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EVALUATION OF WIRE LOCALIZATION IN MANAGEMENT OF NON-PALPABLE BREAST CANCER IN EGYPT

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Abstract

Breast-conserving surgery (BCS) is considered the gold-standard treatment for early breast cancer. Various techniques were proposed for identifying non-palpable breast tumors, but the most popular one is the wire-guided localization (WGL technique). The most important drawback of BCS is the possible presence of microscopic tumor at or close to the margin of excision.

The work highlighted significance of screening programs in early detection and recent advances in the management of early non palpable breast cancer. This was a prospective study on 30 patients with a single non-palpable breast lesion. A preoperative USG or MMG-guided hook wire localization technique was performed then intraoperative frozen section was done.

The results showed that 30 patients were treated with wire-guided localization and BCS, andintraoperative frozen sections. According to positive margins, patient age, menopausal status, tumor size and histologic type were associated with increased risk of positive margins. The re-excision at the time of original operation was 6/30(20%), without second operation. Postoperative complications were 5(16.7%) due to neo-adjuvant chemotherapy, size of mass, specimen volume, margin status and LNs affection.

Keywords: Wire-guided localization, Non-palpable Breast cancer, Breast-conserving surgery

Introduction

Breast cancer is the commonest cancer among females with 25%-35% non-palpable at the time of diagnosis (American Cancer Society, 2017). National Cancer Institute reported that breast cancer was commonest cause of cancer death among females (21%) of all cancer mortality (Elattar, 2015).

Advanced breast cancer screening techni-\ques as; ultrasonography, mammography and breast MRI in early detection of many non-palpable breast lesions and their availability increased the number of non-palpable breast lesions requiring surgery (Sarlos *et al,* 2015). Diagnosis of a breast lump or suspicious ones should be made by a combination of clinical assessment, radiological imaging, and tissue sample taking for cytological or histological analysis, so called triple assessment (Smith and Cokkinides, 2013).
Through the years the classification of early breast cancer has changed as the disease has changed in presentation. More than 50% of the breast cancers were diagnosed in the United States (Cady *et al,* 2015).

Breast conserving surgery has been a recognized method of treatment of early breast cancer. The treatment methods include quadrantectomy or skin sparing mastectomy combined with ipsilateral axillary nodal dissection followed by radiotherapy. Modified radical mastectomy was effective for some patients, but breast conservation therapy proved to be optimal treatment for the majority patients (Singletary, 2001). These lesions need special way of localization to help for intraoperative identification and excision. Wire-guided localization (WGL) proved to be the standard one for many years for localization of non-palpable breast lesions using either ultrasound or mammography preoperative (Sajid *et al,* 2015).

A thin and hooked wire is inserted into the lesion, and the surgeon uses the wire and standard imaging to identify and remove the lesion with good cosmetic result and few complications and excellent results regarding margin status, total of operations, and

excess breast tissue excision (Krekel *et al,* 2013).

Ultrasound-guided surgical clips placement for breast cancer localization prior to neo-adjuvant chemotherapy before surgical treatment was recommended. Neo-adjuvant chemotherapy was the standard pre-operative treatment, in locally advanced cases that converted the inoperable masses into operable one with less complications and better cosmetic outcome (Masroor *et al,* 2016). Radiotherapy reduced the risk of isolated local recurrence by approximately 66%, and radiotherapy proved to be effective for patients underwent breast conservation surgery (Costa *et al,* 2004).

Adjuvant systemic therapy includes endocrine therapy as tamoxifen, the widely used adjuvant systemic therapy for most postmenopausal women. Cytotoxic chemotherapy, regimen was a combination of cyclophosphami- I de, methotrexate and 5-flurouracil (CMF). The 5-fluorouracil, adriamycine and cyclophosphamide (FAC) stressed on the primary chemotherapy value to increase conservative surgery as a predictor of outcome (Falo *et al,* 2005).

This work aimed to highlight the significance of screening programs, early detection and recent advances in the management of early non palpable breast cancer.

Patients and Methods

The present study was a prospective cohort study of 30 patients diagnosed as non-palpable breast cancer and underwent US or mammographic wire localization and wide local excision with frozen section. It was conducted in the period from February 2019 till February 2021 on 30 patients. The study protocol was approved by the ethical committee and all patients gave informed consent to participate in the study. Participants in the present study were selected based on: Non-palpable breast mass discovered by mammography, ultrasonography during screening and non-palpable breast mass post neo-adjuvant chemotherapy. Exclusion criteria: Palpable breast mass, elderly > 75 years, contra indication for conservative breast surgery (1^{st} & 2^{nd} trimester of pregnancy and disseminated malignancy), and axillary lymph nodes positive and negative breast by mammography

All patients were subjected to: A- Pre-operative clinical and laboratory assessment: Careful history taking, Clinical examination, Radiological assessment (breast ultrasound, mammography abdominal US), Pathological assessment, & US or mammographic guided wire localization. B- All operations were carried out by General Surgery Staff, Ain-Shams University Hospitals and Mostafa Kamel Military Hospital. All patients were subjected to wide local excision with frozen section and to SLNB.

Operative technique: Wire localization and frozen section: 1. Preoperative US wire localization (Fig. 1a), 2. Position: Supine, with arms abducted at 90^{o} degree from chest, 3. General anesthesia, 4. Antisepsis of operative site, 5. Incision: elliptical circumferential along Langer's line or according to mass site (Fig 1b). 6. Skin flaps elevated and identification of wire and bringing of wire at site of dissection (Fig 1c). 7. Dissection done around tumor with safety margin about 1cm around mass guided by wire localization (Fig 1d). 8. Marking resected specimen using sutures as superior, inferior, medial, lateral, anterior and posterior for identification of clearance margins and orientation (Fig 1e). 9. Resection completed (Fig 1f). 10. Specimen inspected properly for tumor relation to margins. All marked surfaces and margin closed to tumor underwent frozen section biopsy for confirmation of clearance (Fig 1g). 11, Clips were put in all direction of mass bed at site of resection (Fig 1h), & l2. Negative safety wound margin closure by good hemostasis without drainage (Fig 1i).

Sentinel lymph node dissection (patent blue): 1. Injection of patent blue dye in retro areolar region (Fig. 2a). 2. Massage breast 15 min. helping dye enter lymphatic (Fig. 2b). 3. Incision was marked below axillary hairline (Fig. 2c), 4. Incision done deepened till clavipectoral fascia and dissection till

blue lymphatic (Fig. 2d). 5. Blue SLN seen (Fig. 2e), and 6. Resection of SLN, for frozen section for result to close layer after good hemostasis without drain (Fig. 2f)

Outcome intervention: Postoperative complications (wound infection, seroma, hemorrhage, lymphedema…), and time of hospital stay and Readmission rate.

Statistical analysis: Data were computed using SPSS versions, and were expressed in the form of mean ± SD while categorical data were expressed in the form of count and percent. Comparison of continuous data was performed utilizing student t test, while categorical data were done using Chi-square test. P value less than 0.05 was significant.

Results

The results were shown in tables (1 to 13) and figures (1 to 15).

Table 1: Descriptive table for demographic data of patients.

Demographic Data		Total No. 30
Age	Mean ± SD	43.63 ± 10.57
	Range	23 – 62
Menopausal status	Premenopausal	14 (46.7%)
	Postmenopausal	16 (53.3%)
Family history	No	21 (70.0%)
	Yes	9 (30.0%)

Table 2: Histological type and indication of mammography of patients.

Items		Total no. = 30
Indication for mammography	Nonspecific breast complaints	11 (36.7%)
	Screening	17 (56.7%)
	Post neo-adjuvant chemotherapy	2 (6.7%)
Histological type	Intra-ductal ca	21 (70.0%)
	Intra-lobular ca	2 (6.7%)
	DCIS	7 (23.3%)

Table 3: Descriptive table for mammographic; US findings and WGL timing of patients.

Mammogram or US findings		Total no. = 30
Site	Upper external	21 (70.0%)
	Lower external	1 (3.3%)
	Lower internal	1 (3.3%)
	Upper internal	7 (23.3%)
Size (mm)	Mean ± SD	11.83 ± 3.84
	Range	4 – 19
Shape	Round	3 (10.0%)
	Oval	10 (33.3%)
	Irregular	17 (56.7%)
BIRADS classification	4	19 (63.3%)
	5	11 (36.7%)
Side	Right	17 (56.7%)
	Left	13 (43.3%)
Diagnosing findings by US	No	11 (36.7%)
	Yes	19 (63.3%)
US guided wire localization time (min.)	Mean ± SD	13.17 ± 2.56
	Range	8 – 18

Table 4: Operative data of patients.

Operation Data		Total no. = 30
Resection time (min.)	Mean ± SD	32.57 ± 7.00
	Range	20 – 40
Frozen section time (min.)	Mean ± SD	17.69 ± 2.61
	Range	12 – 21
Total operative time (min.)	Mean ± SD	49.67 ± 8.47
	Range	33 – 60
Specimen volume (mm^3)	Mean ± SD	139.93 ± 50.86
	Range	66 – 220
Margin status	Negative	24 (80.0%)
	Positive	6 (20.0%)
Intra operative re-excision	No	24 (80.0%)
	Yes	6 (20.0%)
Drains	No	21 (70.0%)
	Yes	9 (30.0%)

Operative data safety, intra operative re-excision 6/30 (20%) & frozen section sensitivity (100%), without second operation.

Table 5: Patients' pathogenesis

Pathology		Total No. 30
Histological grade	I	9 (30.0%)
	II	15 (50.0%)
	III	5 (20.0%)
LNs affection	Negative	21 (70.0%)
	Positive	9 (30.0%)
ER status	No	7 (23.3%)
	Yes	23 (76.7%)
PR	No	13 (43.3%)
	Yes	17 (56.7%)
HER2 status	No	24 (80.0%)
	Yes	6 (20.0%)

Table 6: Postoperative data of patients.

Postoperative data		Total no. 30
Hospital stay (days)	Mean ± SD	1.57 ± 0.68
	Range	1 – 3
Complications	Non complicated	25 (83.3%)
	Complicated	5 (16.7%)
Type of complications	Seroma	2 (6.7%)
	Infection	2 (6.7%)
	Delay healing	1 (3.3%)
	Lymphedema	1 (3.3%)

Post-operative: some patients showed one complication, but one patient with lymphedema who needed for readmission for reassurance and conservative treatment.

Table 7: Comparison between complicated and non-complicated cases of demographic data.

Variations		Non complicated No. = 25	Complicated No. = 5	Test value	P-value	Significance
Age	Mean ± SD	42.24 ± 9.49	50.60 ± 14.05	-1.663•	0.108	NS
	Range	23 – 58	27 – 62			
Menopausal status	Premenopausal	12 (48.0%)	2 (40.0%)	0.107*	0.743	NS
	Postmenopausal	13 (52.0%)	3 (60.0%)			
Family history	No	17 (68.0%)	4 (80.0%)	0.286*	0.593	NS
	Yes	8 (32.0%)	1 (20.0%)			

No significant difference between both groups according demographic data.

Table 8: Complicated and non-complicated cases among histological type and mammography indication

Variations		Non complicated No. = 25	Complicated No. = 5	Test value	P-value	Significance
Mammography indication	Non-specific breast complaints	10 (40.0%)	1 (20.0%)	10.749*	0.005	HS
	Screening	15 (60.0%)	2 (40.0%)			
	Post neo-adjuvant chemotherapy	0 (0.0%)	2 (40.0%)			
Histological type	Invasive ductal ca	18 (72.0%)	3 (60.0%)	11.486*	0.003	HS
	Invasive lobular ca	0 (0.0%)	2 (40.0%)			
	DCIS	7 (28.0%)	0 (0.0%)			

Highly significant difference as histological type as invasive lobular, patients with neo-adjuvant chemotherapy more complications.

Table 9: Complicated and non-complicated cases as to mammography and US finding.

Mammogram or US findings		Non complicated No. = 25	Complicated No. = 5	Test value	P-value	Significance
Site	Upper external	18 (72.0%)	3 (60.0%)	5.314*	0.150	NS
	Lower external	0 (0.0%)	1 (20.0%)			
	Lower internal	1 (4.0%)	0 (0.0%)			
	Upper internal	6 (24.0%)	1 (20.0%)			
Size (mm)	Mean ± SD	11.12 ± 3.64	15.40 ± 2.88	-2.465•	0.020	S
	Range	4 – 19	12 – 19			
Shape	Round	3 (12.0%)	0 (0.0%)	1.496*	0.473	NS
	Oval	9 (36.0%)	1 (20.0%)			
	Irregular	13 (52.0%)	4 (80.0%)			
BIRADS classification	4	18 (72.0%)	1 (20.0%)	4.852*	0.028	S
	5	7 (28.0%)	4 (80.0%)			
Side	Right	13 (52.0%)	4 (80.0%)	1.330*	0.249	NS
	Left	12 (48.0%)	1 (20.0%)			
Diagnosis by US	No	11 (44.0%)	0 (0.0%)	3.474*	0.062	NS
	Yes	14 (56.0%)	5 (100.0%)			
US guided wire localization time (min.)	Mean ± SD	13.00 ± 2.52	14.00 ± 2.92	-0.792•	0.435	NS
	Range	8 – 17	11 – 18			

Significant difference as to mass size and BIRADS classification, bigger size more complications.

Table 10: Complicated and non-complicated cases according operative data.

Operation data		Non complicated No. = 25	Complicated No. = 5	Test value	P-value	Significance
Resection time (min.)	Mean ± SD	33.20 ± 6.60	29.40 ± 8.88	1.112•	0.275	NS
	Range	20 - 40	20 – 40			
Frozen section time (min.)	Mean ± SD	17.83 ± 2.39	17.00 ± 3.74	0.644•	0.525	NS
	Range	12 - 21	12 – 20			
Total operative time (min.)	Mean ± SD	50.32 ± 7.70	46.40 ± 12.22	0.942•	0.354	NS
	Range	34 - 60	33 – 59			
Specimen volume	Mean ± SD	129.64 ± 48.66	191.40 ± 24.02	-2.743•	0.010	S
	Range	66 - 220	160 – 216			
Margin status	Negative	22 (88.0%)	2 (40.0%)	6.000*	0.014	S
	Positive	3 (12.0%)	3 (60.0%)			
Intra operative re-excision	No	22 (88.0%)	2 (40.0%)	6.000*	0.014	S
	Yes	3 (12.0%)	3 (60.0%)			
	Yes	0 (0.0%)	1 (20.0%)			
Drains	No	18 (72.0%)	3 (60.0%)	0.286*	0.593	NS
	Yes	7 (28.0%)	2 (40.0%)			

Significant difference as to specimen volume, margin status and intra operative re-excision as when increase specimen volume and positive margin led to more complications.

Table 11: Complicated and non-complicated cases due to pathology

Pathology		Non complicated No. = 25	Complicated No. = 5	Test value	P-value	Significance
Histological grade	I	9 (36.0%)	0 (0.0%)	6.720*	0.035	S
	II	13 (52.0%)	2 (40.0%)			
	III	3 (12.0%)	3 (60.0%)			
LNs affection	Negative	20 (80.0%)	1 (20.0%)	7.143*	0.008	HS
	Positive	5 (20.0%)	4 (80.0%)			
ER status	No	7 (28.0%)	0 (0.0%)	1.826*	0.177	NS
	Yes	18 (72.0%)	5 (100.0%)			
PR	No	10 (40.0%)	3 (60.0%)	0.679*	0.410	NS
	Yes	15 (60.0%)	2 (40.0%)			
HER2 status	No	20 (80.0%)	4 (80.0%)	0.000*	1.000	NS
	Yes	5 (20.0%)	1 (20.0%)			

Significant differences as to histological grades,G3 more than G2 & G1, with high significant in LNs affections and SLNB.

Table 12: Complicated and non-complicated cases according postoperative data.

Postoperative data		Non complicated No. = 25	Complicated No. = 5	Test value	P-value	Significance
Hospital stay (days)	Mean ± SD	1.36 ± 0.49	2.60 ± 0.55	-5.077•	0.000	HS
	Range	1 – 2	2 – 3			

Highly significant differences as to hospital stay as more hospital days more risk of complications.

Table 13: Comparison between margin status cases according age, menopausal status, size, histological types and grades.

Variations		Margin status Negative No. = 24	Positive No. = 6	Test value	P-value	Significance
Age	Mean ± SD	41.38 ± 10.18	52.67 ± 6.98	-2.553•	0.016	S
	Range	23 – 59	45 – 62			
Menopausal status	Premenopausal	14 (58.3%)	0 (0.0%)	6.563*	0.010	S
	Postmenopausal	10 (41.7%)	6 (100.0%)			
Size (mm)	Mean ± SD	10.88 ± 3.27	15.67 ± 3.78	-3.115•	0.004	HS
	Range	4 – 16	10 – 19			
Histological type	Intra-ductal ca	17 (70.8%)	4 (66.7%)	9.762*	0.008	HS
	Intra-lobular ca	0 (0.0%)	2 (33.3%)			
	DCIS	7 (29.2%)	0 (0.0%)			
Histological grade	I	9 (37.5%)	0 (0.0%)	3.333*	0.189	NS
	II	11 (45.8%)	4 (66.7%)			
	III	4 (16.7%)	2 (33.3%)			

Highly significant differences between safety margin as to mass size and histological type as larger mass more positive safety margin than small one and invasive lobular more positive safety margin than invasive ductal than DCIS. And significantly safety margin was positive in old age, post-menopausal than younger and premenopausal.

Discussion

In the present study, 11 patients underwent MMG-guided hook wire localization and 19 patients underwent USG-guided hook wire localization. This agreed with Demirala *et al.* (2016) who with 83 patients where 56 patients underwent MMG-guided hook wire localization and 27 patients underwent USG-guided hook wire localization. Also, this agreed with Eggemann *et al.* (2014) reported that sonographically estimated margin of ≥ 4 mm was associated with an adequate pathological margin of ≥ 1 mm in 100% of tumors without a high grade intraductal component. They added that intra-operative ultrasonography was a safe and feasible one to have clear surgical margins by BCS. The present lesions were visible in 63.3% by ultrasound, but 36.7% were not visible. This agreed with Krekel *et al.* (2011) who found lesions were visible in 61.76% by ultrasound & 38.23% not visible. Also, the median tumor size was 11.83mm^3 range (4-19) in masses, and with the mammography examination mass was irregular in 13(52%), round in 3(12%) and oval in 9(36%). Krekel *et al.* (2011) found that the median tumor size was 8mm^3 ranged (4-19) in masses, and by mammography examination irregular mass in 28(41.18%), round in 15 (10.29%) and oval in 1 (14.71%).

In the present study, 21/30(70%) had invasive ductal carcinoma, in situ duct cancer 7 (23.3%), invasive lobular 2(6.7%). This agreed with Shin *et al.* (2010), with 72 impalpable cancers found 39(54%) invasive ductal 23(32%) noninvasive ductal, lobular carcinoma 4(6%), tubular 1(1%) & colloid 5(7%).

In the present study, dominate intermediate grade 2 tumor was in 15/30(50%), with moderate differentiated, G1 stage in 9(30%) patients and G3 stage in 5(20%) patients. Gaur *et al.* (2013) reported the tumor grades were G1 stage in 17(25%) patients, G2 stage in 41 (60.29%) and G3 stage in 10(14.71%) patients, but in all of them G 2 stage dominated.

In the present study, 80% of patients had negative margins, and positive surgical margins were significantly influenced by age, menopausal status and highly significantly with tumor size, and histologic type of tumor. Small tumors of lobular histologic type were also associated with an increased risk of close or positive resection margins. Rubio *et al.* (2016) reported a negative resection margin in 45(86.6%) breast cancer patients by using WL at BCS. They added that rate of positive surgical margins was significantly influenced by age, menopausal status, tumor size, and histologic grade and type of tumor, elderly postmenopausal women were at risk for positive surgical margins, and that small tumors of lobular histologic type and intermediate grade of differentiation were associated with an increased risk of close or positive resection margins Also, Fillion *et al.* (2012) among 122 patients treated with WGL, negative margins were 82%. Volders *et al.* (2016) reported a tumor-free margin of 626(72.7%) breast cancer patients who underwent WL at BCS

In the present study, effectiveness of intraoperative frozen section, a re-excision was 20%, and with 100% accuracy, which permitted an immediate correction of the adequacy of excision but with an elongation of surgery time of 12-21 minutes. Dorel-Le Theo *et al*. (2013) reported frozen section accuracy of 89%. Esbona *et al.* (2013) reported the effectiveness of intraoperative frozen section, a re-excision of 10%, accuracy of 91%, and permitted an immediate correction of the adequacy of excision but with an elongation of the surgery time of 13-27 minutes.

In the present study, the median excision volume was 139.93 mm^3 ranged (66-220), mean resection time was 32.57 min. and lumpectomy with SLNB 60 min. Eggemann *et al.* (2016) reported lumpectomies without SLNB 40 min comparing to median excision volume of 94mm^3 ranged (10-352), mean operative time was 36 min. and lumpectomy with SLNB 68 min. lumpectomies without SLNB 49 min

In the present study, 5/30(16.6%) of patients had complications of whom wound infection was in 2/30(6.7%) with mild erythema

responded to oral antibiotics, 2/30 (6.7%) had seromas treated by aspiration and one of them post neo-adjuvant with healing delay. Last lymphedema patient (3.3%) needed hospitalization for reassurance, physiotherapy and conservative treatment. In the present study, there were significantly relation between complication and LNs affection, histological grade, tumor type & size, specimen volume resected, margin status & neo-adjuvant chemotherapy. Demiral *et al.* (2016) reported patients had complications; wound infection in 3% of patients with slightly increased infection rate due to their transferred from radiology to surgery during which sterility was disrupted, 13 patients had wound infections, 6 with mild erythema responded to oral antibiotics, and 7 had incisions opened for drainage. They added that 0.8% hematomas were due to biopsy and 0.2% with a vasovagal reaction due directly to the localization procedure, a woman had a vasovagal reaction during the localization procedure recovered after lying down and had biopsy under local anesthesia without incident, and none hospitalization was indicated.

Authors' contributions: All authors equally contributed in this study and neither has any especial interest nor received fund.

Conclusion

Validity of imaging-guided hook wire loc alization biopsy of non-palpable breast lesions proved. Cooperation of surgeon, radiologist and pathologist increased successful outcome of hook wire localization technique.

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Explanation of figures

Fig. 1: Preoperative US wire localization. Fig. 2: Incision. Fig. 3: Elevation of skin flaps. Fig. 4: Dissection. Fig. 5: Marking of resected specimen. Fig. 6: Resection of the specimen. Fig. 7: Specimen for frozen section. Fig. 8: Cliping of resection side. Fig. 9: Closure with good haemostasis. Fig. 10: Injection of methylene blue dye in retro areolar region. Fig. 11: Massage breast. Fig. 12: Site of Incision. 13: Blue lymphatics. Fig. 14: Blue SLN. Fig. 15: i. SLN frozen section. ii. Wound closure