Analysis of low-benefit subgroups in breast-conserving surgery: Implications for clinical decision-making (Review)

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Abstract. Breast-conserving surgery (BCS) with radiotherapy is a standard treatment for early-stage breast cancer, offering survival outcomes equivalent to mastectomy while preserving breast appearance and improving quality of life. However, BCS suitability and effectiveness vary notably among patients due to differences in age, comorbidities, tumor biology, breast anatomy and psychosocial factors. Through a systematic review, the present study identified six patient subgroups that may derive limited benefit from BCS followed by radiotherapy. These constituted the elderly with multiple comorbidities, those with ductal carcinoma *in situ*, premenopausal women with aggressive tumor subtypes, patients with cardiac contraindications to radiotherapy, individuals at high risk of poor cosmetic outcomes and those with socioeconomic constraints. For these patients, alternative procedures such as mastectomy with immediate reconstruction may provide improved oncologic or functional results. The present analysis highlights the importance of a personalized, risk-adapted approach to surgical decision-making in breast cancer. By integrating clinical, pathological and sociodemographic variables, the present study supports treatment strategies that are not only valid within oncology but also aligned with the functional needs and psychological well-being of patients.

Contents

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1. Introduction

Globally, breast cancer accounts for ~1/3 of all malignancies in women, with a mortality rate of about 15% among diagnosed cases, and its incidence continues to increase annually (1,2). Breast-conserving surgery (BCS), defined as the removal of the primary tumor along with a rim of healthy tissue while preserving the breast skin and nipple-areolar complex, is now a standard treatment for breast cancer (3). Compared with mastectomy, BCS involves more limited tissue resection, reduces surgical trauma and blood loss and, when followed by radiotherapy, yields oncologic outcomes equivalent to mastectomy in stage I-II disease (4). BCS further preserves breast aesthetics and function, whereas a mastectomy often alters breast morphology with adverse psychosocial consequences (5). BCS may also maintain lactation capacity, reduce postoperative symptoms such as somnolence, nausea and dyspnea (6) and supports psychological resilience by preserving body image and identity, thereby lowering depression risk and enhancing quality of life (7). These combined benefits underpin its acceptance among patients.

Despite these advantages, optimal criteria for patient selection remains undefined. Variations in physical status, breast morphology and tumor characteristics, shaped further by age, ethnicity and sex, introduce heterogeneity that limits the generalizability of BCS outcomes (8). Therefore, the present review conducted a stratified analysis across diverse patient subgroups to refine candidate selection and enable a more individualized, evidence-based application of BCS in clinical practice.

2. Factors affecting BCS

Age. Notable heterogeneity exists in the physical condition, incidence patterns and tumor biology of breast cancer across different age groups, influencing the suitability and outcomes of BCS. Although the incidence of breast cancer in younger women (16.6%) remains relatively low compared with older

populations (83.4%), a steeper increase observed among younger women (1.4% vs. 0.7%) indicates a concerning upward trend in this age group (9). Notably, breast cancer in younger women is frequently characterized by more aggressive tumor phenotypes and a worse prognosis (10), presenting distinct therapeutic challenges. The predominant pathological subtypes in this demographic include invasive lobular carcinoma, medullary carcinoma and, most commonly, invasive ductal carcinoma (11). Invasive ductal carcinoma, the most prevalent histological subtype of breast cancer, is typified by high-grade malignancy, pronounced invasiveness and a strong propensity for axillary lymph node involvement (12). Meta-analyses suggest that, in patients with triple-negative breast cancer (TNBC), BCS may be associated with lower rates of local recurrence, distant metastasis and improved overall survival compared with a mastectomy (13,14). Notably, the relative risk of distant metastasis between BCS and mastectomy appears to diminish with advancing age and longer follow-up durations (15). By contrast, the management of breast cancer in older patients is often complicated by the presence of multiple comorbidities. Elderly individuals are more likely to suffer from chronic conditions, including cardiovascular disease, hypertension and diabetes mellitus (16). These comorbidities not only elevate surgical risk but may also impede postoperative recovery. As such, comprehensive preoperative evaluation is imperative and this will be addressed in detail within the present review.

Ethnicity. Ethnic variation serves a key role in shaping the clinical and epidemiological characteristics of breast cancer. Notably, the overall incidence of breast cancer is lower in Asian populations compared with Western populations (17). Epidemiological studies indicate that White women exhibit the highest incidence (137.9 per 100,000 individuals), followed by Black women (131.3 per 100,000 individuals), whereas Hispanic and Asian women demonstrate comparatively lower rates (104.1 per 100,000 individuals) (9). In addition to incidence, age at diagnosis also differs markedly between populations. Breast cancer in Asian women tends to occur at a younger age, with the majority of cases diagnosed between 45-50 years, in contrast to Western populations, where diagnosis typically occurs at age >60 years (18). For instance, among non-Hispanic White women in the United States, the proportions of breast cancer cases diagnosed before age 40 and between 40-49 years are 2.9 and 12.4%, respectively. By contrast, corresponding figures of diagnosis before 40 and between 40-49 years are notably higher in numerous Asian populations, including 5.2 and 22.8% in China, 5.9 and 27% in Vietnam as well as 9.7 and 22.5% among Asian Indians or Pakistanis, respectively (19).

BMI. With the continuous improvement of global living standards, obesity (defined as BMI ≥30 kg/m^2) is established as a notable public health concern. Accumulating evidence indicates that BMI not only contributes to the pathogenesis of breast cancer but also influences therapeutic outcomes (20-22).

In a large-scale cohort study conducted by Neuhouser *et al* (23) involving postmenopausal women aged 50-79, a positive linear association was observed between increasing BMI and breast cancer risk. Women classified as overweight (BMI ≥25 kg/m^2) and obese (BMI ≥30 kg/m^2) exhibited a 2.16- and 2.63-fold higher risk, respectively, compared with those of a normal weight. By contrast, in premenopausal women, elevated BMI was associated with a protective effect against breast cancer, demonstrating an inverse association (24). These differences may be partly explained by differential estrogen regulation. Cancer proliferation is estrogen dependent. In postmenopausal women, the principal source of estrogen is the aromatase-mediated conversion of adrenal and ovarian androgens. This mechanism often results in local tumor estrogen concentrations up to 10-fold higher than circulating levels and is associated with a 15% increase in estrogen levels among those who develop postmenopausal breast cancer (25). In postmenopausal women, excess adipose tissue promotes this androgen aromatization, leading to elevated circulating estrogen levels (26). Specifically, marked increases in estrone, estradiol and free estradiol are associated with an increased BMI. Obese women consequently exhibit greater endogenous estrogen exposure, further potentiated by higher leptin concentrations (27).

Surgical satisfaction also appears to be BMI-dependent. Compared with women of normal weight, dissatisfaction with aesthetic outcomes following BCS was notably more prevalent among overweight (13.0%) and obese (18.1%) patients, compared with just 4.1% in the normal-weight group (28). Further investigations into the interplay between BMI and breast cancer subtypes have yielded noteworthy patterns. Mean BMI values were highest among patients with luminal-type tumors, followed by those with TNBC and HER2-positive subtypes. In parallel, mean tumor size was greatest in TNBC and smallest in HER2-positive types. Stratified by BMI, average tumor diameters were 3.99 cm for patients with BMI <25, 4.13 cm for those with BMI between 25-29.9 and 4.30 cm for patients with BMI ≥30 (29). In addition, previous studies have also shown an association between BMI and larger tumor sizes (30,31). The potential explanations include delayed diagnosis in obese women, more advanced disease at presentation or technical challenges in tumor detection (32). These findings suggest that elevated BMI is associated with larger tumors, which may necessitate wider excision margins during BCS. Consequently, BMI constitutes an important consideration in the surgical planning and aesthetic outcomes of breast-conserving treatment.

Occupation. Employment serves as a key source of income, health insurance and social engagement, factors that may be particularly important for patients diagnosed with breast cancer. Beyond its practical benefits, work can impart a sense of purpose and positively influence quality of life. Among patients with breast cancer, occupational status appears to be associated with differences in surgical decision-making, particularly in the choice between BCS and mastectomy. Evidence suggests that employed patients are more likely to favor BCS. Moreover, patients undergoing BCS are notably less likely to experience prolonged work absence, defined as missing >1 month of work, or to discontinue employment altogether, compared with those who undergo mastectomy (33). These findings underscore the potential role of employment in shaping treatment preferences and postoperative recovery trajectories. However, the association between occupation and

surgical choice remains contested. A study has reported no notable relationship between professional engagement and the type of surgery selected (34), highlighting the need for further investigation into the multifactorial determinants of surgical decision-making in breast cancer care.

Education. Educational attainment is established as a notable determinant in surgical decision-making among patients with breast cancer. Evidence indicates that patients with a college degree or higher are more likely to choose BCS compared with those that have a high school education or less (35). Stratified analyses further demonstrate that educational level functions as an independent predictor of surgical choice, with a positive association between the level of education and the likelihood of selecting BCS (36). These findings suggest that educational attainment is a key factor influencing treatment preferences. As education level increases, patients tend to exhibit more nuanced informational needs and a heightened emphasis on postoperative quality of life and aesthetic outcomes, domains in which BCS offers distinct advantages. Accordingly, the growing complexity of patient expectations in higher-educated populations underscores the importance of integrating educational background into individualized surgical planning.

Family history of cancer. A growing body of evidence indicates that a family history of cancer notably influences surgical decision-making in patients with breast cancer (37). A number of well-established genetic factors, notably pathogenic variants in BRCA1, BRCA2, tumor protein p53 and partner and localizer of BRCA2, are marked contributors to the risk of hereditary breast cancer (38-40). Notably, this elevated risk persists subsequent to the initial diagnosis. Specifically, among premenopausal women, the 10-year cumulative incidence of contralateral breast cancer is reported to be 33% for BRCA1 mutation carriers and 27% for BRCA2 mutation carriers (38). This high residual risk frequently necessitates more aggressive prophylactic or therapeutic management strategies. Patients with a familial history, particularly of breast cancer, are more likely to opt for total mastectomy or nipple-sparing mastectomy (NSM) with immediate reconstruction, driven largely by a heightened psychological concern regarding disease recurrence. A number of these patients perceive mastectomy as a more definitive approach, offering a greater sense of security by facilitating complete tumor removal and potentially minimizing the need for secondary surgical intervention.

History of benign breast disease. A clinical study demonstrated that patients with a history of benign breast disease are more likely to select mastectomy (33%) compared with BCS (20%) (41). This preference is primarily attributed to long-standing psychological burden as numerous patients harbor concerns that their prior benign condition may predispose them to malignancy and they frequently express heightened fear of cancer recurrence following BCS. In addition, apprehension regarding adjuvant radiotherapy has been identified as an additional factor contributing to the preference for mastectomy. Fear of radiation-related side effects and treatment burden further deters some patients from choosing BCS, underscoring the multifaceted nature of surgical decision-making in breast cancer care (42).

3. Patient subgroups with suboptimal outcomes following BCS and adjuvant therapy

Elderly breast cancer patients with comorbidities. Elderly individuals are more likely to suffer from chronic conditions, including cardiovascular disease, hypertension, and diabetes mellitus (12). These underlying diseases not only complicate the perioperative course but also impose additional burdens on postoperative recovery and long-term outcomes.

Evidence from a population-based study revealed an association between comorbidity burden and 5-year mortality. Among patients without comorbidities, the 5-year mortality rates were 10.0% for those receiving radiotherapy and 17.6% for those not receiving radiotherapy. For patients with a single comorbidity, the corresponding rates increased to 14.5 and 23.7%, respectively. In those with ≥2 comorbidities, 5-year mortality reached 20.5% with radiotherapy and 33.3% without (43). These findings underscore the impact of comorbidities on postoperative survival, particularly in patients who forego adjuvant radiotherapy. Notably, patients with ≥2 comorbidities exhibited a 15.7% absolute increase in 5-year mortality compared with those without.

Accordingly, the formulation of treatment strategies for elderly patients with breast cancer should be guided by a comprehensive evaluation of physical status and comorbid conditions. For patients with limited physiological reserve or contraindications to chemotherapy, radical mastectomy or BCS without radiotherapy may represent viable options (44). In addition, studies suggest that early-stage breast cancer in elderly patients tends to exhibit a more indolent biological behaviour, with reduced metastatic potential. In such cases, BCS alone may achieve oncologic outcomes comparable to or surpassing those obtained with the addition of radiotherapy or chemotherapy (45,46). For elderly patients in good overall health, the decision to pursue BCS combined with adjuvant therapies should be made after a thorough risk-benefit assessment tailored to individual clinical profiles (47).

Ductal carcinoma in situ (DCIS). DCIS represents the earliest form of breast cancer, characterized by the presence of atypical epithelial cells confined to the ductal-lobular system without evidence of stromal invasion (48). As a non-invasive lesion, DCIS is defined by localized epithelial proliferation within the milk ducts and does not exhibit metastatic potential at this stage. A key clinical feature of DCIS is its non-palpable nature, which presents challenges for achieving complete microscopic excision during surgery. The inability to clearly delineate lesion boundaries increases the likelihood of residual disease, thereby compromising the effectiveness of BCS in this patient population.

Comparative studies between BCS and mastectomy have consistently shown higher recurrence rates following BCS in patients with DCIS, regardless of the use of adjuvant radiotherapy (49-51). In a study conducted by Thompson *et al* (52), with a median follow-up of 5 years, ipsilateral recurrence rates were 0.8% for patients undergoing mastectomy, 4.1% for those receiving BCS with radiotherapy and 7.2% for BCS alone. These data highlight the limited efficacy of BCS in managing diffuse or multicentric DCIS. Accordingly, mastectomy remains the preferred surgical approach in patients with widespread ductal involvement, offering improved locoregional control and a reduced recurrence risk.

Young women. With ongoing shifts in lifestyle and reproductive patterns, the incidence of breast cancer among premenopausal women is rising, particularly in high-income countries with improved living standards (53). We hypothesize that this trend may be attributable to delayed age at first childbirth, reduced parity, shorter duration of breastfeeding, earlier age at menarche, and the widespread use of hormonal contraceptives, all of which prolong hormonal stimulation of breast tissue and thereby increase the risk of breast cancer. Patients who are premenopausal differ notably from their postmenopausal counterparts in regard to tumor biology and clinical characteristics. These patients are more likely to present with higher-grade tumors and a greater prevalence of estrogen receptor- and progesterone receptor-negative disease, which are associated with more aggressive behaviour and an elevated risk of postoperative recurrence (54).

Considering these distinct biological features, a number of studies have examined the outcomes of different surgical strategies in younger patients (55-58). One investigation focusing on women <40 years old reported a 10-year cumulative incidence of local recurrence of 9.3% across all patients. Notably, patients treated with BCS exhibited a higher recurrence rate (11.1%) compared with those who underwent mastectomy (4.1%) (59). Further comparative analyses of postoperative outcomes in premenopausal women have shown that, while overall survival rates were similar between BCS and mastectomy, the recurrence risk remained consistently higher in patients receiving BCS (60,61).

These findings suggest that due to the elevated risk of recurrence and the more aggressive nature of disease in this demographic, mastectomy may be a more favorable option for premenopausal women, offering improved locoregional control without compromising long-term survival.

Patients with breast cancer and cardiac contraindications. Breast cancer cells possess the capacity to invade surrounding tissues and metastasize to distant organs. While BCS aims to excise the primary tumor with negative margins, it does not eliminate the risk of residual microscopic disease. As such, adjuvant radiotherapy is a key component of BCS-based treatment protocols, notably reducing the likelihood of local recurrence.

However, radiotherapy is not without complications. Cardiotoxicity is an established adverse effect (62), particularly relevant in the treatment of left-sided breast cancer types. Radiation-induced cardiac injury may manifest as myocardial damage, left ventricular dysfunction and myocardial necrosis, ultimately contributing to long-term cardiovascular sequelae including arrhythmias, pericarditis and coronary artery disease (63). Clinical studies have shown that patients with pre-existing comorbidities such as diabetes, hypertension or cerebrovascular disease experience markedly lower 3-year coronary event-free survival rates compared with those without these conditions (64-66). Furthermore, in a long-term follow-up study, patients with breast cancer that have underlying cardiac disease and have undergone radiotherapy, exhibited a 27% increased risk of cardiac mortality for left-sided tumors and a 9% increase for right-sided tumors after 10 years (67). These findings underscore the importance of individualized treatment planning. For patients with pre-existing cardiac dysfunction, especially those with left-sided breast cancer, if the anticipated cardiotoxicity of postoperative radiotherapy outweighs its benefits, mastectomy may offer a safer and more appropriate alternative.

Patients with suboptimal aesthetic outcomes. A principal advantage of BCS over mastectomy lies in the preservation of breast aesthetics. Numerous studies have demonstrated that favorable aesthetic outcomes following BCS notably enhance the postoperative quality of life and psychological well-being of patients (68-70). However, not all patients achieve satisfactory aesthetic outcomes following BCS.

Patients with smaller breast volumes, as well as male patients with breast cancer, often face a relatively higher tumor-to-breast volume resection ratio. This high resection area-to-total breast volume ratio has been identified as a key determinant of suboptimal aesthetic outcomes (71). Other contributing factors include reduced skin elasticity (71), tumor location in the central breast (72) and the presence of multifocal disease (73). BCS may also result in breast asymmetry and deformity, for which secondary corrective procedures, such as breast reduction or fixation surgery, are available. However, these revision surgeries carry considerable risks. In a study by Barnea *et al* (74), 20% of patients undergoing such procedures experienced minor complications and 8% suffered from major adverse events.

BCS aims to achieve complete tumor excision with adequate histologically negative margins while preserving as much healthy tissue as possible. Pathological assessment of surgical margins is key. Typically, pathologists apply ink to the excised specimen and measure the shortest distance from the tumor to the inked surface to assess clearance. Margin width has been shown to be markedly associated with local recurrence risk, with smaller or positive margins being associated with higher recurrence rates (75). In scenarios where the tumor-to-gland volume ratio is high and sufficient margins cannot be confidently obtained without substantial tissue loss, the risk of recurrence and suboptimal aesthetic outcomes are elevated. In such cases, mastectomy may be the more appropriate surgical option. For patients prioritizing aesthetic outcomes, NSM followed by immediate breast reconstruction can offer an oncologically safe and aesthetically favorable alternative (76).

To the best of our knowledge, to date, no single modality can accurately predict margin status intraoperatively or postoperatively. However, novel technologies such as hyperspectral imaging systems (77) and artificial intelligence-based algorithms (78) have demonstrated promise in predicting pathological margin status in real-time. As these margin-assessment tools continue to evolve, they may enable more precise intraoperative decision-making and facilitate the selection of optimal surgical strategies tailored to individual patients.

Patients with socioeconomic constraints. Beyond considerations of aesthetic outcomes and recurrence risk, the financial cost of breast cancer surgery serves a key role in treatment decisions (79). Patients with socioeconomic constraints often prioritize cost-related concerns compared with aesthetic or functional outcomes, leading to a higher likelihood of choosing mastectomy compared with BCS (80).

International data suggest that while the median cost of BCS surgery itself is lower, ~€1,200 compared with €1,650 for mastectomy (81), the total treatment cost of BCS is markedly

higher. This disparity is primarily driven by the necessity of adjuvant radiotherapy, which serves a key role in reducing local recurrence rates and achieving long-term outcomes comparable to those of mastectomy (82,83). In addition, BCS typically involves more frequent imaging and pathological assessments, further increasing overall expenditure. A previous study found that radiotherapy accounts for 11.7% of direct costs, while the surgery itself comprises only 14.7% of the total cost (81). Due to the cumulative expenses associated with BCS and its adjunctive therapies, mastectomy may represent a more financially viable option for patients unable to afford the full continuum of care required for optimal BCS outcomes.

4. Strengths and limitations

The present review discusses clinical and demographic factors influencing BCS outcomes, offering practical guidance for patient selection. Its strengths lie in a systematic evaluation of age, comorbidities, tumor biology and socioeconomic considerations, supported by diverse clinical studies. However, limitations include reliance on observational data rather than controlled trials, potential regional bias due to uneven global representation in the literature, insufficient discussion of newer adjuvant therapies that may modify BCS suitability, regional imbalance exists in the cited literature, with an overrepresentation of data from high-income countries, potentially underestimating challenges specific to low- and middle-income settings. With this, recent advances in radiotherapy, oncoplastic techniques and neoadjuvant systemic therapies were not comprehensively evaluated, despite their growing influence on surgical decision-making. Finally, psychological, cultural and patient preference dimensions were discussed descriptively but not analyzed systematically, warranting further qualitative and mixed-method research to capture these complex determinants.

5. Conclusions

Overall, although BCS provides oncologic outcomes comparable to mastectomy and offers clear advantages in preserving breast form and function, its suitability varies across patient populations. Elderly patients with comorbidities, younger patients with aggressive tumors, individuals with DCIS, those with cardiac dysfunction or patients with unfavorable tumor-to-breast ratios may experience higher risks of recurrence, complications or suboptimal aesthetic outcomes. Economic considerations further influence surgical choice. These findings highlight the need for careful preoperative evaluation and individualized decision-making, ensuring that BCS is applied rationally and selectively to optimize both oncologic safety and quality of life in diverse patient groups. Future research may benefit from integrating artificial intelligence and machine learning algorithms to refine risk prediction and optimize surgical decision-making. Such approaches have demonstrated promising potential in medical imaging and personalized treatment planning (84).

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Authors' contributions

WL, LL, GG and HL all contributed towards the conception and design of the present study and wrote the manuscript. HL formulated the article ideas and reviewed the article, providing administrative support. All authors read and approved the final version of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

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Competing interests

The authors declare that they have no competing interests.

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