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ORIGINAL ARTICLE

Use of Intraoperative Ultrasound During Breast Conservation Surgery (BCS) for Palpable Breast Cancer: an Extremely Effective Approach with Improved Oncological Outcome

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Abstract
For clinically low-volume breast cancer patients subjected to BCS, there is a concern regarding achieving microscopically negative margins and avoiding inadvertent resection of excessive volume of breast tissue. In this study, we utilized intraoperative ultrasound to guide resection in patients subjected to BCS. This was compared with palpation-guided resection. A total of 80 patients of invasive breast carcinoma (T1-2, N0-1, M0) (39 patients in USG-guided BCS (group A) and 41 patients in palpation-guided BCS (group B)) were enrolled. In group A, intraoperative localization was performed using a multifrequency 10-MHz linear array ultrasound probe and tumors were excised under USG guidance. In group B, tumor excision was guided by the palpation skills of the surgeon with the aim of achieving grossly negative margin circumferentially. Specimen volume was measured using water displacement technique. One out of 39 patients (2.56%) in group A and 5 out of 41(12.19%) in group B had positive margin in histopathology report. Mean of specimen volume in groups A and B was 42.67 and 57.97 ml respectively ($P = 0.011$). Mean of excess volume removed in study group was 4.19 ml and in control group, it was 24.11 ml ($P = < 0.01$). Mean of calculated resection ratio in study group was 1.1 and in control group was 1.73 ($P = 0.01$). Use of intraoperative ultrasound during BCS may help in improving margin clearance, reducing additional procedures, and preserving the normal breast parenchyma. The safety, ease, and effectivity of this technique may result in its wider application in future.

Keywords Intraoperative ultrasound · Margins · Excessive volume resection · Additional surgery

Introduction

Breast cancer is the most common malignancy among women in the world [1]. Several trials have demonstrated comparable results with regard to disease-free and overall survival between mastectomy and BCS combined with radiotherapy, and the latter has become the standard of care for early-stage breast cancer [2, 3]. For clinically low-volume breast cancer patients subjected to BCS, there is always a concern regarding achieving microscopically negative margins and to avoid inadvertent resection of excessive volume of breast tissue. In this prospective study, we utilized intraoperative ultrasound to guide resection with optimum margins in patients subjected to BCS. This was compared with palpation-guided resection. We found significantly better results in terms of margin negativity and at the same time avoiding excessive volume of breast tissue being resected.

Material and Methodology

The aim of the study was to evaluate the efficacy of intraoperative ultrasonography in the excision of palpable breast cancer during breast conservation surgery. Results of ultrasonography guided excision of palpable breast cancers were compared with palpation-guided excision of breast cancer in terms of—margin status, need for additional procedures—margin revision or mastectomy and to assess volume of normal breast tissue excised.

This study was done in the Department of Surgical Oncology, with the help of the Department of Radiodiagnosis and the Department of Pathology at Bhagwan Mahaveer Cancer Hospital and Research Centre, Jaipur, India.

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Study population consisted of patients of early breast cancer with clinically well-defined palpable lump suitable for breast conservation surgery including cases of palpable invasive breast cancers, (T1-T2, N0-N1) patients, and diagnosed after combination of triple test—physical examination, imaging (mammography/USG of breast/MRI breast), and tissue diagnosis—biopsy. Patients with ductal carcinoma in situ (DCIS), multifocal disease on imaging, history of neoadjuvant therapy, and previous surgical intervention other than core biopsy were not considered for the study.

A total of 80 patients of invasive breast carcinoma were enrolled in the study (T1-2, N0-1, M0) (39 patients in USG-guided BCS (group A) and 41 patients in palpation-guided BCS (group B).

A complete history, physical examination, clinical tumor staging, and requisite investigations for diagnosis and metastatic workup were done. All the relevant details were filled in a proforma specially designed for the study.

In group A, intraoperative localization was performed using a multifrequency 10-MHz linear array ultrasound probe and tumors were excised under USG guidance.

In group B, tumor excision was guided by the palpation skills of the surgeon with the aim of achieving grossly negative margin circumferentially.

Specimen volume measurements were performed by using a water displacement technique. After placement of orientation sutures, specimens were sent for histopathological examinations.

Surgery

Palpation-Guided Surgery

In the palpation-guided surgery group, tumor excision was guided by the palpation skills of the surgeon in the standard manner. In this group, the adequacy of the resection was based on the experience of the surgeon without objective imaging during surgery. The aim of surgical excision was to obtain a rim of healthy adjacent breast tissue around the tumor.

Ultrasound-Guided Surgery

In this group, tumor excision was done under guidance of ultrasound probe (10-MHz linear array ultrasound probe). For ultrasound-guided assistance, an experienced breast radiologist was present and assisted the procedure in the operating room. Under ultrasound guidance, tumors were excised taking adequate margins circumferentially.

Specimen volume measurements were performed by using a water displacement technique. After placement of orientation sutures, specimens were sent for histopathological examinations.

Data

Demographic, clinical, and pathological data including age, menopausal status, tumor location, histopathologic type, T and N stage, grade (Scarf-Bloom-Richardson), the presence of intraductal component, lymphovascular invasion and necrosis, receptor status (ER, PR, HER2-neu), and margin status, tumor- and specimen-related volumes were gathered and calculated resection ratio (CRR) was calculated. Margins were categorized as

1. Negative (no tumor cells at inked margin).
2. Focal positive (3 or less foci of invasive or in situ carcinoma in any inked margin) and
3. Positive (grossly discernible tumor at the inked edge of the specimen).

Need of additional procedures based on histopathological examination report was also notified. Type of additional procedure and histopathological examination report of re-excised or total mastectomy specimens was also documented.

After specimen fixation in formalin solution, all specimens were evaluated for tumor size in length, width, and height using a millimeter ruler and microscopic margin status by histopathologic evaluation of permanent sections. Tumor volume was calculated using $4/3 \times 3.14 \times \text{length}/2 \times \text{width}/2 \times \text{height}/2$ formula. The closest margin of excision was measured and documented.

Calculations

The ratio of the resected volume to the optimal resected volume was calculated from the diameter of the tumor and the three dimensions of the specimen.

- The volume of the tumor was calculated by $4/3\pi r3$.
- The optimal volume required for excision was calculated by adding an arbitrarily chosen "optimal" 1-cm tumor-free resection margin to the lesion radius and converting this value into a volume using the formula $4/3\pi(r + 1\text{ cm})\ 3$.
- The volume of the surgical specimen was calculated using the formula $4/3\pi a\ b\ c$ (with a, b, and c as given in the pathology report). The specimen volume was compared with the optimal excision volume, resulting in a Calculated Resection Ratio (CRR).

Tumor and specimen dimensions for calculation were taken from histopathology report.

Calculated Resection Ratio

To determine the excess tissue resection, the calculated resection ratio (CRR) was defined. The CRR was calculated by dividing the specimen volume by the optimal specimen

volume. In other words, in a perfect excision, the specimen volume would be equal to the optimal specimen volume, and the CRR would be 1.0. If the specimen volume was more than the size of the optimal specimen volume, then the CRR would be > 1.

Statistical Analysis

Continuous variables measured on interval and ratio scale were summarized as mean and standard deviation while nominal and categorical variables as proportions (%).

Unpaired *t* test was used for analysis of ratio and interval scale variables whereas chi-square test and Fisher exact test were used for nominal and categorical variables.

P value < 0.05 was taken as significant.

Medcalc 12.2.1.0 version software was used for all statistical calculations.

Results

Demographically, both the groups were similar.

1. **Age distribution**

The mean age in the study group was 44.66 years (SD, 10.13) while in the control group mean age was 48.42 years (SD, 11.32) with *P* value 0.163 (not significant) (Fig. 1).

The most common age group of patients was 41–50 years with 38.46% patients in study group and 34.15% in the control group.

The percentage of patients below 50 years of age was 70.76% and 66.66% in the study and control group respectively.

Of these, 71.87% in the study group and 60.61% in the control group were premenopausal women. *P* = 0.588 (not significant)

2. **Location of the lump**

Most common location of the breast lump in both the groups was upper outer quadrant (UOQ) (Fig. 2).

In the study group, 22 (56.41%) patients presented with lump in upper outer quadrant.

In the control group, 24 (58.54%) patients presented with lump in upper outer quadrant.

P value is 0.458 (not significant).

3. **Clinical staging**

Most of the patients (63.75%) in both the groups presented with clinically negative axilla (Fig. 3).

In the study group, 23 (58.97%) and 2 (5.13%) patients presented with cT2N0 and cT1N0 stage respectively.

In the control group, 22 (53.66%) and 4 (9.76%) patients presented with cT2N0 and cT1N0 stage respectively.

So, most common clinical stage was cT2N0 (56.25%).

P value is 0.036 (significant).

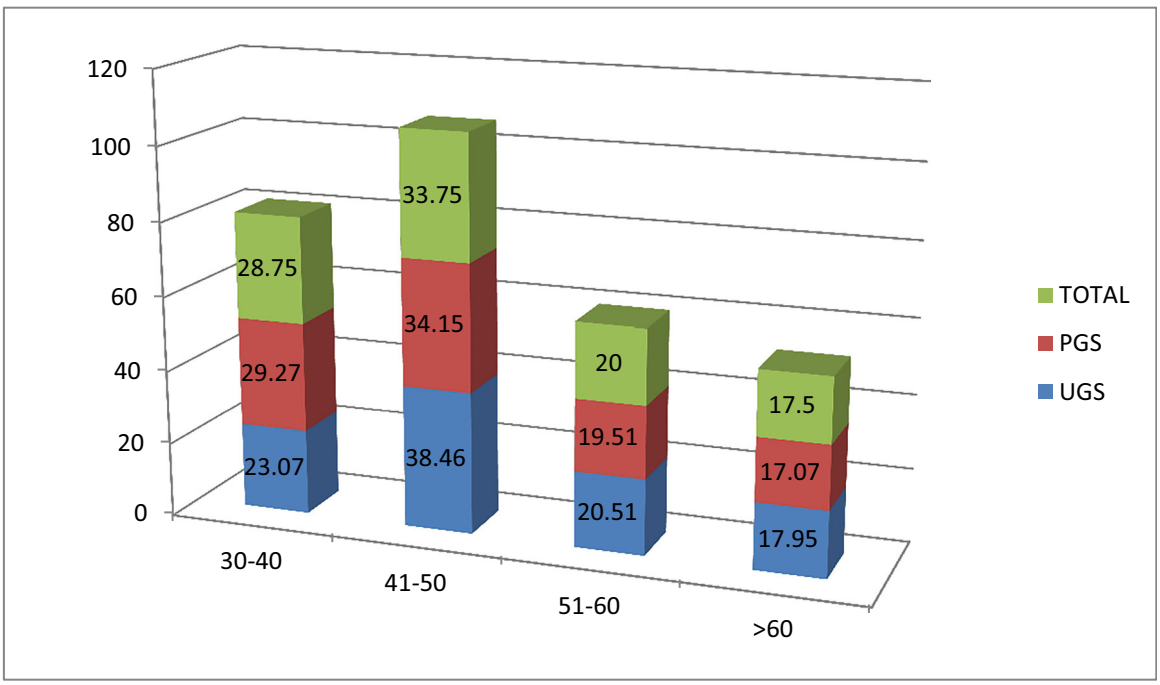

Fig. 1 Age distribution

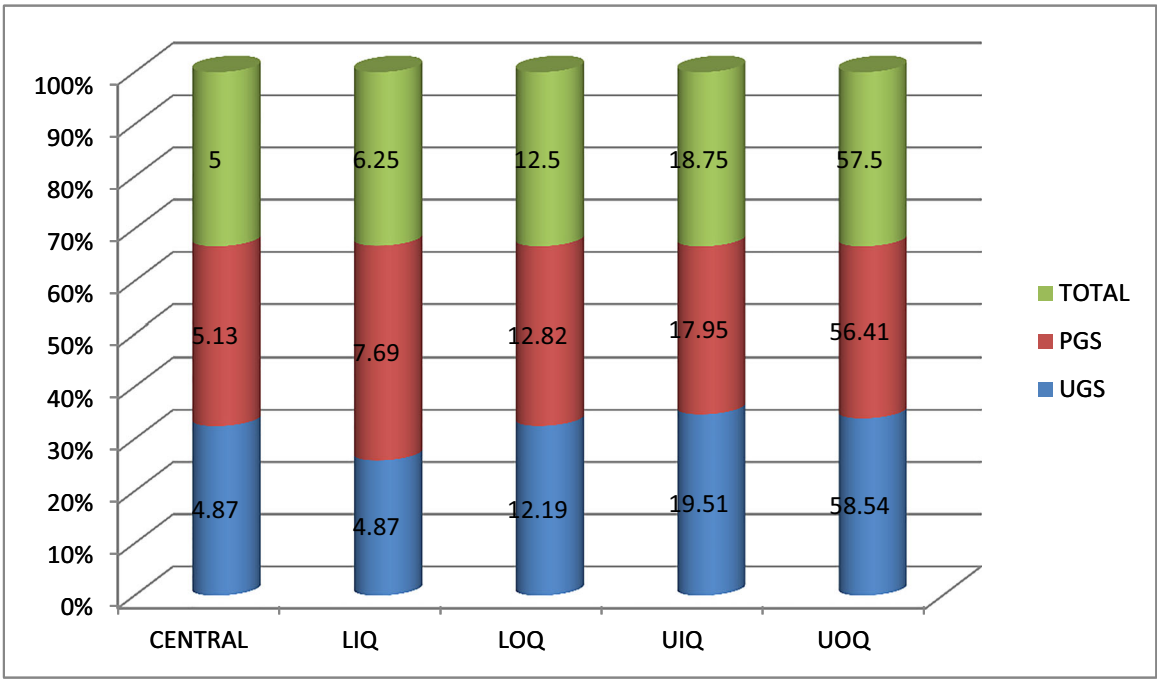

Fig. 2 Site of lump

4. BIRADS scoring

Most common BIRADS score in both the groups was 5 (58.75%) (Fig. 4).

In the study group, 23 patients (58.97%) had BIRADS 5 score.

In the control group, 24 patients (58.54%) had BIRADS 5 score.

P value was 0.861 (not significant).

5. Margin status

Out of 39 patients, one patient (2.56%) in the study group and out of 41 patients, 5 patients (12.19%) in the control group had positive margin in pathology report (Fig. 5).

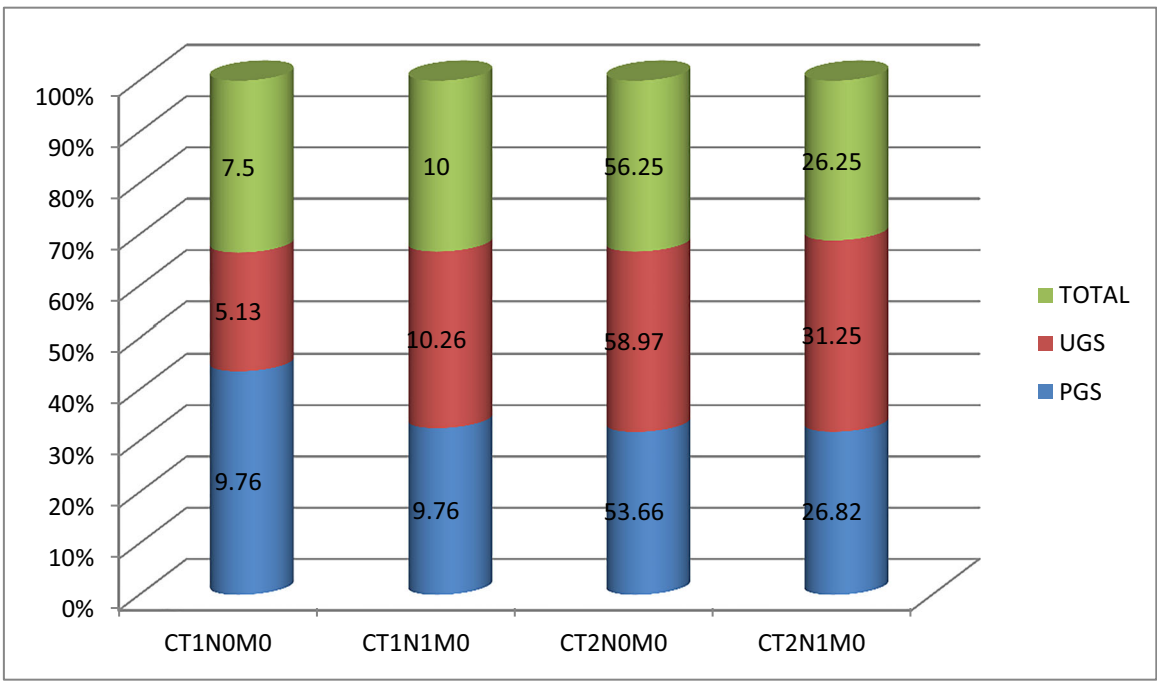

Fig. 3 Clinical stage

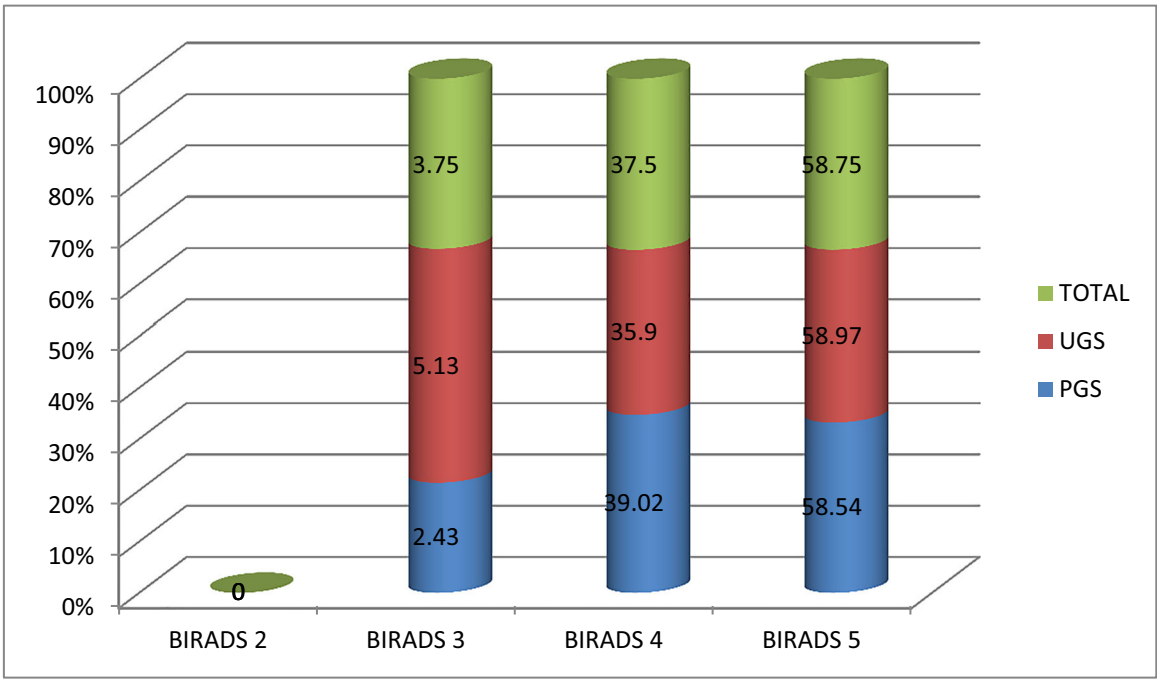

Fig. 4 Birads category

6. Specimen Volume

Mean of specimen volume in group A was 42.67 ml and in group, B it was 57.97 ml ($P = 0.011$).

Mean of excess volume removed in the study group was 4.19 ml and in the control group, it was 24.11 ml ($P = < 0.01$) (Fig. 6).

7. Calculated Resection Ratio

Mean of calculated resection ratio in the study group was 1.1 and in the control group was 1.73 ($P = 0.01$) (Fig. 7).

Although the mean of tumor volume and mean of optimal specimen volumes were more (7.64 cm^3 and 36.20 cm^3 respectively) in the study group in comparison with the control group (6.74 cm^3 and 33.86 cm^3), the mean specimen volume

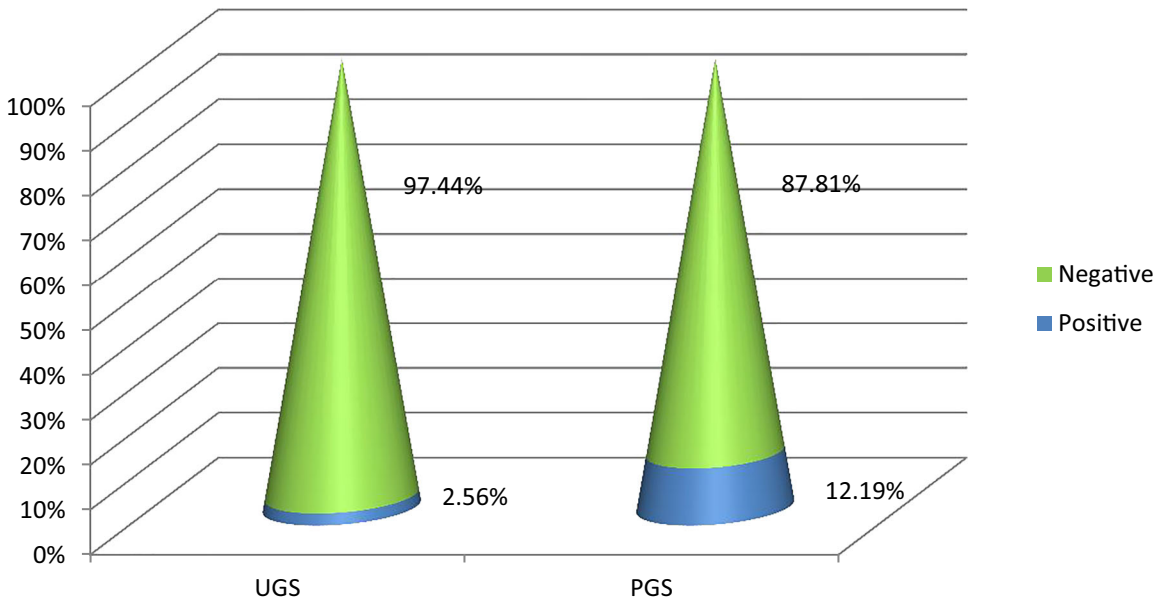

Fig. 5 Margin status

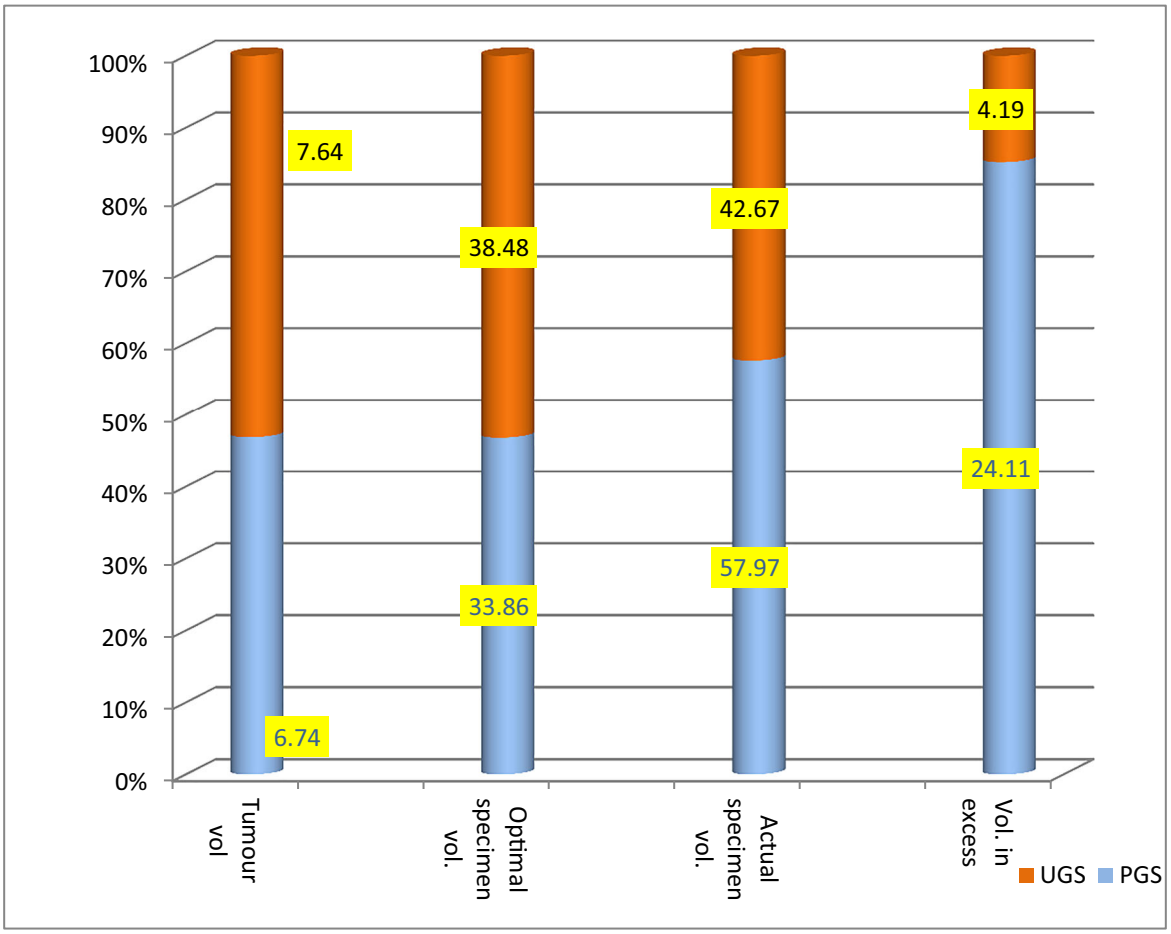

Fig. 6 Volume in excess

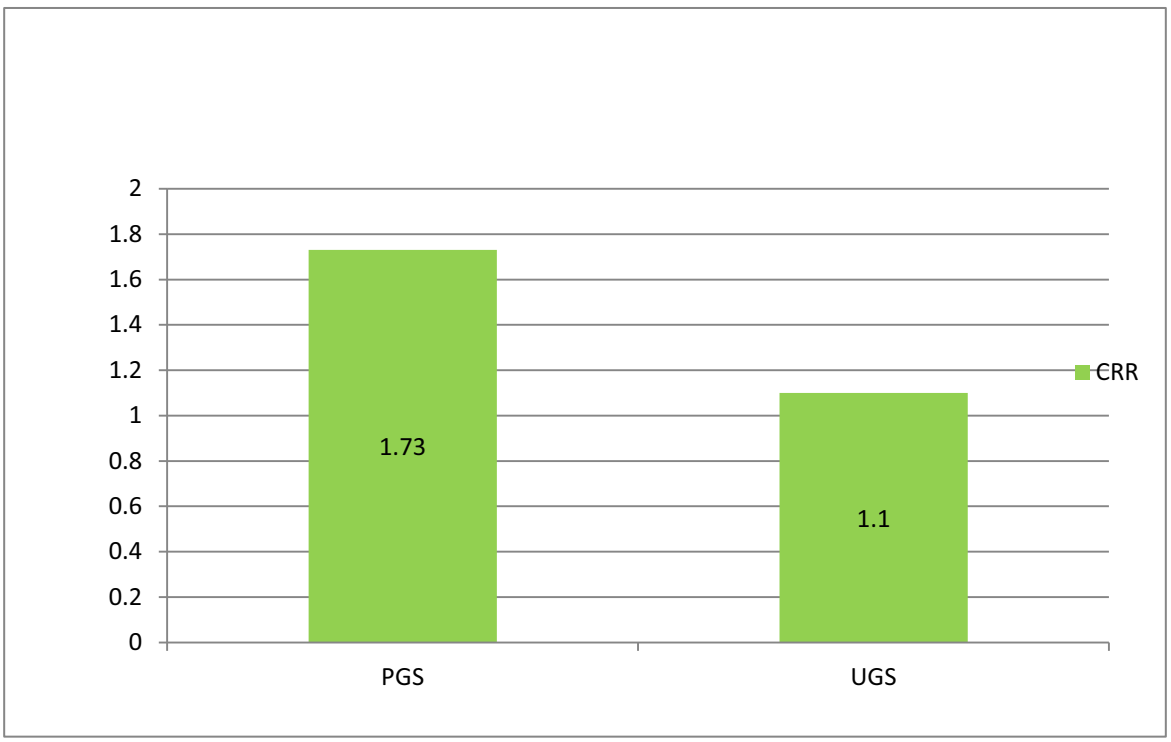

Fig. 7 Calculated resection ratio(CRR)

of the palpation-guided surgery group was significantly high (57.97 ml) in comparison with the ultrasound-guided surgery group (42.67 ml).

In the study group, only 1 patient (2.56%) had positive margin in pathology report; therefore, it underwent margin revision in second sitting. In the control group, 5 patients (12.19%) had positive margins in pathology report; hence, it needed second surgery. Two patients underwent revision of margins and the rest of the 3 patients underwent mastectomy ($P = 0.355$).

Above mentioned results are comparable with other reference studies and justify the intraoperative use of ultrasound for excision of early palpable breast cancer.

Discussion

Various techniques have been used to localize breast lesions during BCS. In daily practice, the excision of palpable breast cancer is guided by palpation. The adequacy of this procedure is based on preoperative imaging techniques and the experience and tactile abilities of the surgeon. However, excision of the tumor mass by this "palpation-guided" procedure can be problematic, especially in dense breasts. Indeed, in previous retrospective study, 22.5% of all palpation-guided tumor excisions presented with tumor-involved surgical margins [4]. Other studies have also reported a high incidence of positive margins after initial excision, ranging from 20 to 60% [5–7].

Examining the breasts by ultrasound was first described by Wild and Neal [8]. Its application has expanded from preoperative assessment and diagnostic guidance to intraoperative localization of breast cancers. Intraoperative ultrasound guidance (IOUS) was developed in 1988 [9]. It is an ultrasound probe that is used to localize the breast tumor in the operating theater with an intention to improve surgical accuracy of breast cancer excision.

US guidance offers some benefits over needle localization guidance in terms of non-palpable breast cancer. US guidance provides better operational anatomy coordination which helps a surgeon to end up with better margin clearance which leads to less re-excision rates and also better cosmetic outcomes. Palpable breast cancer patients should benefit from US-guided lumpectomy as it was reported for non-palpable breast cancer patients [10–12].

Marcia M. Moore et al. (2001) conducted the first study for evaluation of role of intraoperative ultrasound in lumpectomy for palpable breast cancer. They found out that surgical accuracy was improved with intraoperative ultrasound-guided surgery. Margin status was improved, patient satisfaction was equivalent, and cost was not affected using ultrasound technology. Intraoperative ultrasound appears especially efficacious for women whose preoperative mammogram shows dense parenchyma surrounding the lesion. Finally, they concluded that the use of intraoperative ultrasound optimizes the surgeon's ability to obtain satisfactory margins for breast-conserving techniques in patients with breast cancer. Patient satisfaction was excellent and a cost saving was most likely realized [12]. In a study done by Davis K.M. et al. (2011), patients who underwent lumpectomy with the help of intraoperative ultrasound were significantly less likely to have an involved margin (41% vs. 9%, $P = 0.01$) and less likely to require a re-excision (34% vs. 9%, $P = 0.04$). The lumpectomy volumes in the intraoperative ultrasound group were smaller than the volumes in the lumpectomy alone group. They concluded that intraoperative use of ultrasound can decrease the rate of positive margins and re-excision procedures in patients with palpable breast cancers [13].

Nicole MA Krekel et al. COBALT trial 2013 in their study found that 2 (3%) of 65 patients allocated with USG-guided surgery had margins involved by tumor compared with 12 (17%) of 69 who were assigned to palpation-guided surgery (difference 14%, 95% CI 4–25; $P = 0.0093$). Specimen weight and volume were both significantly lower with USG-guided surgery than palpation-guided surgery. USG-guided surgery resulted in smaller excision volumes (38 (SD 26) vs. 57 (41) cm^3; difference 19 cm^3, 95% CI 7–31; $P = 0.002$. [14]

Hasan Karanlik et al. 2015 in their study observed positive margins in 5 (6%) of the patients in the US-guided group and 14 (17%) of the patients in the palpation-guided group ($P = 0.03$). Mean resection volume in palpation-guided surgery group was 108.1 cm^3 and in USG-guided surgery group, it was 89.9 cm^3 with P value 0.048 [15].

Conclusion

Use of intraoperative ultrasound for excision of palpable breast cancer is a newer concept aimed to provide help in

- improving margin clearance,
- reducing additional procedures and
- reducing excision volume of normal breast parenchyma

This study shows that the use of intraoperative ultrasound is safe, easy, effective and may result in wider application of this technique.

Breast cancer is very common in Indian population and now breast conservation surgery is a well-accepted approach. But until now, there is limited literature available regarding use of intraoperative ultrasound for excision of palpable breast cancer and its effectiveness during breast conservation surgery in India.

Recommendations

Intraoperative ultrasound for excision of palpable breast cancer is an effective procedure with a short learning curve and can be easily applied in routine practice.

1. Intraoperative ultrasound for excision of palpable breast cancer is an oncologically safe procedure in early breast cancer patients.
2. The technique of use of intraoperative ultrasound for excision of palpable breast cancer needs to be standardized.
3. Use of this technique in breast conservation surgery after NACT can also be explored.
4. A randomized controlled trial with larger number of patients required to establish the use of IOUS in routine practice.
5. Randomized controlled trials with longer follow-up are required to know the cosmetic outcome and patient satisfaction.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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