4 Radiotherapy related factors

Higher radiation dose and additional radiotherapy-boost are often reported to correlate negatively with the cosmetic result of BCT [6, 8, 11, 19, 21, 26, 32, 33, 35, 37, 40]. It was observed that excellent cosmetic ratings decreased with increasing radiation dose (50 Gy vs $>$ 65 Gy) to the entire breast ($P = 0.02$) [40]. Some studies did not specify the amount of radiation dose in detail, but only described the negative effect of radiotherapy on cosmesis [8, 11, 21]. Patients who received radiotherapy had significantly higher asymmetry scores compared to those without radiation therapy ($P = 0.008$) [21]. Several studies concluded that radiotherapy-boost had the greatest effect on the overall cosmetic outcome after BCT [6, 19, 26, 32, 33, 35], whereby electron boost gave better results than photon boost [6, 19, 33].

It was also observed that axillary lymph node irradiation had a significantly negative impact [17, 23, 25, 43]. Thus, the extensiveness of radiotherapy fields, treatment volume, tangential breast fields vs. three or more fields, all influenced the final outcome ($P = 0.034$) [40].

3.5 Chemotherapy- and hormonal related factors

Despite the fact that chemotherapy and hormonal therapy are systemic modalities, these factors appear to influence the final cosmetic result. In one of the older studies, premenopausal patients who got adjuvant chemotherapy, were compared to postmenopausal patients receiving tamoxifen 30 mg. Patients receiving chemotherapy had poorer cosmetic results ($P = 0.004$) [33]. In other study reports, this negative effect of chemotherapy was confirmed [6, 8, 15, 17, 23, 24, 33]. In various studies, concomitant chemotherapy and radiotherapy was shown to have a profound effect on cosmesis [25, 26, 38]. One study correlated tamoxifen with a worse outcome ($P = 0.025$) [32]. Tamoxifen combined with radiotherapy appeared also significantly associated with more breast fibrosis ($P = 0.004$) [23].

We conclude that adjuvant systemic therapy in general has a negative effect on final cosmetic outcome.

Neoadjuvant chemotherapy (NACT) is increasingly being used in breast cancer treatment. Often, it results in reduction of the tumor (size) and thereby increasing the rate of

BCT [53, 54]. One review described that cosmetic outcome after NACT was divided in two single cohort studies [55]. Both studies showed acceptable cosmetic outcomes. One of these studies compared the satisfaction of patients treated with BCT and oncoplastic breast surgery (OPBS) and patients without OPBS after NACT. The satisfaction about the cosmetic outcome was comparable for both groups (P = 0.52): 86% of the patients were satisfied to very satisfied [56]. Another study concluded that excision volumes were smaller in the patients receiving NACT (P = 0.04). Patients receiving BCT after NACT assessed cosmetic outcome more often as good to excellent compared to patients receiving BCT without NACT (92% vs. 80%, P = 0.03) [57].

Despite the fact that only a few studies specifically investigated the cosmetic outcome of BCT after NACT, we conclude that NACT mostly has a positive effect. The most logical conclusion seems that NACT results in reduction of tumor volume, thus resulting in smaller excisions leading to better cosmesis.

4. Discussion and conclusions

The current narrative review represents a comprehensive overview concerning factors that may influence cosmetic outcome for breast cancer patients treated with BCT. BCT, including radiotherapy, by definition, can lead to deformation of the treated breast which may result in patient dissatisfaction with the final cosmetic outcome. In general most patients (64–92%) assess the cosmetic outcome of their treated breast as excellent to good after BCT [12, 14, 15, 18, 20, 21, 23, 24, 31, 34, 35, 38, 40, 44, 46, 48, 51].

Based on the present data we conclude that no unambiguous agreement exists on assessment tools for cosmetic outcome. Variety of scales and instruments, and combination of these tools, are used to assess cosmesis. The majority of reports use some subjective assessment based on comparison with the untreated breast. Three, or, -more commonly-, four point scales are used to distinguish, using criteria similar to those described by Harris *et al.* [9]. 5-point Likert scales and even an 11-point structured questionnaire are also used to assess cosmetic outcome. Most rating scales are based on assessment of the total cosmetic outcome. Few, however, analyze more details, such as shape, volume, change in nipple position, surgical scar, or color of the skin. Subjective assessments were either performed by patients themselves, by health professionals or both. With the introduction of computer technology, specific software has been developed to objectively assess the cosmetic effects of BCT. Objective measurement of cosmetic outcome with specific software, however, is considered to be the most accurate evaluation of only asymmetry [38, 58].

By reviewing various factors that might influence outcome by multivariable- and univariable analysis we found the following factors to be most relevant (in order of importance): tumor size with concomitant extensiveness of the primary tumor and it's surgical resection (lymph node) irradiation, BMI and age (both higher) and adjuvant systemic therapy. Knowledge of these factors may be important, not only for patients when they are counselled, but also for professionals who treat these breast cancer patients. The comprehensive knowledge of these effective factors can influence a better choice or method of treatment(s) for these patients.

Naturally, some factors cannot be modified, such as age and tumor size. Other factors, however, are potentially modifiable and therefore render an opportunity for improvement of cosmetic outcomes. This relates mainly to surgery and radiotherapy related factors, such as type and location of incision, use of oncoplastic techniques, radiotherapy fields and total volume and indication for a radiotherapy boost. NACT, of course, might influence tumor size and can thus be considered a modifiable modality.

It has been observed that the results of univariable- and multivariable analysis are different, since some of the studies included factors that were found with univariable- but not multivariable analysis. Cosmetic outcome after BCT can be influenced by many factors: if this is not corrected, particularly in non-randomized studies, the findings may be under- or overestimated due to confounding factors.

One limitation in the present review is the fact that in the past few years, surgery- and irradiation techniques, as well as systemic treatment regimes, have been enhanced, changed and further upgraded. Because of this fact, comparison of various different studies over time has become difficult.

We strongly recommend the development by some form of Delphi analysis, with consensus, a universal easily usable uniform objective measuring or scoring instrument for assessment of cosmetic outcome after BCT. We also suggest that using this objective measuring instrument would help a preoperative prediction model to determine the individual cosmetic outcome, which can then be potentially helpful for counselling of breast cancer patients. The present analysis may be helpful in this matter. Since surgical, systemic and irradiation techniques are continuously developing, it remains important to keep evaluating the cosmetic results after BCT.

Author contributions

ABA and RR conceived and designed the review. ABA searched the literature and selected the articles with the help of RR. ABA and LJ retrieved data from the articles and conducted data synthesis. ABA and RR wrote the manuscript. ABA, RR, SMB, LJ and VTH critically reviewed and revised the manuscript and approved its final version.

Ethics approval and consent to participate

Not applicable.

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Conflict of interest

The authors declare no conflict of interest.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at https://ejgo.imrpress.com/EN/10.31083/j.ejgo.2021.03.2285.

Statement of human rights and Statement on the welfare of animals

This article does not contain any studies with human participants or animals performed by any of the authors.

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