

Assessment of Laparoscopically Harvested Omental Flap Used in Immediate Reconstruction in Breast Cancer Cases Eligible for Breast Conservative Surgery

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Abstract

Background and Purpose: Breast conservative surgery is considered a standard surgical modality for treatment of early breast cancer. Omental pedicled flap is used for volume replacement after breast conservative surgery.

Aim of Study: The aim of this study was to assess the fate of laparoscopically harvested omental flap used in immediate reconstruction in breast cancer cases eligible for breast conservative surgery.

Patients and Methods: Ten female patients were included in this retrospective study which was conducted at The Surgical Oncology Unit, Department of General Surgery, Tanta University Hospitals, from June 2016 to July 2018. Every patient was subjected to mammography with complementary ultrasonography, Doppler ultrasound and Tru-cut needle biopsy from the omental flap and histopathology with different stains.

Results: Nodules were detected in 40% of cases which were proved to be benign in nature by Histopathology. Doppler revealed that two cases had partial infarction and degeneration of the omental flap. Histopathology revealed minimal inflammatory reaction, extensive fat necrosis and dense fibrosis in 50% of the studied cases. Vasculitis was detected in 30% of the studied cases. No recurrence of malignancy could be detected over the follow-up period. With CD31, various degrees of neovascularization were detected in the omental flap, mild in 20% of cases, moderate in 40% of cases and severe in 40% of cases. With CD8, T-Killer cells were found mild in 50% of cases and moderate in 40% of cases. CD44 detected presence of stem cells in 20% of cases.

Conclusion: The laparoscopically harvested omental flap had a promising oncological safety during the follow up. In spite of the fibrosis and nodulation found, no change was observed in the shape or contour of the breast. The inflammatory reaction and enhanced local immunity by the omentum is not studied as a possible preventive factor for recurrence. Vasculitis, angiogenesis and the presence of stem cells are not studied as a possible potentiating factor for recurrence of

breast cancer. So, long term follow-up is essential to see whether the omental flap could be a barrier against recurrence or it may enhance it.

Key Words: Breast cancer – Breast conservative surgery – Omental flap.

Introduction

BREAST conservative surgery is considered the treatment of choice in early breast cancer [1,2]. Some studies have proved that immediate breast reconstruction is better than delayed reconstruction both aesthetically and functionally [3].

Pure autologous tissue reconstruction is more desirable because of its durability, better appearance, softness, warmth, avoidance of implant-related complications, and resistance to the effect of postoperative irradiation [4,5]. The use of the omental flap for breast cancer was first described by Kiricuta in 1963 [6]. More than a decade later, Arnold et al described a one-stage reconstruction of the breast using a transposed greater omentum. [7] Saltz et al., were the first to describe the laparoscopically harvested the omental flap for repair of soft tissue defects in 1993 [8]. A few years later, Costa et al., described the laparoscopically harvested omental flap for breast reconstruction and its use in the treatment of Poland syndrome in 1998 [9].

Recently investigators have shown that the omentum can be activated in the presence of foreign bodies. Once activated, the thin sheet like organ enlarges in size and mass wherein the new cells are predominantly non-fat stromal cells [10,11]. These stromal cells are a rich source of growth factors like fibroblast growth factor (FGB) and vascular endothelial growth factor (VEGF) and

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express adult stem cell markers including SDF-1a, CXCR4, WT-1, as well as pluripotent embryonic stem cell markers; Nanog, Oct-4, and SSEA-1 [10,12,13]. Data suggests that the omentum contains the potent ability of tissue regeneration and may be useful for treatment of various types of diseases involving tissue damages [14]. In this study we aimed to assess the fate of laparoscopically harvested omental flap used in immediate reconstruction in breast cancer cases eligible for breast conservative surgery.

Patients and Methods

This is a retrospective study including 10 female patients with breast cancer eligible for breast conservative surgery. It was conducted at The Surgical Oncology Unit, Department of General Surgery, Tanta University Hospitals. The duration of this study was 26 months, started from the 1st of June 2016 to the 31st of July 2018. They were operated on for local excision of breast cancer with immediate reconstruction of the breast with pedicled omental flap harvested with laparoscope. Every patient was called upon at least 6 months after finishing chemoradiotherapy. So the follow-up period ranged from 6 to 12 months. This study was approved by the ethics committee of our institution; informed consent was obtained from all patients after full explanation of the procedure. It was approved by the Research Ethical Committee, Faculty of Medicine, Tanta University.

Patients selection criteria:

Inclusion criterion:

Female patients eligible for breast conservative surgery with immediate breast reconstruction with volume replacement using laparoscopically harvested omental flap.

Exclusion criteria:

Patients with graft necrosis, patients with local recurrence and patients with soft tissue or bone metastasis.

Every patient in this study was subjected to the following:

1- History taking:

Complete history taking with emphasizing on breast complains in details:

- Personal data and reproductive history.
- Complaint: Breast lump, pain, axillary swelling, nipple discharge ... etc.
- Positive family history of breast cancer.
- Concomitant medical or surgical problems.

2- Clinical examination:

General examination:

- For presence of incisional hernia.
- To exclude soft tissue or bone metastasis.

Breast examination including:

- Breast contour, skin, nipple areola complex and symmetry.
- Breast mass (number, size, site, multiplicity and fixation).
- Any nipple discharge.
- Axilla and ipsilateral arm.
- Contralateral breast and axilla.

3- Investigational studies:

a- Laboratory investigations:

Relevant laboratory workup:

- Complete blood count.
- Coagulation profile (bleeding time, clotting time, prothrombin activity).
- Liver function tests as ALT, AST and alkaline phosphatase.
- Tumor markers (CEA, CA 15.3).

b- Imaging investigations:

- Mammography with complementary ultrasonography of the breast to assess the density of the breast and the omental flap, presence of any masses, calcifications and the axillary lymph nodes.

- Doppler ultrasound of the breast to assess the vascularity of the omental flap.

c- Histopathological investigation:

- Tru-Cut needle biopsy taken from every patient for Histopathological study, different stains were used in the study:

1- Conventional stains (H&E) in every case.

2- Special stains:

- a- P63 to prove the presence of sclerosing adenosis.
- b- CD44 to prove the presence of stem cells.
- c- CD8 to prove the presence of T-Killer cells.
- d- CD31 to prove the presence of neovascularization.

Statistical analysis:

The collected data were organized, tabulated and statistically analyzed using SPSS version 25 (Statistical Package for Social Studies) created by IBM, Illinois, Chicago, USA. We used descriptive statistics, where data were expressed as number and percentage.

Results

This study included 10 patients who underwent immediate breast reconstruction with volume replacement using laparoscopically harvested omental flap following breast conservative surgery and were followed-up from June 2016 to July 2018 at least 6 months following chemoradiotherapy. The ages of the studied patients ranged from 26 to 72 years old, with mean age 44.7 ± 12.21 .

Regarding mammography with complementary ultrasonography, 40% of cases had mixed fatty glandular density, 20% were fatty, 20% were micronodular, whereas 20% were mixed fibrofatty. No masses were detected in 50% of the studied cases. No calcification was detected in any case during the follow up period. One case had a benign looking cyst. Nodules were detected in 40% of cases which were proved to be benign in nature by Tru-Cut needle biopsy and Histopathology.

By using Doppler, most cases showed normal vascularity of the omental flap, these were 80% of the studied cases. Two cases revealed partial infarction and degeneration of the omental flap, mostly due to the radiotherapy effect postoperatively. Histopathological examination of these 2 cases revealed fat necrosis and fibrosis with no recurrence.

Histopathological exam detected various degrees of inflammatory reaction, mostly was minimal in 50% of the studied cases as shown in Table (1). Fig. (1) shows infiltration of the fat tissue by lymphocytes, macrophages and plasma cells. Fat necrosis was obvious in the omental flap. It was detected to be extensive in 50% of the studied cases as shown in Table (2), Fig. (2) shows an example of moderate fat necrosis in one of the studied cases.

The degree of fibrosis detected was mostly dense during the follow-up period in 50% of the studied cases as shown in Table (3), Fig. (3) shows replacement of the fatty tissue of the omental flap by collagen fibers in one of the cases. Vasculitis was detected in 30% of the studied cases, most probably due to the effect of radiotherapy postoperatively, Fig. (4) shows an example of vasculitis in one of the cases.

No recurrence of malignancy could be detected in any of the studied cases over the follow-up period. CD31, an indicator for vasculo-endothelial cells, detection was somehow related to the degree of fibrosis found in histopathology, various degrees

of neovascularization developed in the omental flap after implantation, found to be mild in 20% of cases, moderate in 40% of cases and severe in 40% of cases, possibly by the angiogenetic factors of the omentum, Fig. (5) shows neovascularization detected in one of the cases. CD8, an indicator of the presence of T-Killer cells, percentages was somehow related to the degree of inflammatory reaction found, mild presence was found in 50% of cases, moderate presence was found in 40% of cases and severe presence was found in 10% of cases, Fig. (6) shows the detection of T-Killer cells in one of the cases. CD44, an indicator for stem cells, was found in 20% of cases, Fig. (7) shows the CD44 stain in two cases.

Table (1): Inflammatory reaction in histopathological samples.

Interpretation	Inflammatory reaction in histopathology	
	No.	%
Minimal	5	50
Mild	2	20
Moderate	2	20
Severe	1	10
Total	10	100

Table (2): Fat necrosis in histopathological samples of studied patients.

Interpretation	Fat necrosis in Histopathology	
	No.	%
Mild	2	20
Moderate	3	30
Extensive	5	50
Total	10	100

Table (3): Fibrosis in histopathological samples of studied patients.

Interpretation	Fibrosis in Histopathology	
	No.	%
Mild	3	30
Dense	5	50
Keloid	2	20
Total	10	100

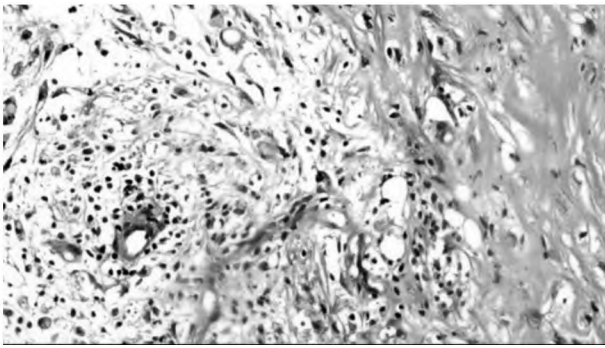


Fig. (1): Moderate inflammatory reaction in one of the cases by H&E.

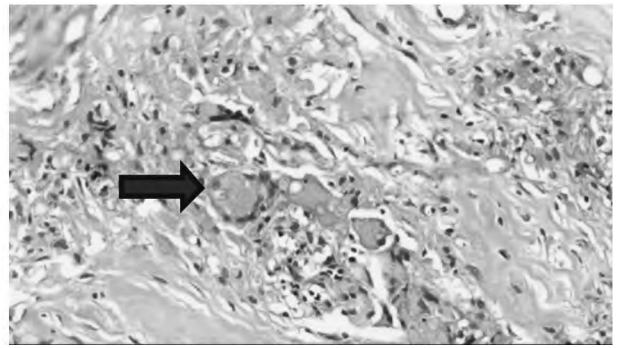


Fig. (2): Moderate fat necrosis in one of the cases by H&E.

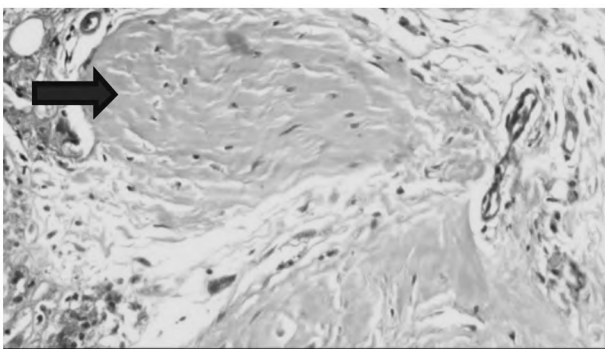


Fig. (3): Dense fibrosis in one of the cases by H&E.

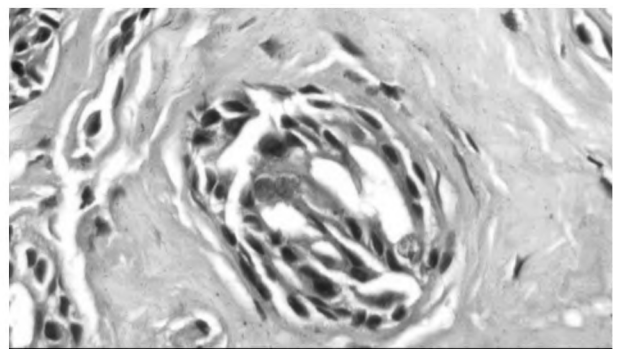


Fig. (4): Vasculitis with endothelial proliferation in one of the cases by H&E.

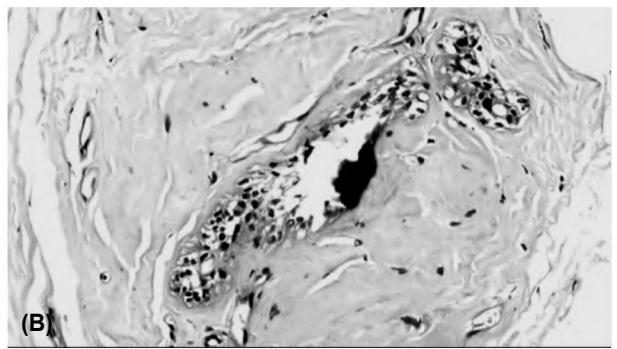
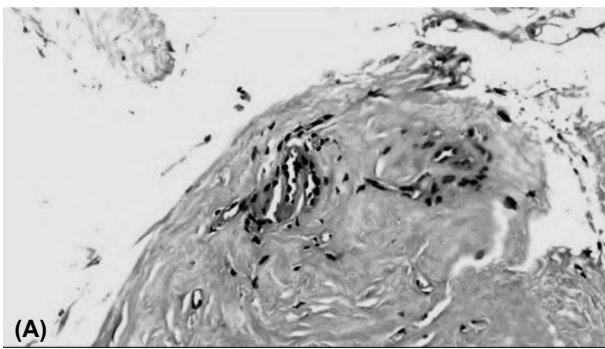


Fig. (5): Neovascularization detected in one of the cases, (a) X40 and (b) X100.

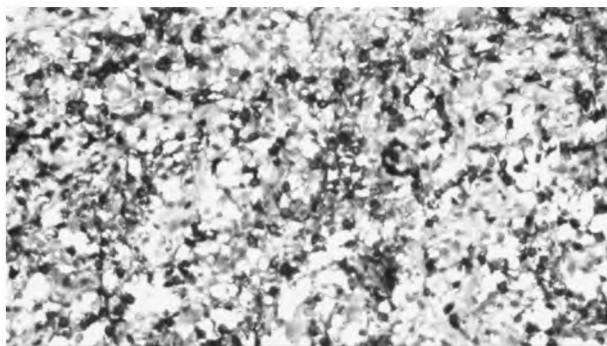


Fig. (6): The detection of T-Killer cells.

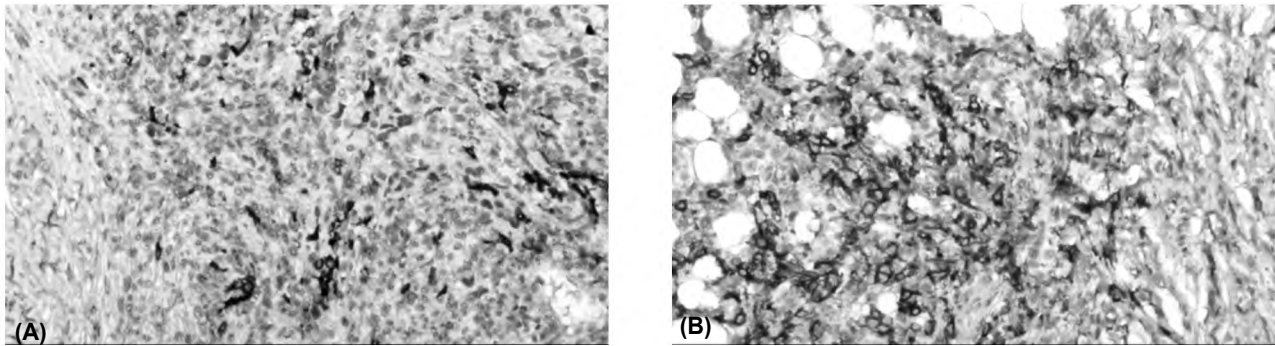


Fig. (7): CD44 stain in two cases, (a) X100 and (b) X100.

Discussion

Kiricuta and Popescu (1973) first described harvesting omental flaps through a laparotomy that was associated with several complications and disadvantages [15]. It was not until earlier in the millennium that the introduction of laparoscopy as a technique for harvesting the flap and that the number of cases started to increase [8]. The advantages of laparoscopy results in minimizing the effects of dissection on the donor site, the incisions visible to the patients and their scars, a decreased operative time, and associated complications [16,17].

One of the different modalities of volume replacement in breast oncoplastic surgery is the use of omental pedicled flap [18]. Like other autologous flaps, this flap serves well for patients who might refuse or cannot afford the insertion of prosthetic materials in their bodies [19].

In the review of the literature agreement was concluded on advantageous properties of the omentum in terms of its malleability to any shape. Advantages were identified for the use of the omental flap in terms of outcome, mainly its superior aesthetics, its availability in all patients, the omentum's rich blood supply that supports healing and its immunogenic properties that prevent infections [20,21].

Two questions should be answered. First, bringing an intraabdominal organ into a subcutaneous position where it would be exposed to external radiation that would modulate its properties. Second, bringing an innocent intraabdominal organ into direct contact with cancer bed, would carry a potential risk of transporting malignancy into the abdomen. The fate of that omental flap that was transposed into the breast is not well studied. Very few reports are available in the literature but not covering all the aspects. In this study we tried to find out the final outcome of the flap based on studying its vascularity (by Doppler), shape (by

imaging studies) and the potential immune function or risk factor for recurrence (by Histopathology).

A total number of 10 female patients eligible for immediate breast reconstruction with volume replacement using laparoscopically harvested omental flap following breast conservative surgery were included in this study.

The patients age ranged from 26 to 72 years old with mean age 44.7 ± 12.21 . Zaha and Inamine (2010) published a large study examining laparoscopically harvested omental flaps among 96 women. They evaluated a relatively older group of women (mean age 49 years) [17]. Khater (2013) published a study for evaluation of pedicled omental flap delivered through a minilaparotomy for immediate breast reconstruction in obese patients for 24 patients with mean age of 57.54 years. 22 However, The age of the patients has no value in the final assessment of either the oncologic safety or the aesthetic outcome of the procedure [23]. Nevertheless, we observed that the patients felt satisfied with preserving the breast whatever its residual shape or contour.

The viability of the omental flap can be studied intraoperatively through laser Doppler flowmetry [24]. Or postoperatively by exposing a small part of the flap through the skin [16]. In the present study, viability of the omental flap was assessed postoperatively by Doppler, which revealed partial infarction and degeneration in 20% of the studied cases, probably due to the effect of radiation received postoperatively. That would be attributed to the improper mapping and improper adjustment of the radiation dosage, as Trombetta et al. (2010) reported in their study. [25] Costa et al (2011) reported an increase in size of free flaps up to 6 months postoperatively, which was attributed to the temporary ischemia. [26] Khater (2013) in his study noted that flap survival was excellent, with only a single case of partial necrosis (4%) [22]. This high discrepancy among findings regarding

the viability of the flap could be related to the difference in patients' response to radiation dosage improperly adjusted.

Regarding mammography with complementary ultrasonography, 40% of cases had mixed fatty glandular density, 20% were fatty, 20% were micronodular, whereas 20% were mixed fibrofatty. No masses were detected in 50% of the studied cases. No calcification was detected in any case during the follow-up period. One case had a small cyst, which was proved by Histopathology to have a benign nature. Nodules were detected in 40% of cases due to partial fibrosis from fat necrosis and Tru-Cut needle biopsy and Histopathological study proved their benign nature. That is probably due to the effect of external radiation taken postoperatively because the omental tissue tolerance to radiation is different from the breast tissue [25,27,28]. No recurrence of tumor was detected as proved by histopathology.

Histopathological exam detected various degrees of inflammatory reaction, it was minimal in 50% of the studied cases. The immune system has the power to modulate the damage effect of radiation on normal and tumor tissue. It can contribute to cancer cure, on the other hand it can influence acute and late radiation side effects, which in many ways resemble acute and chronic inflammatory disease states [29]. CD8, an indicator of the presence of T-Killer cells, percentages were somehow related to the degree of inflammatory reaction found, mild presence was found in 50% of cases and moderate presence was found in 40% of cases. These findings are compatible with the innate property of the omentum [30].

Fat necrosis was obvious in the omental flap. It was detected to be extensive in 50% of the studied cases. This was probably due to the omental exposure to radiation extraabdominally leading to partial infarction and degeneration [25,27,28]. Guan D et al. (2015) observed fat necrotic nodule in 12.5% of cases among 24 cases with laparoscopic harvested omental flap [31]. Zaha et al. (2017) observed fat necrosis occurred in 5.2% of patients. 32 The high incidence of fat necrosis in the present study may be related to increased response to postoperative radiation. This adverse effect was reported by Garsa et al. (2013) in cases receiving interstitial brachytherapy. They also reported that fat necrosis is associated with worse qualitative and quantitative cosmetic outcomes [33]. Therefore, minimizing exposure volumes, may decrease the incidence of fat necrosis and improve cosmesis.

In the present study, the degree of fibrosis detected was mostly dense during the follow-up period in 50% of the studied cases. Some studies suggested a genetic factor for excessive fibrotic response to radiation. Grossberg et al., conducted a study in 2018 aiming for validation of a genomic marker for radiation fibrosis. The C-509T allele in transforming growth factor β 1 (TGFB 1) is a key determinant of breast fibrosis risk. Assessing TGFB 1 genotype may facilitate a more personalized approach to locoregional treatment decisions in breast cancer [34].

In the present study, vasculitis was detected in 30% of the studied cases. Most probably due to the innate property of the omentum to produce capillary ingrowth, also would be as an inflammatory response to external radiation [13,35,36]. No studies in the literature reported vasculitis in the omental flap used for immediate breast reconstruction following breast conservative surgery.

Over the short period of follow-up in the present study, no recurrence of malignancy could be detected in any of the studied cases. Moran et al., in a recent meta-analysis of 33 studies including 28,162 patients who underwent breast conservative surgery and omental flap reconstruction for stage I and II invasive breast cancer revealed a median prevalence of ipsilateral breast tumor recurrence of 5.3% in a median follow-up period of 79.2 months [37]. Compared with this meta-analysis, Zaha et al. (2017) reported lower local recurrence rate with a longer median follow-up period of 90 months, which suggests the oncological safety of the laparoscopically harvested omental flap procedure [32].

In the present study, we used CD31 marker to measure angiogenesis in the omental flap. There was an increase in the number of vessels noted suggesting neo-angiogenesis. We reported mild increase in 20% of cases, moderate increase in 40% of cases and severe increase in 40% of cases. This stain is an indicator for vasculo-endothelial cells. The higher was the vasculo-endothelial cells found, the higher the degree of fibrosis on Histopathological study.

CD44 stain is a marker for stem cells. In the present study, we reported 2 positive cases out of 10 (20%). No studies regarding this point were found in the literature. However, some studies reported CD44 as a marker of breast cancer cells. 38,39 Other studies used it as a prognostic factor for breast cancer. Whenever it is expressed in high percentage in the breast cancer it worsens the

prognosis [40]. Consequently, increased expression of CD44 in the omentum would be considered as a predictor of recurrence.

Conclusion:

Tumor should be completely eradicated before the use of omental flap as a volume replacement after breast conservative surgery. The laparoscopically harvested omental flap had a promising oncological safety during the follow up. The omental flap can achieve a good cosmetic outcome in breast reconstruction after breast conservative surgery. In spite of the fibrosis and nodulation found, no change was observed in the shape or contour of the breast. Any nodule detected during the follow up should be biopsied and examined histopathologically. The inflammatory reaction and enhanced local immunity by the omentum is not studied as a possible preventive factor for recurrence. Vasculitis due to angiogenesis and inflammatory reaction is not studied well as a potential enhancing factor for recurrence. The presence of CD44 in the omental flap is not studied as it would potentiate the recurrence of breast cancer.

Recommendations:

Long term follow-up is essential to see whether the omental flap could be a barrier against the recurrence of tumor due to its immunological function, or it can enhance the recurrence due to its angiogenetic capabilities together with production of stem cells in some cases.

Limitations:

This is a single-centre experience and represents a limited number of patients.

Financial support and sponsorship:

Nil.

Conflicts of interest:

There are no conflicts of interest.

Authors' contributions:

All authors had equal role in design, work, statistical analysis and manuscript writing.

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تقييم سديلة الثرب المستخلصة عن طريق المنظار الجراحي المستخدمة فى التقويم الفورى فى حالات الجراحات التحفظية لسرطان الثدي

جراحة أورام الثدي التحفظية تعتبر الحل الأمثل لعلاج سرطان الثدي المبكر. يتم استخدام سديلة الثرب المستخلصة عن طريق المنظار الجراحي كوسيلة تعويضية لحجم الثدي بعد استئصال الورم. تهدف هذه الدراسة لتقييم سديلة الثرب المستخلصة عن طريق المنظار الجراحي المستخدمة فى التقويم الفورى فى حالات الجراحات التحفظية لسرطان الثدي.

هذه دراسة بأثر رجعى تم إجراؤها على عشرة حالات من النساء اللائى قد أجريت لهن جراحة تحفظية من إعادة إنشاء الثدي بأستخدام سديلة الثرب المستخلصة عن طريق المنظار الجراحي وذلك بعد استئصال الورم من الثدي. تمت الدراسة بقسم جراحة الأورام بكلية الطب، جامعة طنطا. وقد تم تعريض الحالات ضمن الدراسة للفحوصات الإكلينيكية، أشعة المأموجرام والموجات فوق الصوتية المكملة لها، الدوبلر وتحليل الأنسجة لتقييم سديلة الثرب المستخدمة.

سديلة الثرب المستخلصة عن طريق المنظار الجراحي كان لها أثر واعد كطريقة آمنة عند استخدامها كوسيلة تعويضية لحجم الثدي عند إجراء الجراحة التحفظية لاستئصال الورم. بالرغم من ظهور بعد العقيدات بالثدي فى بعض الحالات ضمن الدراسة إلا أنها لم يكن لها تأثير واضح على الشكل العام للثدي. لم تتم دراسة رد الفعل الالتهابى وزيادة المناعة الموضعية للثرب كوسيلة لمنع رجوع الورم مجدداً، كما لم تتم دراسة ظهور أوعية دموية جديد وظهور الخلايا الجذعية فى بعض الحالات ضمن الدراسة كعامل محفز لرجوع الورم مجدداً، ويرجع ذلك للحاجة لعدد أكبر من الحالات ومدة دراسة أطول.