Research Article / Araştırma Makalesi

The Efficacy of Using Intraoperative Ultrasound and Frozen Pathology in Breast Conserving Surgery on Safe Surgical Boundary

Meme Koruyucu Cerrahide İntraoperatif Ultrason ve Frozen Patoloji Kullanımının Güvenli Cerrahi Sınır Üzerindeki Etkinliği

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Abstract

Background: Breast cancer is the most common cancer in women over the age of 40. The lifetime risk is around 12%. Today, breast cancer patients are diagnosed at an early stage thanks to screening programs, and thus mortality has decreased to around 25-30%. The positivity or closeness of surgical margins in breast conserving surgery varies between 5-60%. Negativity of surgical margins is very important to prevent future recurrent breast cancer, to prevent recurrent surgeries, and to prevent additional treatments. In this study, we aimed to investigate the efficacy of intraoperative ultrasonography and frozen section use in breast cancers treated with breast conserving surgery in obtaining safe surgical margins and in postoperative cosmetic terms.
Materials and Methods: This study includes 150 patients diagnosed with breast cancer and treated with breast conserving surgery in between January 2015 and January 2019. The presence of distant metastases and multifocal or centrally located tumor involvement in the breasts were investigated. The localization of the tumor was marked anatomically by preoperative ultrasonography in all patients. The operation was started 15 minutes after the injection. The tumor was completely excised, leaving at least 1 cm of intact tissue around the tumor, including the skin, on the preoperatively marked area, including the underlying muscle fascia. Medial and superior borders were marked with string. This excised tissue block was examined with intraoperative ultrasonography.
Results: The mean age of the patients was 48,3± 9.7 years. While the tumor was located in the right breast in 83 (55.3%) of the patients, it was located in the left breast in 67 (44.7%) patients. The tumor was located in the upper outer quadrant in 67 (44.7%) patients, in the upper inner quadrant in 53 (35.3%) patients, and in the lower outer quadrant in 30 (20%) patients. Axillary dissection was performed in 21 (14 %) of the patients because sentinel lymph node was positive. In histological typing, 141 (94 %) patients were ductal carcinoma and 9 (6 %) patients were lobular carcinoma.
Conclusions: As a result of our study and literature review, we think that frozen examination together with intraoperative ultrasonography is a simple, easily applicable and cosmetically good method to determine the safe surgical margin in breast conserving surgery.

Key Words: Breast cancer, Ultrasonography, Surgical margin, Frozen section

Öz

Amaç: Meme kanseri 40 yaş üstü kadınlarda en sık görülen kanserdir. Yaşam boyu risk %12 civarındadır. Günümüzde tarama programları sayesinde meme kanseri hastalarına erken tanı konulmakta ve bu sayede ölüm oranları %25-30 civarına düşmektedir. Meme Koruyucu Cerrahi'de cerrahi sınırların pozitifliği veya yakınlığı %5-60 arasında değişmektedir. İleride tekrar meme kanseri oluşmasını önlemek, tekrarlayan ameliyatları önlemek ve ek tedavilerin önüne geçmek için cerrahi sınırların negatifliği çok önemlidir. Bu çalışmada Meme Koruyucu Cerrahi ile tedavi edilen meme kanserlerinde intraoperatif ultrasonografi ve frozen kesit kullanımının güvenli cerrahi sınır elde etmede ve postoperatif kozmetik açıdan etkinliğini araştırmayı amaçladık.
Materyal ve Metod: Bu çalışma, Ocak 2015 ile Ocak 2019 tarihleri arasında meme kanseri tanısı alan ve Meme Koruyucu Cerrahi ile tedavi edilen 150 hastayı içermektedir. Memelerde uzak metastaz varlığı ve multifokal ya da santral yerleşimli tümör tutulumu araştırıldı. Tüm hastalarda tümörün lokalizasyonu preoperatif ultrasonografi ile anatomik olarak işaretlendi. Tümör tamamen eksize edildi ve altta yatan kas fasyası da dahil olmak üzere ameliyat öncesi işaretli alanda deri de dahil olmak üzere tümörün çevresinde en az 1 cm sağlam doku bırakıldı. Medial ve superior sınırlar ip ile işaretlendi. Eksize edilen bu doku bloğu intraoperatif ultrasonografi ile incelendi.
Bulgular: Hastaların yaş ortalaması 48,3± 9,7 idi. Tümör hastaların 83 (%55,3)'ünde sağ memede yerleşirken, 67 (%44,7) hastada sol memede yerleşmişti. Tümör 67 (%44,7) hastada üst dış kadranda, 53 (%35,3) hastada üst iç kadranda, 30 (%20) hastada alt dış kadranda yerleşmişti. Hastaların 21'ine (%14) sentinel lenf nodu pozitifliği nedeniyle aksiller diseksiyon uygulandı. Histolojik tiplendirmede 141 (%94) hasta duktal karsinom ve 9 (%6) hasta lobüler karsinomdu.
Sonuç: Çalışmamız ve literatür taraması sonucunda intraoperatif ultrasonografi ile birlikte frozen incelemenin Meme Koruyucu Cerrahi'de güvenli cerrahi sınırı belirlemede basit, kolay uygulanabilir ve kozmetik açıdan iyi bir yöntem olduğunu düşünüyoruz.

Anahtar Kelimeler: Meme kanseri, Ultrasonografi, Cerrahi sınır, Frozen inceleme

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Received / Geliş tarihi: 15.05.2023

Accepted / Kabul tarihi: 01.06.2023

DOI: 10.35440/hutfd.1297280

Introduction

Breast cancer is the most common cancer in women over the age of 40. The lifetime risk is around 12%. Today, breast cancer patients are diagnosed at an early stage thanks to screening programs, and thus mortality has decreased to around 25-30% (1). There is also a serious regression in the median tumor diameter due to early diagnosis. As a result of these developments, breast conserving surgery (BCS) is used more widely as a safe surgical option in breast cancer surgery (2). The positivity or closeness of surgical margins in BCS varies between 5-60%. Negativity of surgical margins is very important to prevent future recurrent breast cancer, to prevent recurrent surgeries, and to prevent additional treatments (3,4). In order to obtain the safe surgical margin in BCS, radiological methods such as wire marking, palpation-guided advancement, ultrasound (USG), radiofrequency spectroscopy and intraoperative frozen pathology are used (5). Intraoperative ultrasound was first used in the last years of 1980 to obtain a safe surgical margin in BCS (6). There are studies reporting successful results of using intraoperative USG in determining negative surgical margins in palpable or non-palpable early stage breast cancers. This reduces repetitive surgeries and additional treatments (7).

In this study, we aimed to investigate the efficacy of intraoperative USG and frozen section use in breast cancers treated with BCS in obtaining safe surgical margins and in postoperative cosmetic terms.

Materials and Methods

This study includes 150 patients diagnosed with breast cancer and treated with Breast Conserving Surgery at Health Sciences University Gazi Yaşargil Health Application and Research Center and Memorial Diyarbakır Hospital between January 2015 and January 2019. Patient files were reviewed retrospectively. This study was designed according to the Declaration of Helsinki. Since it was a retrospective study, ethics committee approval was obtained on 05.05.2023 with protocol number 402 from the clinical research ethics committee of Health Sciences University Gazi Yaşargil Training and Research Hospital.

The treatment to be applied to all patients was explained in detail and a consent form was obtained. After histopathological diagnosis of breast cancer was made in all patients, PET CT and bilateral breast magnetic resonance scanning were performed. The presence of distant metastases and multifocal or centrally located tumor involvement in the breasts were investigated. As a clinical approach, BCS was not recommended in patients with multiple focal tumors and central tumor localization. Patients who were suitable for BCS were informed about the radiotherapy and possible chemotherapy they would receive in the post-operative period.

The localization of the tumor was marked anatomically by preoperative USG in all patients. After the patient was intubated, methylene blue was injected around the areola or sentinel lymph node sampling. The operation was started 15 minutes after the injection. The tumor was completely excised, leaving at least 1 cm of intact tissue around the tumor, including the skin, on the preoperatively marked area, including the underlying muscle fascia. Medial and superior borders were marked with string. This excised tissue block was examined with intraoperative USG and it was checked that the tumor was in the middle and that sufficient healthy tissue was left around it (Figure 1).

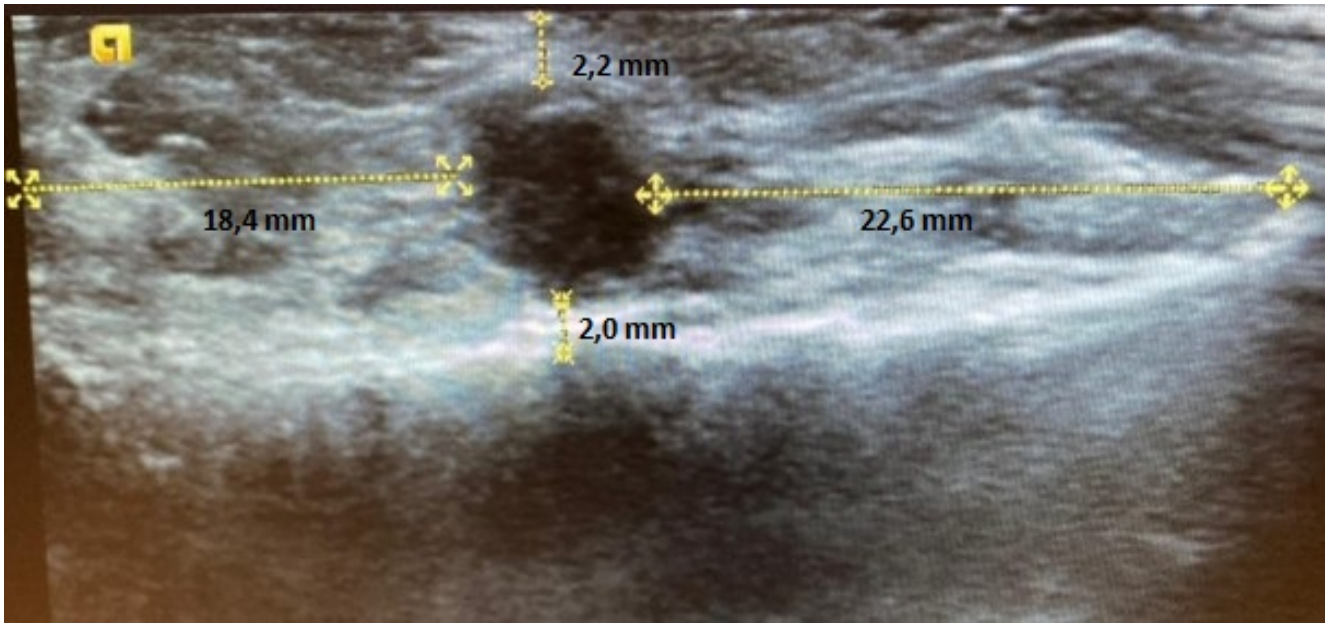

Figure 1. USG image of the sample after excision

Then, the lymph nodes stained with methylene blue through an incision made in the axilla were excised and sent to frozen pathology together with the removed tissue. If the frozen pathology result was positive, the positive surgical margin was excised again. Axillary lymph node dissection was completed if the sentinel lymph node was frozen and the tumor was positive. Axillary drain was placed in patients who underwent axillary lymph node dissection. The drain was removed when the daily drainage amount fell below 30 cc. After wound healing, patients were referred to relevant clinics for radiotherapy and/or chemotherapy. The mean follow-up period was 40±10 months.

Demographic information of the patients, tumor location, tumor size, sentinel lymph node positivity, tumor surgical margin positivity, presence of postoperative complications, tumor stage according to the pathology result, and whether there was a recurrent tumor were scanned. Data were analyzed as mean and percentage by simple manual calculation.

A four-point Likert scale was used to determine patients' cosmetic satisfaction (8). Accordingly, the operated breast was compared with the healthy breast. Classifies outcomes as excellent, good, fair, or poor. 'Excellent' meant identical to the untreated breast and 'poor' indicated a marked difference with the untreated breast.

Results

The mean age of the patients was 48,3± 9.7 years. While the tumor was located in the right breast in 83 (55.3%) of the patients, it was located in the left breast in 67 (44.7%) patients. The tumor was located in the upper outer quadrant in 67 (44.7%) patients, in the upper inner quadrant in 53 (35.3%) patients, and in the lower outer quadrant in 30 (20%) patients. Axillary dissection was performed in 21 (14 %) of the patients because sentinel lymph node was positive. The drainage tube inserted in the patients who underwent axillary dissection was removed in an average of 3 days. As the surgical margin was positive in 6 (4 %) patients as a result of frozen pathology, the relevant surgical margin was enlarged by 2 cm. Two were medial and one was inferior border. The mean size of the tumors was 18.58± 8.72 (9-28) mm. The mean volume of the excised sample was 88±48.52 mm^3. In the early postoperative follow-up, seroma accumulated in 7 (4,66 %) patients. No seroma remained after two aspirations. While the tumor was stage I in 106 (70.66%) patients, it was stage II in 44 (29.34%) patients. In histological typing, 141 (94 %) patients were ductal carcinoma and 9 (6 %) patients were lobular carcinoma. Tumor receptor investigations resulted as follows. Estrogen receptor was positive in 106 (70,66 %) of the patients and negative in 44 (29,34 %) of them. Progesterone receptor was positive in 88 (58,66%) of the patients and negative in 62 (41,34%) of them. Human epidermal growth factor receptor-2 was positive in 34 (22,66 %) of the patients and negative in 116 (77,34%) of them. 32 (21.33%) of the patients had received neoadjuvant chemotherapy. Patients completed adjuvant chemotherapy and radiotherapy. Local recurrence was observed in 5 (3.33 %) of the patients after 24 months. These patients underwent mastectomy. All of the patients were patients who underwent axillary dissection. No additional pathology was observed during the follow-up of the patients. When the cosmetic satisfaction scale was evaluated, 58 (38.66 %) patients said excellent, 70 (46.66 %) patients said good, 22 (14.68 %) patients said fair. No patient said poor. The mean response time to the frozen result was 38 minutes (30-65 minutes). The demographic information and data of the patients are summarized in table 1.

Table 1. Patient and tumor characteristics.

Variables	
Age,years	48,3± 9.7
Tumor size, mm	18.58± 8.72
Excision volume, mm^3	88±48.52
Histologic type n, (%)	
Ductal	141 (94)
Lobular	9 (6)
Tumor localization n, (%)	
Right	83 (55.3)
Left	67 (44.7)
Upper outer quadrant	67 (44.7)
Upper inner quadrant	53 (35.3)
Lower outer quadrant	30 (20)
Tumor stage n,(%)	
Stage I	106 (70.66)
Stage II	44 (29,34)
Lymph node status n,(%)	
Positive	21 (14)
Negative	129 (86)
Receptor status n,(%)	
ER +/-	106 (70,66)/ 44 (29,34)
PR +/-	88 (58,66)/ 62 (41,34)
HER-2 +/-	34 (22,66)/ 116 (77,34)

Data are presented as mean standard deviation or n (%). ER: estrogen receptor, PR: progesterone receptor, HER-2: human epidermal growth factor receptor 2.

Discussion

In suitable patients, BCS and adjuvant radiotherapy are as effective and safe as mastectomy (2). A safe surgical margin and successful cosmetic results are important criteria for surgeons for BCS to be successful (9). Positive surgical margins lead to local recurrences and repeated surgical interventions, negatively affecting patient satisfaction and comfort (10). Therefore, it is very important to obtain R0 resection in the first surgical operation (11). USG has been used safely for many years in the diagnosis of breast diseases and for histopathological sampling. Later, it was revealed that tumors that were not visible on mammography could be detected by USG (12). Schwartz et al. used intraoperative USG to detect and excise non-palpable breast tumors (13). Hu et al. compared USG and wire marking guidance in the excision of non-palpable breast cancer in their study. They operated 262 patients under USG guidance. They found a positive surgical margin rate of 4,6%. The intraoperative re-excision rate was 11.1%. These rates were found to be higher in the group with wire marking. This rate is lower in our

study. In our study, the rate of surgical margin positivity was found to be 3,5% and the rates were approximately similar (3).

Krekel et al. In their study, they divided patients with palpable breast cancer into two groups. They performed surgery under palpation guidance and USG guidance. While the positive margin rate was 3% in the USG group, this rate was 17% in the palpation group. The rate in the USG group is consistent with our study (14).

Haloua et al. In their study, they shared the cosmetic and patient satisfaction results of BCS patients who were performed with intraoperative USG. While the rate of patients who reported only negative feedback on patient satisfaction was 2%, only 6% of patients reported dissatisfaction in terms of cosmetics. They reported the re-excision rate as 2%. We see that these data are compatible with our study (15). In two separate studies by Kayser and Hau, they achieved excellent or good cosmetic results in 93% of patients according to their subjective evaluations (16,17). This rate was 86% in our study and there was no poor in our study.

Corsi et al. In the article they wrote, they stated that in order to determine the tumor localization for BCS, sonographic localization with a high-frequency probe could be performed with wire marking, dye injection, and marking on the skin. After excision, the sample can be examined with USG to check whether a safe surgical margin is provided (18,19). In our study, postoperative margin safety was checked with USG and frozen section in accordance with the procedure.

Intraoperative frozen examination is preferred by many surgeons to minimize the risk of repetitive surgery. With this pathological examination, a safe surgical margin of around 90% is obtained (20). In our study, we used USG guided surgical margin control and frozen examination to minimize the risk of possible recurrence and recurrent surgery. A more precise safe surgical margin was obtained with this procedure. It increased patient satisfaction by reducing the number of repetitive surgeries, as well as reducing health expenditures (21). Olsha et al. stated in their study that problematic surgical margins can be easily detected with USG and re-excision can be performed in the same session, and this result is consistent with our study (22). Usually the cause of positive margins is the intraductal component, and intraductal components may not be visible on USG. Examination of the resected sample with USG with frozen section reduces this possibility and prevents possible local recurrence and repetitive surgeries (23,24).

The use of USG also clearly reveals structures such as fibrosis, mastopathy, and fibrocysts that exist in dense breast tissues. In this way, the surgeon excises a lower volume of breast tissue, avoiding unnecessary resection (25). In addition, frozen can identify these benign lesions close to the intraoperative incision. The use of preoperative USG helps in incision planning, determining the proximity of the tumor to the skin and making a more controlled incision.

In the study conducted by Ko et al., they investigated the usefulness of frozen section for surgical margin safety in 509 patients who underwent breast-conserving surgery. BCS was performed in 437 (85.9%) patients, and mastectomy was performed in 72 (14.1%) patients. Average turnaround time was 40 minutes. A positive margin was found in 123 (24.16%) patients. In our study, surgical margin positivity was found as 3.33 %. We think that the use of intraoperative USG reduces this rate. In our study, no patient underwent total mastectomy. The mean turnaround time was similar (26).

Osaka et al. In the study conducted by Frozen, the positive margin rate was found to be 30.3%. The recurrence rate in the preserved breast was found to be 0.1% in the follow-ups. In our study, while the positive margin rate was lower, the recurrence rate was higher (27).

Conclusion

The use of intraoperative USG and frozen section is a cheap, non-traumatic and time-consuming procedure. It offers the possibility of re-excision in the same session if necessary. As a result of our study and literature review, we think that frozen examination together with intraoperative USG is a simple, easily applicable and cosmetically good method to determine the safe surgical margin in BCS.

Limitation

The limitations of the study are the absence of a control group, its retrospective nature, and the low number of patients.

Ethical Approval: *Declaration of Helsinki. Since it was a retrospective study, ethics committee approval was obtained on 05.05.2023 with protocol number 402 from the clinical research ethics committee of Health Sciences University Gazi Yaşargil Training and Research Hospital.*

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Concept: A.T., E.D.
Literature Review: A.T., E.D., E.G.
Design : A.T., E.G.
Data acquisition: A.T., E.D.
Analysis and interpretation: A.T., E.D.
Writing manuscript: A.T., E.D.
Critical revision of manuscript: A.T., E.G.

Conflict of Interest: *The authors have no conflicts of interest to declare.*

Financial Disclosure: *Authors declared no financial support.*

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