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Intraoperative ultrasound guidance in breast-conserving surgery shows superiority in oncological outcome, long-term cosmetic and patient-reported outcomes: Final outcomes of a randomized controlled trial (COBALT)

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Abstract

Background: The multicenter randomized controlled COBALT trial demonstrated that ultrasound-guided breast-conserving surgery (USS) results in a significant reduction of margin involvement (3.1% vs. 13%) and excision volumes compared to palpation-guided surgery (PGS).

The aim of the present study was to determine long term oncological and patient-reported outcomes including quality of life (QoL), together with their progress over time.

Methods: 134 patients with T1–T2 breast cancer were randomized to USS (N = 65) or PGS (N = 69). Cosmetic outcomes were assessed with the Breast Cancer Conservative Treatment cosmetic results (BCCT.core) software, panel-evaluation and patient self-evaluation on a 4-point Likert-scale. QoL was measured using the EORTC QLQ-C30/-BR23 questionnaire.

Results: No locoregional recurrences were reported after mean follow-up of 41 months. Seven patients (5%) developed distant metastatic disease (USS 6.3%, PGS 4.4%, p = 0.466), of whom six died of disease (95.5% overall survival). USS achieved better cosmetic outcomes compared to PGS, with poor outcomes of 11% and 21% respectively, a result mainly attributable to mastectomies due to involved margins following PGS. There was no difference after 1 and 3 years in cosmetic outcome. Dissatisfied patients included those with larger excision volumes, additional local therapies and worse QoL. Patients with poor/fair cosmetic outcomes scored significantly lower on aspects of QoL, including breast-symptoms, body image and sexual enjoyment.

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Conclusion: By significantly reducing positive margin status and lowering resection volumes, USS improves the rate of good cosmetic outcomes and increases patient-satisfaction. Considering the large impact of cosmetic outcome on QoL, USS has great potential to improve QoL following breast-conserving therapy.

Keywords: Breast cancer; Ultrasound guided surgey; Palpation guided surgery; Margins; Cosmetic outcome; Quality of life

Introduction

Breast conserving therapy (BCT) is the established standard of care for women with early stage breast cancer, attaining disease-free and overall survival rates comparable to mastectomy.[1] BCT refers to a combination of breast conserving surgery (BCS) followed by whole breast irradiation to eradicate possible microscopic residual disease.

The primary goal of BCS is to remove the tumor while attaining clear margins, as margins positive for tumor cells are associated with an increased risk of local recurrence and require additional local therapies such as radiotherapy boost, re-excision or even mastectomy.[2] Positive margin incidences of up to 23% have been reported in BCS.[3]

The current population of breast cancer survivors is growing due to the increasing incidence of breast cancer, improved survival as a result of screening and to more effective treatment options. As a consequence, secondary goals such as cosmetic outcome and quality of life (QoL) are becoming increasingly important. However, fair or poor cosmetic outcomes are still observed in up to one third of all patients who undergo BCS.[4–10] Poor cosmetic outcome negatively influences different aspects of QoL.[10–12]

The two key determinants of cosmetic outcome are a larger excision volume and the administration of secondary radiotherapy.[5–7,9,13,14] For this reason, the achievement of tumor-free margins while excising a small volume of breast tissue during the initial procedure is crucial to both oncological and cosmetic outcomes.

The Cosmetic Outcome of the Breast After Lumpectomy Treatment (COBALT) trial was the first randomized multicenter trial comparing ultrasound-guided surgery (USS) with standard palpation-guided surgery (PGS). The implementation of USS led to a dramatic reduction in margin involvement and fewer additional local therapies. Moreover, USS allowed optimal excision volumes to be achieved, whereas PGS resulted in volumes almost twice optimal.[15]

The current analysis aims to assess the long-term oncological, cosmetic and patient-reported outcomes, including patient satisfaction and QoL.

Patients and methods

The COBALT trial was performed in accordance with the Declaration of Helsinki, guidelines for Good Clinical Practice, and the CONSORT statement. Central and local independent medical ethics review boards of the participating hospitals approved the study protocol (http://www.TrialRegister.nl, number NTR2579).

The COBALT trial was a comparative, two-arm, parallel group, randomized controlled trial undertaken in six hospitals in the Netherlands between 2010 and 2012. 134 patients with early stage (T1–T2, N0–N1) palpable invasive breast cancer were scheduled to undergo BCS.[15] The sample size was calculated based on the primary endpoints: resection volume and margin status. Secondary endpoints included oncological outcome, cosmetic outcome and QoL.

Surgical technique

During the ultrasound-guided procedure, the surgeon used a portable 14 MHz ultrasonography probe (Toshiba Viamo, Tokyo, Japan). The method of USS has been described previously.[15]

Briefly, the surgeon located the tumor by palpation and ultrasonography, compared findings with the pre-operatively digital images and measured the tumor diameter, the lesion-to skin distance, and the lesion-to-fascia distance. Then the tumor margins were marked on the skin. Dissection was assisted by placing the ultrasonography probe repeatedly in or around the wound at different angles, to visualize the tumor margins continuously, thereby checking attainment of adequate resection margins. During USS, surgeons did not guide the incision by palpation. After excision, the specimen was scanned ex vivo by ultrasonography so additional tissue could be excised if the tumor excision appeared incomplete. During PGS, surgeons used their fingers to palpate the tumor, retract it, and guide the dissection.

Although the definition of tumor-free margins used in the current study was “no tumor cells at the margin”, the aim for all surgeons was to achieve complete tumor removal with a surgically-feasible healthy tissue margin of up to an arbitrarily chosen 1 cm. The closure of the lumpectomy cavity did not involve oncoplastic surgery techniques. All included patients received radiotherapy as part of BCT.

Follow-up

The study protocol follow-up has been extensively described.[15,16] Briefly, patients received standard

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