




Why Breast-Conserving Therapy Should be Considered Treatment of Choice in Early-Stage Breast Cancer Patients

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After a diagnosis of breast cancer has been made, a major choice a patient with early-stage breast cancer needs to make, along with her surgeon, is between breast-conserving surgery followed by radiation therapy (breast-conserving therapy [BCT]) or mastectomy, which may be followed by breast reconstruction (BR). In discussing the pros and cons of these options, quality-of-life considerations will be an important topic as there are no differences in survival rates.¹

Quality of life (QoL) is relatively high in breast cancer patients following treatment, but there is conflicting evidence about possible differences in QoL after different treatment options.^{2–4} In a large multicenter cohort study that compared QoL between breast cancer patients following BCT, mastectomy without reconstruction, and mastectomy followed by implant or autologous BR, we showed the added value of breast preservation and reconstruction over mastectomy without reconstruction.⁵ However, no clinically relevant differences in overall health-related QoL were found between BCT, implant BR, and autologous BR. In this study, we included a generic preference-based QoL instrument instead of only a disease-specific QoL instrument, to ensure that the overall health effects of the various surgical treatment pathways would also be included. After studying these overall health

effects, we found that postoperative complications had a large and long-lasting negative impact on the QoL of patients, specifically following autologous BR.⁵

Next to QoL considerations, there are also societal arguments to take into account. Healthcare budgets are under substantial strain due to increasing healthcare costs. Society, policy makers, and insurance companies are therefore confronted with complex choices about which medical interventions need to be reimbursed. In this process, cost effectiveness of the interventions is an important argument. This is not only relevant when choosing between different surgical pathways for breast cancer treatment but also when the reimbursement of these surgical pathways is in competition with other allocations of the healthcare budget. This is particularly the case when choices are being made between different postmastectomy BR options, as these are not life-prolonging. A article published in *Annals of Surgical Oncology* in 2019 was the first to review studies on the cost effectiveness of breast cancer surgery.⁴ Typical in such cost-effectiveness assessments is the use of quality-adjusted life-years (QALYs), a metric for both quality and quantity of life. How patients value their QoL, for instance by filling out a validated generic QoL instrument, can be coupled with health state scores ranging from 0 (referring to the value of ‘death’ as a health state) to 1 (the value of perfect health), also known as utility scores. Therefore, in these and other cost-effectiveness analyses, including our own, QoL is an essential part of the analyses. In health economics, one always looks for a reasonable balance between costs and effects, in this case QoL effects.

The results of the review showed that “Breast-conserving therapy yielded the highest mean utility score at 0.79, whereas mastectomy yielded a mean utility score of

0.75. Among reconstruction health states, implant reconstruction had a lower score than autologous reconstruction (0.64 implant vs. latissimus dorsi 0.69 and TRAM/DIEP 0.71)."

There was a lot of variation in the methods used in the papers included in this review. Studies varied in the way health state assessments were performed. In half of the studies, these were estimated by healthcare professionals, in one-third of the studies they were estimated by the general public, and in only one-sixth of the studies assessments were reported by the patients themselves. Although each method may have its own strengths and weaknesses, we strongly favor health state assessments by patients, as in the end it is their own health that is evaluated; or as Yoon et al. state, "the legitimacy of a patient-reported utility by first-hand experience is difficult to overcome".⁴ Results from their review show that many cost-effectiveness studies in this field have used 'expert' opinions to estimate the value of the different BR outcomes. This may cause bias because if experts are enthusiastic about the improved breast appearance after, for example, autologous BR, and do not think that the potential (donor site) complications produce much disutility, the results are pushed towards a favorable outcome for autologous BR that has a high risk of complications and little additional overall health-related QoL benefits compared with implant BR or BCT.^{2,6} In other words, as long as experts instead of patients value the outcomes of benefits and risks, the outcomes of the related studies become dependent on the perception of these experts.

To overcome this weakness, we performed a state-of-the-art cost-effectiveness analysis with the dataset mentioned above, using patient-derived QoL values by means of the EQ-5D.⁷ Because we used this instrument and were able to estimate all the hospital-related costs associated with the various surgical treatment pathways, including follow-up surveillance costs, we were able to estimate the cost effectiveness in terms of costs per QALY. In line with the review by Yoon et al. we found that BCT had the most favorable cost-effectiveness ratio compared with the other options. BCT resulted in comparable QoL, with lower costs compared with implant BR and autologous BR, and showed better QoL, with higher costs than mastectomy without reconstruction. In our study, QoL outcomes and costs of, in particular, autologous BR were affected by the relatively high occurrence of complications. If reconstruction following mastectomy was performed, implant BR was more cost effective than autologous BR. However, recent findings regarding the long-term adverse effects of breast implants may put these favorable cost-effectiveness outcomes of implant BR (over autologous BR) in a different light. Women with breast implants appear to have a considerably larger risk of the development of a rare and

potentially lethal anaplastic large cell lymphoma (BIA-ALCL) than was previously assumed.⁸⁻¹⁰ This news has been widely picked up by the media and has led to a ban on certain breast implant types in some countries around the world.¹¹ It has also led to fear and many questions among patients who have previously undergone implant BR, and among patients who are about to make a choice with respect to whether and which type of BR they would opt for.^{12,13} However, please note that often radiation therapy is indicated after breast-conserving surgery, which is sometimes associated with adverse effects such as edema, fibrosis, a more sensitive breast, or, in rare cases, radiation-associated angiosarcoma. As breast cancer survivors grow in number with increasing life expectancy, research on these adverse radiation effects becomes increasingly relevant to find strategies to reduce them and to improve our knowledge, and, consequently, our decision counseling. Overall, these findings ask for a careful discussion with the patient about the risks and benefits of each treatment option.

Thus, do the favorable outcomes of BCT, both in terms of QoL and cost effectiveness, mean that clinicians should always advise BCT for patients with early-stage breast cancer? We think that such a mechanistic implementation would miss the point of the results presented. Rather, our results support BCT as a very sound surgical option for eligible patients. If patients have a clear preference for the expected outcomes of the reconstruction options and/or are reluctant towards the possible adverse effects of radiation therapy, and are willing to trade-off the risk of complications or have a high penetrance pathogenic mutation, then BR could and should be considered. From a health policy point of view, cost considerations might provide an additional argument. Health policy should look beyond the patient in question and should also consider the lost opportunities of other patients if money is spent on the patient in question. However, it is important to realize that cost-effectiveness ratios are based on group outcomes. In reality, 'average patients' do not exist and one could argue that cost effectiveness will most likely improve if treatments are allocated rationally and in line with the preferences of a well-informed individual patient.

In conclusion, BCT is generally associated with fewer complications, similar overall health-related QoL, and lower resource use, leading to superior cost effectiveness compared with mastectomy followed by BR.⁷ We therefore believe that BCT is a very sound surgical option for eligible patients with early-stage breast cancer, for whom BCT is an oncologically safe alternative. Large differences still exist between countries in the rates at which BCT and mastectomy are performed. For example, in Denmark the mean BCT rate is around 68%, compared with around 59% in The Netherlands.¹⁴ This suggests there may be room for

changes in clinical practice aimed at increasing the BCT rate. For this, an important challenge is educating breast cancer patients about the differences between treatments, with respect to survival, expected QoL, cosmetic outcomes, visits to the hospital, and the short- and long-term adverse effects of adjuvant treatments. No one-size-fits-all solution exists for this group of patients; therefore, careful and preferably standardized exploration of the value the patient attributes to all aspects of her future treatment process and outcomes is warranted.

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