Comparative study between The Effect of Ultrasound-guided versus palpation-guided conservative breast surgery on cosmetic outcome in palpable early breast cancer patients

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Background: In conservative breast surgery (CBS), the larger the volume of breast tissue resected the poorer the cosmetic outcome, therefor, introduction of ultrasonography in the excision of palpable breast cancer aims to minimize heathy tissue excision and ensure oncologically-safe excision, hence, better cosmetic outcome than in palpation-guided surgery (PGS).

Aim: A comparison between ultrasound-guided surgery (UGS) for palpable breast cancer with PGS on safety margin, re-excision rate and cosmetic outcome.

Methods/design: This is a prospective randomized controlled study conducted on 79 female patients with palpable early breast cancer. Patients were randomized to underwent either UGS or PGS. Mean distance between the tumor and the resection margin, re-excision rate, operative time, cosmetic outcome and patient satisfaction were assessed.

Statistical analysis used: Data management and statistical analysis were done using SPSS version 28 (IBM, Armonk, New York, United States). Quantitative data were assessed for normality using the Shapiro-Wilk test and direct data visualization methods. According to normality, quantitative data were summarized as means and standard deviations. Categorical data were summarized as numbers and percentages. Quantitative data were compared between the studied groups using independent t-test. Categorical data were compared using the Chi-square test. Multivariate logistic regression analysis was done to predict good to excellent patient satisfaction. All statistical tests were two-sided. P values less than 0.05 were considered significant.

Results: The UGS group revealed significantly higher excellent panel evaluation (48.7% vs. 22.5%, P = 0.028) and patient satisfaction (61.5% vs. 30%). The UGS group demonstrated significantly longer operative time but significantly lower re-resection rate and distance from tumor to resection margin (0.62 ±0.16 vs. 1.72 ±0.35 cm, P < 0.001) The predictors of the outcomes were tumor T stage (T2 stages associated with less satisfaction), tumor to resection margin distance (the more distance the less satisfaction), and ultrasound use.

Conclusion: UGS prove to be superior to the PGS as it significantly decreases re-excision rates and improves overall cosmetic outcome and patient satisfaction.

Keywords: Breast-conserving surgery (BCS), patient satisfaction, cosmetic outcomes, ultrasound-guided surgery.

Key Messages: UGS prove to be superior to the PGS as it improves overall cosmetic outcome and patient satisfaction.

Introduction

Breast-conserving surgery (BCS) with sentinel lymph node sampling become the main procedure, whenever possible, for the management of patients with breast cancer aiming for preservation of healthy breast tissue and the healthy axillary lymph nodes. Such procedure improve patient`s quality of life through better aesthetic appearance (Compared to mastectomy) and avoid limited mobility and arm edema associated with axillary clearance via less invasive sentinel lymph node biopsy and hence improve the functional outcome.[1-3]

With application of screening program, the incidence of diagnosing breast cancer in early stage while the tumor still small or even impalpable increase significantly.[4]

In palpable tumors, palpation can easily localize the mass intraoperatively, however, oncologically safe excision with adequate negative margins together with minimal healthy tissue removed as possible may be achieved better with the use of intraoperative ultrasound (IOUS) to objectively measure the distance from the tumor margin to the resection margin, rather than using the traditional subjective palpation-guided surgery. The use of IOUS allow the surgeon to visualize the tumor along the course of tumor resection and measure a safe distance for oncologically safe resection.[5]

The volume of the tissue excised generally affect the cosmetic outcomes after BCS, the larger volume excised the less favorable cosmetic outcomes.[6]

Subjects and Methods

Study design:

This is a prospective, blind, randomized, controlled study conducted on 79 female patients with palpable early breast cancer and take place at Benha University Hospital, general surgery department in the period from November 2022 to November 2023.

The present study has been reported in line with CONSORT criteria (Consolidated Standards of Reporting Trials).[7]

Inclusion criteria:

Female patients diagnosed as early (T1-2, N 0-1) invasive breast cancer and fit for BCS.

Exclusion criteria:

1. Patients with unpalpable breast cancer or carcinoma in-situ.
2. T3 andT4 breast carcinoma (Locally advanced tumor).
3. Metastatic breast cancer.
4. Recurrent cases of breast cancer.
5. Breast sarcomas.
6. Benign breast lump.
7. patients unwilling or unfit for BCS.

Randomization method:

Using an excel sheet, a randomization sequence with a 1:1 allocation using random block sizes of 2 and 4 via an independent doctor. The allocation of treatment was determined by a researcher not included in the team of the present study using sequential opening of opaque, numbered, sealed envelopes. After randomization, none of the patient was excluded from the study.

Sample size calculation:

Calculation of sample size was conducted using an online software (https://clincalc.com/stats/samplesize.aspx).

After obtaining the approval on the present study via ethical committee of the faculty of medicine, Benha University. Seventy-nine female patients were randomly assigned into the following two groups:

Group A, subjected to ultrasound-guided surgery (UGS),

Group B, subjected to palpation-guided surgery (PGS).

A written informed consent was obtained from the participants. The benefits and hazards of the different methods of surgeries were thoroughly explained. All patients were assessed via a multidisciplinary team (Including specialized doctor from the general surgery, medical oncology, radiology, radiotherapy and pathology).

All patients included in the study underwent the following:

1. A full history documentation and clinical examination.
2. Laboratory investigations, including full blood picture, liver and renal function tests, fasting and 2-hour postprandial blood glucose measurement and tumor marker assessment (CA 15–3).
3. Bilateral mammography and breast ultrasound.
4. Metastatic work up investigation (Plain chest X-ray, pelvi-abdominal ultrasound and bone scan (When indicated)).

5. Tissue diagnosis: In the form of tru-cut biopsy from the breast mass. tru-cut biopsy or fine needle cytology from axillary lymph nodes when suspicious nodes were detected by axillary ultrasound.

Surgical technique:

All cases were performed via the same surgical team under general anaesthesia aiming to obtain a safety margin up to 1 cm around the malignant mass. No oncoplastic techniques were used to close the cavity after excision of the tumor allowing seroma formation.

Ultrasound-guided surgery (UGS):

Before skin incision, the surgeon performed an assessment to the lesion using THI 14-MHz US probe (LOGIQ™ e portable ultrasound, Philadelphia, USA was used) under supervision of an experienced radiologist **(Figs. 1,2).**

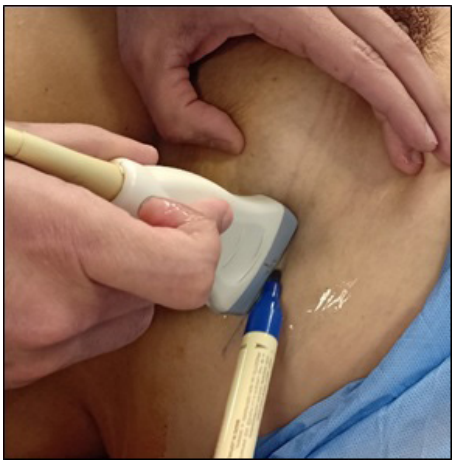

Fig 1: Precise marking of the tumor site using the ultrasound.

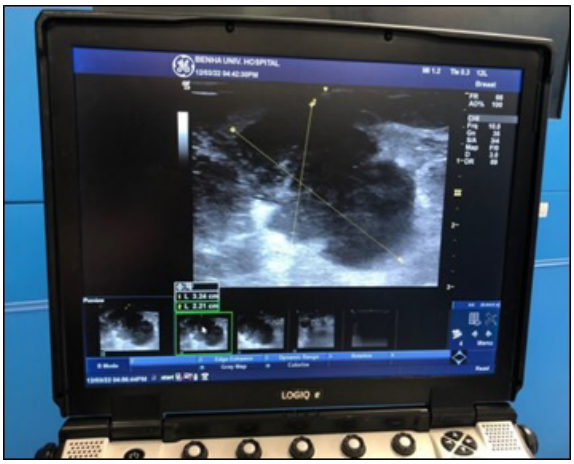

Fig 2: US assessment of the lesion.

Then, the probe of the US unit was enclosed in a sterile surgical glove filled with sterile gel hence it can be applied inside the surgical wound **(Fig. 3).**

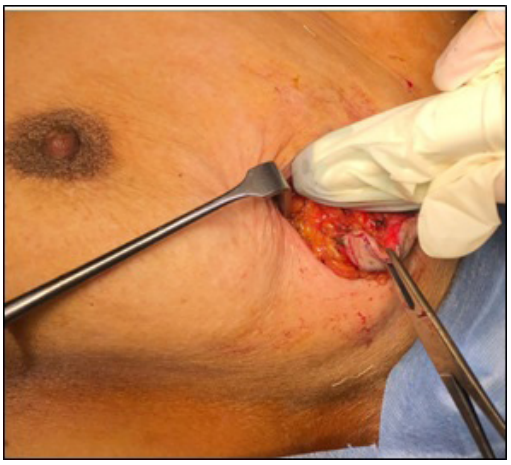

Fig 3: Application of the US probe inside the wound to aid the dissection.

The breast was fixed by the assistant hand in a way that making the mass as close to the skin as possible. Precise localization of the tumor was marked on the skin using the US then, skin incision was made and skin flaps were raised. Ultrasound probe was applied inside the wound by the surgeon and under supervision and guidance of the radiologist to assess the position of the tumor and guide the dissection together with the palpation ensuring adequate safety margin.

Dissection continued posteriorly between the lesion and pectoral fascia with repeated application of the probe to assess the depth of the lesion and safety margin **(Fig. 4).**

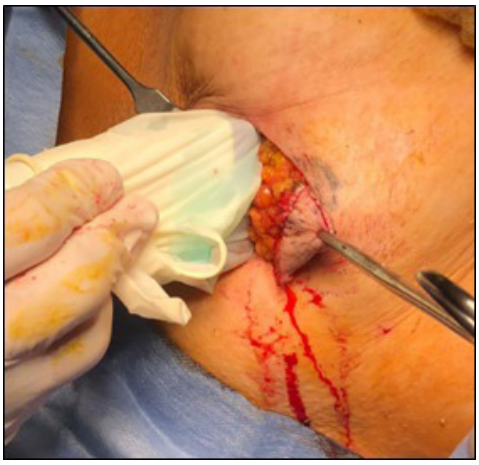

Fig 4: Assessment of the posterior margin using the US probe.

After complete excision of the tumor, orientation of the specimen was done using sutures and the specimen was re-assessed by the US to ensure complete, safe excision of the mass then, the specimen was sent for frozen section assessment by a pathologist so that positive margins were

resected.

The cavity after excision was marked using titanium clips to guide radiotherapy then proper hemostasis assured and closure of the skin without drain was done using 3/0 vicryl sutures (No oncoplastic methods or tissue mobilization were used).

Palpation-guided surgery:

In PGS, the excision was guided by palpation using the index finger to palpate and retract the mass and guide the dissection. The specimen was dealt with in the same manner as UGS group and the cavity was marked by titanium clips and the wound was closed without drain.

Management of the axilla:

Patients with clinically and radiologically negative axillary lymph nodes were subjected to sentinel lymph node sampling using patent blue dye (Combined peri-tumoral and retro-areolar injection technique were done). Then, the sentinel nodes were sent to be assessed by frozen section and if they were positive for metastasis, axillary lymph node dissection was done.

Patients with clinical or radiological positive axillary lymph node proved by preoperative FNAC underwent axillary clearance immediately.

Patient Follow-Up:

Patients were assessed at 1, 3 and 6 months postoperatively by patient self-evaluation questionnaire (To assess patient satisfaction) and standardized 4- viewpoint digital photographs of the breast (One frontal, one lateral and two oblique pictures from the neck to the waist).

End points:

Mean distance between the tumor and the resection margin, rate of intraoperative re-excision, time of the operation (Excluding axillary surgery time), cosmetic outcome and patient satisfaction

Cosmetic outcome assessment and scoring:

The cosmetic outcomes were assessed using panel- and self- evaluation. In these methods, a comparison between the cosmetic end-result of the treated breast with the healthy breast were done and scored using the 4-point Likert scale, classifying the results into "excellent", "good", "fair" or "poor" results. The "excellent" results referred as (Similar to the healthy breast) while "poor" results meant (Marked distortion or difference between the treated and healthy breast).

Panel Evaluation:

The photographs were evaluated by A three-member panel (Consisting of a breast surgeon and two laymen). The breast surgeon did not perform the surgery. The study arm and the patient`s information were hidden to the panel members. Four-view point photographs of each case at the specific follow-up time point were reviewed. Points to be reviewed include breast contour, volume, degree of deformity, position of the nipple, scar and overall cosmetic end-result.

Patient Cosmetic Self-Evaluation:

A composite questionnaire was used which include questions on the degree of similarity between the treated and the healthy breast on different parameters as firmness, position of the nipple, breast contour and size, surgical scar appearance, final cosmetic outcome, and the degree of satisfaction with the final appearance of the breast.

Results

General characteristics

As shown in **(Table 1),** the two groups were comparable regarding age (P = 0.652), BMI (P = 0.695), tumor type (P = 0.379), and tumor stage (P = 0.184).

The UGS group demonstrated significantly higher operative time (28 ±4 vs. 17 ±3 min, P < 0.001) but significantly lower re-resection rate (7.7% vs. 35%, P = 0.003) and distance from tumor to resection margin (0.62 ±0.16 vs. 1.72 ±0.35 cm, P < 0.001) **(Table 1, Fig. 5).**

Regarding satisfaction, the UGS group revealed significantly higher excellent panel evaluation (48.7% vs. 22.5%, P = 0.028) and patient satisfaction (61.5% vs. 30%, P = 0.006) **(Table 1, Fig 6).**

Agreement between the panel and patient evaluation

In the UGS group, there was a moderate agreement between panel evaluation and patient self-evaluation (Kappa = 0.539, P < 0.001). Additionally, in the palpation group, a good agreement was observed (Kappa = 0.7, P < 0.001), with an obvious tendency in the patients for a higher evaluation in both groups **(Table 2)**.

- **Prediction of good to excellent patients' satisfaction**

Multivariate logistic regression analysis was done to predict good to excellent patient satisfaction. The predictors were T2 stage (Associated with less satisfaction; OR = 0.099, 95% CI = 0.02 – 0.483, P = 0.044), tumor to resection margin distance (The more distance the less satisfaction; OR = 0.104, 95% CI = 0.035 – 0.310, P <0.001), and

ultrasound use (Associated with better satisfaction; OR = 5.547, 95% CI = 1.773 – 17.358, P = 0.003), controlling for age and BMI **(Table 3).**

Data management and statistical analysis were done using SPSS version 28 (IBM, Armonk, New York, United States). Quantitative data were assessed for normality using the Shapiro-Wilk test and direct data visualization methods. According to normality, quantitative data were summarized as means and standard deviations. Categorical data were summarized as numbers and percentages. Quantitative data were compared between the studied groups using independent t-test. Categorical data were compared using the Chi-square test. Multivariate logistic regression analysis was done to predict good to excellent patient satisfaction. All statistical tests were two-sided. P values less than 0.05 were considered significant.

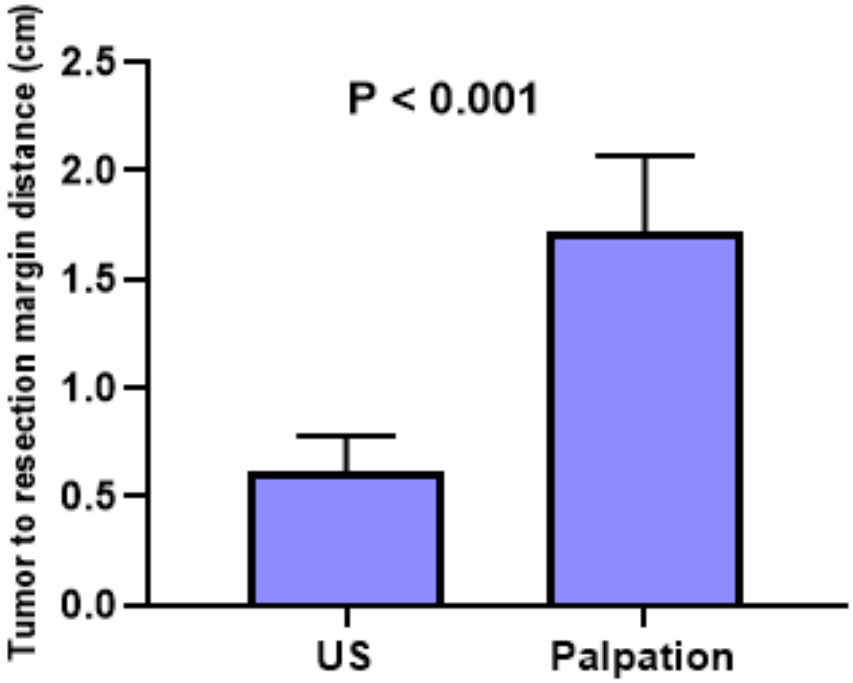

Fig 5: Tumor to resection margin distance in the studied groups.

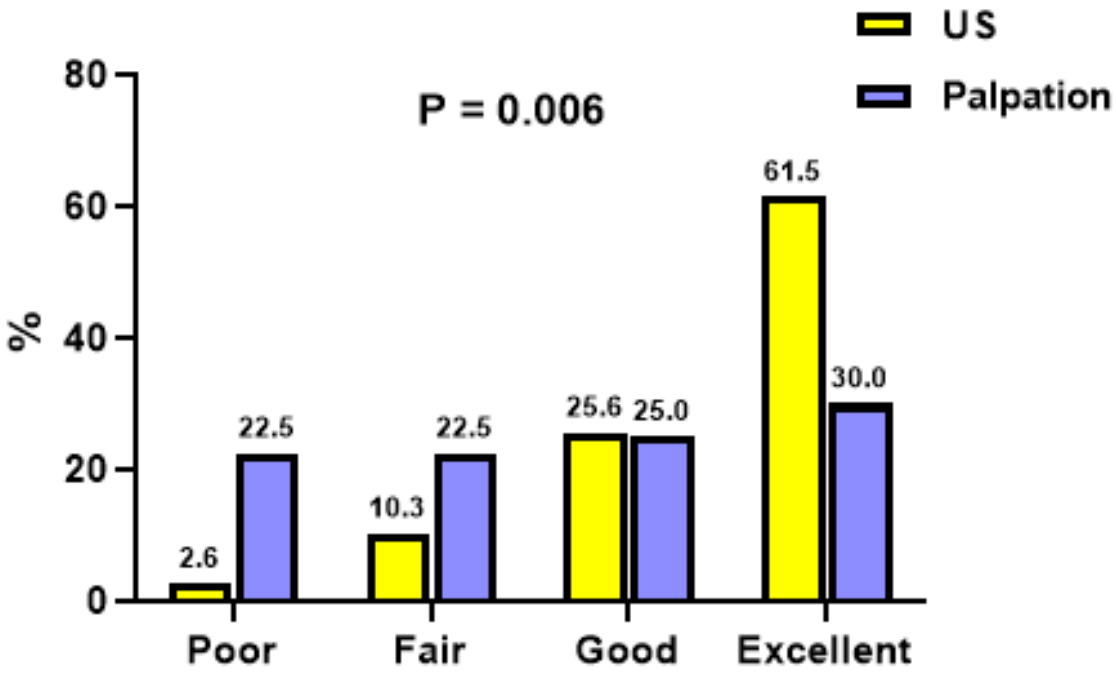

Fig 6: Patient satisfaction in the studied groups.

Table 1: General and clinical characteristics of the studied groups

	US (n = 39)	Palpation (N = 40)	P-value
Age (years)	50 ±8	49 ±8	0.652
BMI	30 ±6	29 ±6	0.695
Tumor type			
IDC	28 (71.8)	25 (62.5)	0.379
ILC	11 (28.2)	15 (37.5)	
Tumor T stage			
T1	11 (28.2)	17 (42.5)	0.184
T2	28 (71.8)	23 (57.5)	
Operation time (min)	28 ±4	17 ±3	<0.001
Re-resection	3 (7.7)	14 (35)	0.003
Tumor to resection margin distance (cm)	0.62 ±0.16	1.72 ±0.35	<0.001
Panel evaluation			
Poor	2 (5.1)	10 (25)	0.028
Fair	8 (20.5)	9 (22.5)	
Good	10 (25.6)	12 (30)	
Excellent	19 (48.7)	9 (22.5)	
Patient cosmetic self-evaluation			
Poor	1 (2.6)	9 (22.5)	0.006
Fair	4 (10.3)	9 (22.5)	
Good	10 (25.6)	10 (25)	
Excellent	24 (61.5)	12 (30)	

Data are presented as mean ±SD or number (percentage); IDC: Infiltrating duct carcinoma; ILC: Infiltrating lobular carcinoma; Significant P-values are marked in bold.

Table 2: Agreement between the panel and patient evaluation in each studied group

		Patient cosmetic self-evaluation						
	Panel evaluation	**Total**	**Poor**	**Fair**	**Good**	**Excellent**	**Kappa**	**P-value**
Ultrasound								
	Poor	2	1 (50)	1 (50)	0 (0)	0 (0)	0.539	<0.001
	Fair	8	0 (0)	3 (37.5)	5 (62.5)	0 (0)		
	Good	10	0 (0)	0 (0)	5 (50)	5 (50)		
	Excellent	19	0 (0)	0 (0)	0 (0)	19 (100)		
Palpation								
	Poor	10	8 (80)	2 (20)	0 (0)	0 (0)	0.7	<0.001
	Fair0	9	1 (11.1)	6 (66.7)	2 (22.2)	0 (0)		
	Good	12	0 (0)	1 (8.3)	8 (66.7)	3 (25)		
	Excellent	9	0 (0)	0 (0)	0 (0)	9 (100)		

Data are presented as number (percentage). Significant P-values are marked in bold.

Table 3: Multivariate logistic regression analysis to predict good to excellent patient satisfaction

	OR (95% CI)†	P-value
Tumor type	1.714 (0.563 - 5.222)	0.343
T2 stage	0.099 (0.02 - 0.483)	0.044
Tumor to resection margin distance	0.104 (0.035 - 0.310)	<0.001
Ultrasound use	5.547 (1.773 - 17.358)	0.003

†Adjusted for age and BMI; OR: odds ratio; 95% CI: 95% confidence interval; Significant P-values are marked in bold.

Discussion

The main goal of the BCS is to achieve the best oncological outcome together with good cosmetic results, however, the aim to achieve the best attainable cosmetic outcome gain more and more attention recently. Several studies show the benefit of using the US in BCS as it minimizes the amount of healthy breast tissue resection and reduce the incidence of margin involvement, hence, reduce the need for additional treatments together with healthcare costs.[8,9]

The present study shows a significantly lower re-resection rate (7.7% vs. 35%, P = 0.003) and distance from tumor to resection margin (0.62 ±0.16 vs. 1.72 ±0.35 cm, P < 0.001) in UGS group compared to PGS one. In studies by Rahusen et al. and Snider et al. comparing UGS and wire-guided surgery revealed the superiority of UGS regarding minimizing pre-operative stress and discomfort, smaller breast volume excised and improving safety margins (Hence avoid the need for higher boost dose of radiotherapy, re-excision or even mastectomy).[10,11]

In the present study, the UGS group , despite significantly longer operative time (28 ±4 vs. 17 ±3 min, P < 0.001), revealed significantly higher excellent panel evaluation (48.7% vs. 22.5%, P = 0.028) and patient satisfaction (61.5% vs. 30%, P = 0.006). Moreover, 85% of patients reported either good to excellent cosmetic outcomes in UGS group which is comparable to the results reported by Losken et al. (83 %) and Eichler et al. (87 %) after BCS.[12,13]

The frequently used subjective methods to analyze cosmetic outcomes were panel evaluation and the patient self-evaluation methods. Patient self-evaluation and assessment of the surgical cosmetic outcome is of a great value, although patients mostly report a better result than that by the professionals. On the other hand, panel-evaluation was considered to be the most reliable subjective method for evaluation of the outcomes.[14,15] The present study shows a moderate agreement between panel evaluation and patient self-evaluation (Kappa = 0.539, P < 0.001) in the UGS group and a good agreement (Kappa = 0.7, P < 0.001) in PGS group, with an obvious tendency in the patients for a better evaluation in both groups.

In this study, factors that predict "poor" to "fair" cosmetic outcomes were T2 stage and larger safety margin, however, several studies revealed Other factors including the tumor site,[16,17] wound complications,[18] and the amount of radiotherapy (Including radiotherapy boost).[18–20]

In a Studies by Barnett GC et al. and Immink JM et al., the incidence of breast shrinkage or induration increased in patients who had "fair" or "poor" cosmetic results few months after surgery, hence, highlighting the significance of minimizing the mount of breast tissue resected as possible.[21,22]

Patient`s quality of life is dramatically affected when the cosmetic outcome is poor.[23,24] EORTC QLQ-C30 questionnaire was used by Hau et al. which reported that patients with "fair" or "poor" cosmetic outcomes (At 5- and 10-year follow-up) showed a significantly worse quality of life scores.[25] Hence, we can conclude that the use of US in resection of palpable breast mass will improve patient`s quality of life than pGS.

Conclusion

UGS for palpable early breast cancer prove to be superior to the PGS as it significantly reduce re-excision rates and improves overall cosmetic outcome and patient satisfaction which were attributable to the reductions in total excision volumes and the need for additional therapy.

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