Kurdistan Region- Iraq
Ministry of Higher Education and
Scientific Research
University of Sulaimani
College of Nursing



THE EFFECTS OF SENTINEL LYMPH NODE BIOPSY ON THE MANAGEMENT OF EARLY BREAST CANCER WITH A NEGATIVE AXILLARY LYMPH NODE IN HOSPITALS IN SULAIMANI CITY

A DISSERTATION

SUBMITTED TO THE COUNCIL OF THE COLLEGE OF NURSING UNIVERSITY OF SULAIMANI IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTORATE OF PHILOSOPHY IN ADULT NURSING

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بِسْمِ اللهِ الرَّحْمنِ الرَّحِيمِ

مَن جَاءَ بِالْحَسَنَةِ فَلَهُ خَبْرٌ مِنْهَا وَمَن جَاءَ بِالْسَيِّئَةِ فَلا يُجْزَى الَّذِينَ عَمِلُوا السَّيِّئَاتِ إِلاَّ مَا كَانُوا يَعْمَلُونَ السَّيِّئَاتِ إِلاَّ مَا كَانُوا يَعْمَلُونَ

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Biopsy on the Management of Early Breast Cancer with a Negative
Axillary Lymph Node in Hospitals in Sulaimani City" was prepared by
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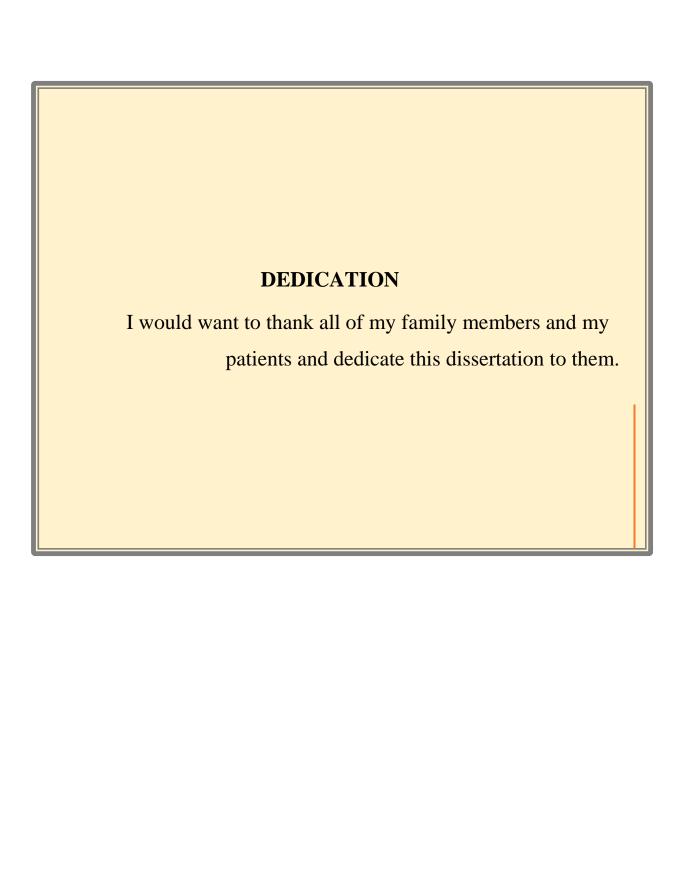
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ACKNOWLEDGEMENT

At the onset, great thanks to **God**, the merciful, glorious, and compassionate I am so thankful for forgiveness, and kindness and grace give us hope.

I would also like to express my thanks to Dr. Nizar Mohamad Tawfeeq, my research supervisor, for his guidance and support.

Provide thanks to the former dean, Dr. Zhiyan Salah, and the new dean, Dr. Muhammad Rashid, for their cooperation.

Special thanks to our Adult Nursing Department's Dr. Niyan Hakim Ismael, and Dr. Khanda Mustafa Ahmed for their cooperation and support.

My deep appreciation goes to Dr. Atiya Kareem Mohammed for her assistance and guidance, and many thanks to Dr. Mahabat Hassan Saeed for her guidance.

Sincere appreciation to Dr. Heshu Sulaiman Rahman for her assistance.

Our deepest thanks go to the director of the Smart Health Tower Hospital, Dr. Abdul Wahid Mohmmed, and their surgical team in the operation department for their cooperation, as well as the nurses working in the ward for their help during data collection.

Also, my deepest thanks to the director of the Soma General Surgical Hospital and Dr. Abbas Tahir with their surgical team for their help during data collection.

Appreciation also goes to the University of Sulaimani, the College of Nursing, the Deanship of the College, and the Post-Graduate Unit, for providing me with the opportunity to learn.

Lastly, special thanks go to the study participants for being generous with their time and commitments. God willing, they will be cured permanently.

ABSTRACT

Background: Advanced surgical procedures for axillary staging are less invasive. Many patients, continued to experience side effects such as infections, hematomas, seromas, paresthesia, shoulder stiffness, and arm swelling, which delayed adjuvant therapy.

<u>Aim:</u> The current study aimed to assess the effects of sentinel lymph node biopsy on the management of early breast cancer with negative axillary nodes.

Methods: An observational analytic study was carried out on 110 women undergoing sentinel lymph node biopsy alone or plus sampling from 1st of March 2021 to the 1st of April 2022. The study tools included a structured interviewing questionnaire and an observational checklist. It includes; Sociodemographic features, history of present illness, clinical examination of the breast and axilla, and breast screening. Surgical and non-surgical treatment. Surgical technique for sentinel lymph node biopsy: injection of blue dye peritumorally or into the subareolar space. Post-operative complications.

Results: The identification rate of sentinel nodes was 97.56% in those with sentinel lymph node biopsy alone and 91.8% for those with sentinel lymph node biopsy plus sampling. Patients with positive lymph node and extra-nodal extension metastasis underwent a second operation to remove the metastatic axillary lymph node (p< 0.001). There is a significant association between decreased shoulder range of motion and axillary surgery (p = 0.03).

Conclusion: Biopsy of a sentinel lymph node through Methylene blue injection remains an effective and reliable way to determine whether axillary lymph nodes have metastatic disease, and to make decisions regarding adjuvant systemic therapy. Some patients experienced such complications, which delayed adjuvant therapy and decreased their life quality.

LIST OF CONTENTS

Subjects	Page No.	
Acknowledgment	I	
Abstract	II	
List of Contents	III	
List of Tables	VII	
List of Figures	IX	
List of Abbreviations	X- III	
INTRODUCTION	_	
Introduction	1	
Important of the study	4	
Statement of the problem	5	
Objectives of the study	5	
Research hypothesis	6	
Operational definitions of the terms		
LITERATURE REVIEW		
Overview of breast cancer therapy	8	
Surgical anatomy of the breast	9	
Epidemiology of breast cancer	11	
Risk factors of breast carcinoma	13	
Diagnosis of early breast cancer/ breast screening	15	
Breast Self-Examination	15	
Clinical Breast Examination	16	
Diagnostic Mammography, breast Ultrasound and MRI		
Needle biopsy/cytology	18	
Pathology of breast cancer	19	
Clinical feature of breast cancer	20	
Triple assessment	20	
Pathologic and prognostic staging of breast cancer	20	

The stage of breast cancer by the T, N, and M classifications results of ER/PR and HER2 testing	21
Clinical Staging of the Axillary Nodal Regions	21
Treatment of Early Breast Cancer	24
Axillary surgery	24
Sentinel lymph node biopsy	25
The technique of SLNB procedure	27
Sentinel lymph node biopsy in pregnant women	29
Axillary lymph node dissection	30
Pathology	31
Breast conserving surgery	31
Ductal Carcinoma In Situ	32
Lobular carcinoma in situ	34
Invasive Ductal Carcinoma	35
Breast-conserving surgery after new adjuvant therapy	36
Inflammatory breast cancer	36
Paget Disease of the Breast	37
Mastectomy	38
Simple mastectomy and modified radical mastectomy	38
Nipple sparing mastectomy	39
Chemotherapy	40
Radiation Therapy	40
Endocrine therapy	41
Biological therapy	41
Molecular Subtyping/Biomarker Profile (ER, PR, HER2)	41
Complications after axilla and breast surgery	42
Wound infections	43
Seroma	43
Hematoma	43
Presthesia	44

Range of motion (ROM)	44	
Lymphedema	44	
Recommendations after management of early breast cancer	47	
Recommendations for pre and post -menopausal women	47	
Previous study	47	
PATIENT & METHODS		
Method	49	
Design	49	
Administrative Arrangement and Ethical Approve	51	
Study Setting	51	
Population and Sample	52	
Sample Size	52	
Inclusion criteria	53	
Exclusion criteria	53	
Data Collection	53	
The study instrument	54	
The questionnaire	55	
Validity	57	
Pilot Study	57	
Reliability	58	
Statistical analysis	58	
Descriptive statistics	58	
Inferential statistics	58	
Limitation of the study	59	
RESULTS		
Distribution of the study samples according to socio-demographic characteristics	60	

Distribution of the study samples according to social and personal history	61	
Distribution of the study samples according to patients' complaints and present illness histories	62	
Distribution of the study samples according to patients' past medical histories	63	
Distribution of the study samples according to patients' breast cancer characteristics	64	
Distribution of the study samples according to patients' ultrasound, mammography, and MRI findings of the breast and axilla	65	
Distribution of the study samples according to patients' histological results of a breast core biopsy	67	
The identification rates of sentinel nodes using blue dye for SLNB and SLNB+LAS	68	
Types of breast surgery and their relationships to postoperative complications	71	
Distribution of the study samples according to the patients' histopathology results for the tumor size and axillary involvement of the disease and it is association		
Distribution of the study samples according to patients' non-surgical treatments (systemic therapy)), adjuvant and neo-adjuvant therapy	73	
Distribution of the study samples according to patients' post-operative complications	74	
Distribution of the study samples according to patients' post-operative complications associated with the SLNB alone, SLNB plus LAS, and ALND groups	76	
DISCUSSION		
Patients socio-demographic features	78	
Social and personal history of the study participants	79	
Complaints and present illness histories of the study participants	80	
Past medical histories of the study participants	81	
Breast characteristics of patients' participants	83	

Screening and imaging findings of the participants		
Patients' histological results of a breast core biopsy	85	
Surgical techniques for the SLNB procedure	86	
Breast surgery types and their relationship to long-term complications	87	
Patients' histopathology results for the tumor and axillary involvement of the disease	88	
Patients' non-surgical treatments (systemic therapy)	89	
Complications following breast and axillary surgery	90	
Time to go back to work after surgery	92	
CONCLUSION&RECOMENDATIONS		
Conclusions	94	
Recommendations	95	
Recommendations for further research	96	
REFERENCES	97	
APPENDICES		
Appendix 1: Ethical Approval		
Appendix 2: Formal Permission of Smart and Soma hospital		
Appendix 3: Consent Form		
Appendix 4: Reliability formula		
Appendix 5: Sample size formula		
Appendix 6: English version of the questionnaire		
Appendix 7: List of Expertise		
Appendix 8: Acceptance letter of paper one		
Appendix 9: Acceptance letter of paper two		

List of Tables

S/no Subject		Page No.			
Table 2.1	Early and late post-breast and axillary surgery complications	46			
Table 4.1	Distribution of the study samples according to socio- demographic characteristics	60			
Table 4.2	ble 4.2 Distribution of the study samples according to social and personal history				
Table 4.3	Distribution of the study samples according to patients' complaints and present illness	62			
Table 4.4	Distribution of the study samples according to patients' past medical histories	63			
Table 4.5	Distribution of the study samples according to patients' breast cancer characteristics	64			
Table 4.6	4.6 Distribution of the study samples according to patients' ultrasound, mammography, and MRI findings of the breast and axilla				
Table 4.7	Distribution of the study samples according to patients' histological results of a breast core biopsy	67			
Table 4.8	The identification rates of sentinel nodes using blue dye for SLNB and SLNB+LAS	68			
Table 4.9	Relationship between type of breast surgery and postoperative complications	71			
Table 4.10	Distribution of the study samples according to the patients' histopathology results for the tumor and axillary involvement of the disease	72			
Table 4.11	Distribution of the study samples according to patients' post- operative complications	74			
Table 4.12	Complications associated with the SLNB, SLNB plus LAS, and ALND groups	76			

List of Figures

/no	Subject	Page No.
2.1	Cross-sectional anatomy of the breast	9
2.2	Breast cancer tumors, breast cells mutate and grow	9
2.3	lymphatics axillary nodes and internal mammary lymph nodes	11
2.4	Risk Factors of breast carcinoma, heredity and breast cancer	14
2.5	Breast self-examination	15
2.6	Palpation of the axillary regional lymph nodes	16
2.7	Clustered micro calcifications	17
2.8	Speculated, irregular mass lesion	18
2.9	Pathology of breast cancer	19
2.10	Lymphatic pathway of the breast, the direction of lymph flow.	26
2.11	Injection of Blue dye for SLNB	27
2.12	Blue lymphatic toward the axilla	28
2.13	Sentinel lymph node identification by blue dye	29
2.14	Sentinel lymph nodes removed	29
2.15	Ductal Carcinoma in situ	33
2.16	Lobular carcinoma in situ	35
2.17	Invasive Ductal carcinoma	36
2.18	Inflammatory breast cancer	37
2.19	Paget's disease	38
2.20	Lymphedema after breast cancer treatment	45
3.1	Sketching for research design	50
3.2	Sketching for steps for the participants refined and reached the final	52
3.2	number of 110 in the study	
4.1	Sketching diagram on surgical technique and pathological results	70-71
4.1	of the SLNB	
4.2	The value of the study samples' adjuvant therapy and its	74
T.2	comparison with the value of neoadjuvant therapy	
4.3	Time to go back to their daily normal activities	79

List of Abbreviations

Abbreviations	Words		
ABUS	Automated whole-breast ultrasound		
ACOG	American College of Obstetricians and Gynecologists		
ACOSOG Z0011	The American College of Surgeons Oncology Group Z0011		
ACS	American Cancer Society		
AJCC	American Joint Committee on Cancer		
ALMANAC	Axillary Lymphatic Mapping Against Nodal Axillary Clearance		
ALND	Axillary lymph Node Dissection		
BC	Breast Cancer		
BCS	Breast Conserving Surgery		
BCT	Breast Conserving Therapy		
BD	Blue dye		
BIRAD	Breast Imaging Reporting and Data System		
BRCA	Breast Cancer gene (BReast CAncer gene)		
BSE	Breast Self-Examination		
Ca	Cancer		
CDC	Centers for Disease Control and Prevention		
CI	Confidence Interval		
CISH	Chromogenic In Situ Hybridization		
CMF	Cyclophosphamide, Methotrexate, and 5-Fluorouracil		
	,combination of chemotherapy		
CNB	Core Needle Biopsy		
DCIS	Ductal Carcinoma In Situ		
DM	Diabetes Mellitus		
ER	Estrogen		
ERBB2	erb-b2 receptor tyrosine kinase 2		
ESMO	European Society for Medical Oncology		
F	Frequency		
FISH	Fluorescence In Situ Hybridization		
FNA	Fine Needle Aspiration		
GA	General anestesia		
H&E	Hematoxylin and eosin stain		
HER-2	Human Epidermal Growth factor 2		
HRT	Hormone Replacement Therapy		
IBC	Inflammatory breast cancer		
ICBN	Intercostobrachial nerve		
IDC	Invasive Ductal Carcinoma		

IHC	Immunohistochemically			
IMN	Internal Mammary Nodes			
IR	Identification Rate			
IV	Intravenous Wind (Wi) and the solid and the solid and (67)			
Ki67	Kiel (Ki), number of the original clone (67).			
LAS	lower Axillary Sampling			
LCIS	Lobular Carcinoma In Situ			
LN	Lymph Nodes			
M	Metastasis			
MB	Methylene Blue			
MR	Magnetic Resonance			
MRI	Magnetic Resonance Imaging			
MRM	Modified Radical Mastectomy			
N	Node			
NAC	Neo-Adjuvant Chemotherapy			
NCCN	National Comprehensive Cancer Network			
NCCN	National Comprehensive Cancer Network			
NSM	Nipple Sparing Mastectomy			
NST	No Special Type			
P	Pathology			
PPV	Positive predictive value			
PR	Progesterone			
R	Receptors			
ROM	Shoulder Range Of Motion			
SERMs	Selective estrogen receptor modulators			
SLN	Sentinel Lymph Node			
SLNB	Sentinel Lymph Node Biopsy			
SM	Simple Mastectomy			
SNB	Sentinel Node Biopsy			
SSM	Skin-sparing Mastectomy			
Т	Tumor			
Tis	Tumor in situ			
TNM	Tumor, Node, Metastases			
UK	United Kingdom			
USA	United State of America			
USPSTF	The U.S. Preventive Services Task Force			
VS	Versus			

1. INTRODUCTION

1.1. Introduction

According to cancer statistics, there were 2.26 million cases of female breast cancer (CA), the most prevalent kind of cancer worldwide (Jacques et al., 2021). Most types of breast ca are invasive ductal and lobular carcinoma. Ductal carcinoma in situ (DCIS) is the most prevalent kind of noninvasive breast CA and may lead to invasive breast CA. (Biganzoli, 2020).

For patients with early breast ca, axillary surgery is necessary for assessment and estimating the stage of disease (Mátrai et al., 2022). It has a basic role in the treatment of the early stage of CA. Axillary surgery gives information to instruct adjuvant therapy and preventing local recurrence of cancer (Bromham et al., 2017).

Screening imaging program and the advance surgery techniques used for diagnosis and staging axilla are less invasive for patients with early stages cancer undergoing axillary surgery to remove axillary lymph nodes (LN). It helps clinicians obtain the same facts about the staging of the axilla with reduced morbidity (lymphedema, chronic pain, sensory deficit). Performing axillary lymph node dissection (ALND) for controlling and staging of axilla has been tested again and understanding that it is not necessary for doing major axillary surgery for patients with nodal the disease (Park, Ko UnPark & Ko UnCaudle, 2018).

For women with clinically node-negative operable breast cancer, lower axillary sampling (LAS) is a reliable alternative to whole-axillary clearance and is equally accurate as sentinel node biopsy (SNB) at predicting axillary lymph node (LN) status (Parmar et al., 2013).

Sentinel lymph node biopsy (SLNB) has evolved as the basis of care in the management of axilla and prognosis of early breast cancer. A meta-analysis trial discovered SLNB precisely mapped the sentinel node in 96% of patients with an estimate false negative rate of 7.3% (Chen & Gillanders, 2021). Recognition of sentinel LN, through radioisotope, or visual dye is based on the principle that primary tumors drain to one or more lymph nodes before they spread widely. The negative lymph node means that the tumor is still in its location (Durre, 2022).

An important predictor of survival of breast cancer, and decision-making for treatment depends on the number and the level of involvement of axillary lymph nodes for the disease. When the identified lymph nodes are removed and are clear of metastatic, the remaining axilla is likely to be negative (Josef et al., 2019).

An ultrasound-guided fine needle aspiration (FNA) may be beneficial for patients with clinically suspicious axilla to find out if there have been metastatic dissemination to the axilla. It facilitates the evaluation of patients with an equivocal physical examination. For a clinically negative axilla, SLNB should be planned at the time of surgery with a decision about further management of the axilla, if any pending the results of the SLNB (Thanh & William, 2017).

Less intrusive treatment methods in local therapy, such as surgery and radiotherapy, allow patients to maintain cognitive capability and general well which are the main clinical advantages (Watase et al., 2021).

Breast or axillary procedures have been linked to up to 30% of postoperative problems (wound infection, seroma formation, and hematoma), all of each can be caught early (McNeely et al., 2012; Rizvi et al., 2020). The division of sensory nerves is largely responsible for the sensory sequelae of both SLNB and ALND (Gabriel et al., 2021).

Limitation in shoulder range of motion (ROM), with SLNB showing reduced impairment in comparison to ALND in randomized trials. Studies show that shoulder range of motion (ROM) increases quickly with time (Gabriel et al., 2021).

Seroma develops during axillary and breast surgery as a result of persistent lymphorrhea, which results in a protracted healing period and a higher risk of infection (Radu et al., 2021).

Hematoma rates for breast reduction procedures range from 1.0 to 9.3%. After a breast reduction, intraoperative hypotension may increase the chance of hematoma (Daar et al., 2021). It's typical for wound-related issues to arise after breast surgery. Inadequate cosmesis might result from delayed wound healing (Iqbal et al., 2020).

Removal of the axillary lymph nodes results in a mechanical obstruction that causes a lymph fluid backup and upper limb edema (Dayan, et al., 2020). About 10% of patients experience ALND adverse effect of infection or cellulitis of the arm, chest wall, or breast. Repeated infections increase the risk of developing lymphedema (Gabriel et al., 2021).

Millions of breast cancer patients worldwide are affected by lymphedema (Vassard et al., 2010; Pusic et al., 2013; Wiser et al., 2020). It causes poor physical function, negative psychological impacts, and social effects (Pusic et al., 2013; National Guideline Alliance (UK), 2018).

In spite of upgrading the techniques that are used for the SLNB procedure in most of the developed countries. Sulaimany city still uses blue dye (BD) for this procedure. The SLNB procedure in Smart Health Tower and Soma surgical hospitals begins with localization of the sentinel LN through injection of methylene blue dye 0.079g/ml (0.3mg diluted in 5 ml distal water), or 1% Isosulfan into the parenchyma,

subareolar, or periareolar regions of the breast close to the underlying breast cancer. There is a breast massage. Stain nodes are surgically excised through an axilla incision or the lateral portion of a mastectomy after 20 minutes of injection.

1.2 Importance of the study:

In the management of early-stage breast cancer, axillary staging is an essential part of the surgical procedure. A variety of surgical techniques for the axilla are performed for diagnosis and staging. SLNB accurately represents the condition of all axillary lymph nodes.

This study was undertaken because this is the first time research has been conducted on SLNB among women with early breast cancer in the Kurdistan region of Iraq. Much like the rest of the world, breast CA is the greatest concern of women in this region and has seen an increase in the number of breast cancer cases in recent years in Iraq (Al-Hashimi, 2021).

Although the survival rates for early breast cancer have increased, many patients still encounter a number of problems after undergoing local therapy (breast and axillary surgery). Early and late post-operative problems, such as seroma, hematoma, wound infection, restricted shoulder range of motion, sensory morbidity in the affected arm, and lymphedema, were identified and confirmed by the study's researcher.

These women need medical care to recover from the illness. For that, we need to do such a study on axillary lymph nodes management and complication rate consequences following breast and axillary surgery, which is crucial in determining

whether to use adjuvant systemic treatment or not, that affects survival from the disease.

In Sulaimani City/ Hewa cancer hospital/ Kurdistan Region of Iraq, continuing adjuvant systemic therapies in the management of early breast cancer, depends on the result of SLNB and gene expression profiles.

On the other hand, post-operative follow-up assessment is essential for enhancing women's quality of life, daily activity, and time to go back to work after management and completion of systemic therapy.

1.3 Statement of the problem

The Effects of Sentinel Lymph Node Biopsy on the Management of Early Breast Cancer with Negative Axillary Lymph Node in Hospitals in Sulaimani City.

1.4 Objectives:

1.4.1. Main Objective

To assess the effects of sentinel lymph node biopsy on the management of early breast cancer with negative axillary lymph node in surgical hospitals in Sulaimani City.

1.4.2 Specific Objectives

- **1.** To identify characteristics of patients clinical features with stages 1, 2 of breast cancer
- 2. To recognize patients social and personal history

- **3.** To clarify type and molecular subtype of early breast cancer
- **4.** To assess the identification rate of sentinel node, if the lymph node's Methylene cytology result for sentinel lymph node mapping appropriately reflects the effectiveness of the Methylene Blue injection.
- **5.** To explore histopathology results of axillary lymph node involvement and its association with the breast tumor size
- **6.** To evaluate the pathological outcomes of cases who were submitted for full axillary lymph node dissection for positive SLN.
- 7. To identify patient complications after breast and axillary lymph node surgery

1.5. Research hypothesis

H₁: Sentinel lymph node biopsy using Methylene Blue is accurate in the identification of nodal involvement for the management of early breast cancer.

H₂: Axillary lymph node dissection causes post-operative complications.

1.6. Operational definitions of terms

Sentinel lymph node biopsy: A sentinel lymph node biopsy is surgery to identify, remove and examine a sentinel lymph node to see if it contains cancer cells.

Management: an approach to managing women in the early stages of breast cancer through taking a biopsy at a sentinel node in the armpit.

Early breast cancer: Breast cancer that has not spread beyond the breast or the axillary lymph nodes. This includes ductal carcinoma in situ and stage I, stage IIA, stage IIB, and stage IIIA breast cancers.

Negative axillary lymph node: A lymph node in the armpit that is free of cancer.

Chapter Two Literature Review

2. LITERATURE REVIEW

2.1 Breast Cancer

2.1.1. Overview of Breast Cancer Therapy

The development of breast cancer is a multi-step process involving multiple cell types, and its prevention remains challenging in the world. Early diagnosis of breast cancer is one of the best approaches to prevent this disease. Currently, people have more drug options for the chemoprevention of breast CA, while biological prevention has been recently developed to improve patients' quality of life (Sun, 2017).

Genetic testing is a powerful tool that allows for the detection of BRCA and non-BRCA germline mutations in individuals with high risks of breast ca, which in turn aids in the individualization of treatment (Valencia et al., 2017).

Historically, patients diagnosed with breast ca underwent axillary node dissection (ALND) to stage the axilla. Advancements in diagnostic imaging and surgical technique, however, now allow for nonsurgical or minimally invasive approaches that help clinicians attain the same information with reduced morbidity (Park Ko UnPark &Ko UnCaudle, 2018).

Treatment strategies in local therapy, including surgery and radiotherapy, are becoming less invasive and are enabling the retention of cognitive function and quality of life, which are the key clinical benefits. (Watase et al., 2021)

Adjuvant therapy has played a significant role in improving survival outcomes of patients with early-stage breast cancer (Wolff 2015).

<u>Chapter two</u> <u>Literature review</u>

2.1.2. Surgical Anatomy of the Breast

The boundaries of the mature adult breast are the second rib superiorly, the sixth rib inferiorly (Figure 2.1), the sternal edge medially, and the midaxillary line laterally. Breast tissue extends into the axilla. Posteriorly, the breast lies on top of portions of the deep investing fasciae of the pectoralis major muscle, the serratus anterior muscle, the external abdominal oblique muscles, and the upper extent of the rectus sheath (Michael et al., 2017).

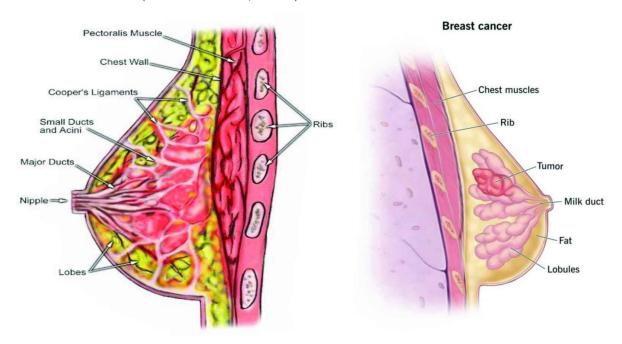


Figure 2.1: Cross-sectional anatomy of the breast (Medscape, 2016)

Figure 2.2: Breast cancer tumors, breast cells mutate and grow (Cleveland Clinic, 2022)

A non-lactating mammary gland comprises glandular (secretory) and adipose (fatty) tissue with fibrous connective tissue called Cooper's ligaments (Figure 2.1). The glandular tissue has 15 to 20 lobes and lobules containing 10 to 100 alveoli (0.12 mm in diameter). The 15–25 ducts drain the alveoli and merge into larger ducts before converging into the central milk duct, which dilates slightly to form the laticiferous sinus before narrowing and opening into the nipple surface as it passes through the nipple. The nipple has different types of 5–9 ducts on average (Biswas et al., 2022).

The structural support system of the breast, made of the superficial fascia, suspensory ligaments, and skin, can also change its fibrous frame with aging and due to the force of gravity. These ligaments account for the dimpling of the skin overlying a carcinoma (Gefen & Dilmoney, 2007).

Lymph is transported through lymphatic vessels. White blood cells, lipids, bacteria, cell detritus, water, and protein make up lymph. Its chemical structure is similar to that of blood plasma. Initial lymphatics (lymph capillaries), precollectors, collectors, lymphatic trunks, and lymph nodes make up the intricate lymph drainage system (Sleigh & Manna, 2022).

The lymphatic drainage of the breast parallels the venous anatomy with intramammary and axillary lymph nodes (Figure 2.3). Deep lymphatic channels communicate with the more superficial cutaneous lymphatic plexus, especially around the nipple in the subareolar plexus. The axillary lymph nodes receive the majority of the subareolar plexus' lymphatic drainage. Normal lymph nodes have a thin (3 mm), moderately lobulated cortex, a fat-filled hilum. The sentinel lymph node can be located by 1 Lymphatic drainage from the subareolar plexus is primarily to axillary lymph nodes. (Jesinger, 2014).

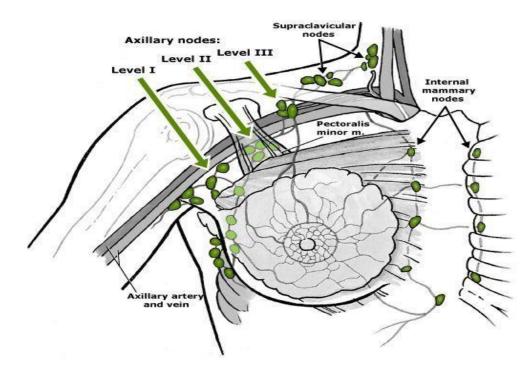


Figure 2.3: lymphatics axillary nodes and internal mammary lymph nodes (Moore& Agur, 2018)

The presence or absence of axillary lymph node involvement is an important predictor of survival in patients with breast cancer, and important treatment decisions are based on it. The number of involved lymph nodes and the level of lymph node involvement are predictors of survival in patients with breast cancer. The aim of SLNB is to identify patients who are node-negative or who have limited volume axillary disease (Josef et al., 2019).

2.1.3. Epidemiology of Breast Cancer

Breast cancer is the most common neoplasm diagnosed amongst women worldwide and is the leading cause of female cancer death. Statistics indicate that approximately 11 % of worldwide breast cancer occurs in China (Li &Mello-Brennan, 2016).

It is considered the most common cause of death in middle-aged women in western countries. In England and wales, 1 in 12 women will develop the disease during their lifetime. The incidence is expected to continue rising as the population

ages, although more slowly than previously thought as the use of hormone replacement therapy (HRT) has reduced in the USA and UK (Norman et al., 2018).

Breast cancer remains the most diagnosed cancer in women globally. It is estimated to have approximately 281,550 new cases and 43,600 deaths in 2021 in the United States. Breast cancers categorized into four molecular subtypes based on the Immunohistochemistry (IHC) including the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), as well as a proliferation marker Ki-67 protein expression. Luminal A (ER/PR+, HER2−, Ki67+ <20%), luminal B (ER/PR+ <20%, HER2−, Ki67+ ≥20%); HER2+ B2 (ER/PR+, HER2 overexpression), HER2 overexpression (ER−, PR−, HER2 overexpression), basal-like triple-negative breast cancer (TNBC, ER−, PR−, and HER2−) (Luo et al., 2022)

Breast cancer case fatality rates illustrate the great disparity in outcomes between regions. Case fatality rates in East Africa reach an unacceptable 59% compared to 19% in the United States. Cancer registries in Connecticut and upper New York State document that the age-adjusted incidence of new breast cancer cases had steadily increased since the mid-1940s. In the 1970s, the probability that a woman in the United States would develop breast cancer at some point in her lifetime was estimated at 1 in 13; in 1980 it was 1 in 11; and in 2004 it was 1 in 8. More than 250 000 new cases of breast cancer were diagnosed in the United States in 2017 (Waks & Winer, 2019).

In most cases, there is no obvious pattern of inheritance for the complex trait of breast cancer, which is influenced by both genetic and non-genetic variables. Analyses based on genome-wide association studies on people of American and European descent have indicated a heritability between 9 and 13%. Also, studies have reported a heritability of 27-31% in Nordic populations (Zavala et al., 2019).

<u>Chapter two</u> <u>Literature review</u>

From 1960 to 1963, 5-year overall survival rates for breast cancer were 63% and 46% in white and African American women, respectively, whereas the rates for 1981 to 1983 were 78% and 64%, respectively. For 2002 to 2008 rates were 92% and 78%, respectively. The size of the primary breast cancer correlates with disease-free and overall survival, but there is a close association between cancer size and axillary lymph node involvement. In general, up to 20% of breast cancer recurrences are local-regional, >60% are distant, and 20% are both local regional and distant (Catherine, 2019)

2.1.4. Risk Factors of breast carcinoma

Demographic & Geographical:

As a woman ages, her risk for breast cancer increases: from birth to age 49 years, there is a1.9% probability of developing invasive breast cancer (1 in 53); from age 50 to 59 years, a 2.3% (1 in 43); from age 60 to 69 years, a 3.5% (1 in 29); and from age 70 years and older, a 6.7% (1 in 15). From birth to death, the probability of developing invasive breast cancer is 12.3%, or 1 in 8. Carcinoma of the breast occurs commonly in the western world, accounting for 3–5% of all deaths in women. In resource-poor countries, it accounts for 1–3% of deaths (Michael, et al., 2017).

Reproductive: High amounts of estrogen exposure, whether endogenous (during ovulation, early menarche and late menopause) or exogenous (from oral contraceptives or hormone replacement treatment), play a role in the development of breast cancer (Howlader, et al., 2014).

Genetic and family history: A high percentage of cases of breast cancer has been demonstrated in women with a genetically conditioned cancer, i.e. mutations in genes BRCA1, BRCA2, syndromes of Li-Fraumeni, Cowden and Peutz-Jeghers. Risk factors for DCIS include family history, the number of first-degree relatives with breast cancer is strongly associated with a woman's risk for the future development of breast cancer (Figure 2.4) (Budny, et al., 2019).

<u>Chapter two</u> <u>Literature review</u>

Comorbidities: Metabolic Syndrome has been consistently and positively associated with the risk of postmenopausal breast cancer (RR 2.01, 95% CI 1.55-2.60). Hyperglycemia and subsequently T2DM have been also shown to increase the risk of cancer (Mili et al., 2021).

Life style: Regular physical exercise and a diet composed mainly of fruits and vegetables likely provide protection against breast cancer (Michael et al., 2017), a generally cancer in both premenopausal and postmenopausal women. The local synthesis of estrogens in the breast adipose tissue is thought to play a significant role in the initiation and progression of breast cancer (Bhardwaj, et al., 2019; Brown, 2021). Healthy lifestyle may lessen the effect of genetic variables on the chance of developing invasive breast cancer (Wu et al., 2013; Arthur, et al., 2020). **Environment and previous radiation:** In which significant doses of radiation to the breast were received. The risk appeared about a decade after treatment and was higher if radiotherapy occurred during breast development (Norman et al., 2018).

Breast density: Women with benign breast disease and extremely dense breasts had a threefold elevated risk of breast cancer over time (Román et al., 2021).

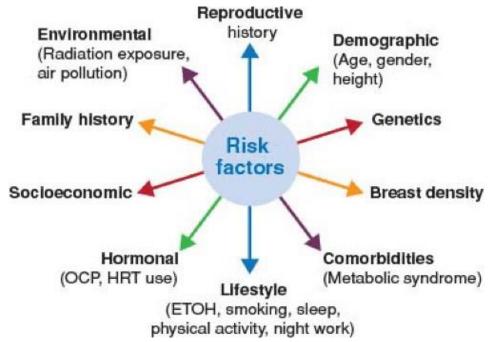


Figure 2.4: Risk Factors of breast carcinoma, heredity and breast cancer (Magdolna, 2002-2019)

2.2. Diagnosis of Early Breast Cancer

2.2.1. Breast screening

2.2.1. a Breast Self-Examination

Breast self-examination (BSE) is an early detection method to prevent breast cancer among women and is an early method of breast cancer screening that can be done easily by women (Figure 2.5), maintains privacy, and does not include invasive procedures (Husna, et al., 2019).

The World Health Organization does recommend BSE to increase women's awareness regarding their health, and the American Cancer Society recommends starting BSE during high school on a monthly basis. A cross-sectional study among students with a mean age of 20.8, in the Ghaza governorate, revealed that knowledge scores about BC and BSE were low (44.2%), and a training program was recommended to increase the level of awareness about BC and practicing BSE (Abo Al-Shiekh et al., 2021).

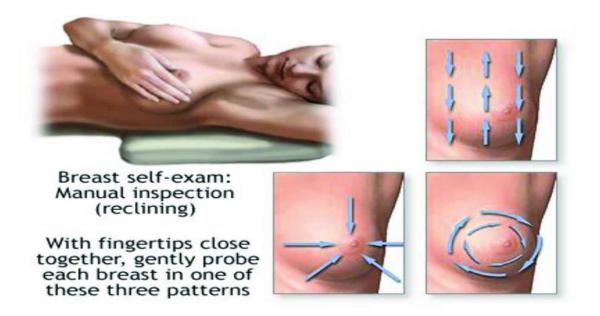


Figure 2.5: Breast self-examination (National Library of Medicine, 1997-2023)

2.2.1. b Clinical Breast Examination

Clinical breast examinations can allow clinicians to educate patients about their breasts and breast cancer, including early detection. Clinical breast examination can help detect some cancers not found by mammography, and clinicians should not override their examination findings if imaging is not supportive of the physical findings (Pandya & Moore 2011). With the patient in the sitting position and the pectoral muscles relaxed, palpation of the regional lymph nodes of the neck, clavicles (infraclavicular and supraclavicular), and axilla is then performed (figure 2.6) (Michael, et al., 2017).

The National Comprehensive Cancer Network and ACOG recommend clinical breast examinations every 1 to 3 years, but the American Cancer Society and the USPSTF do not recommend clinical breast examinations (ACOG, 2019).

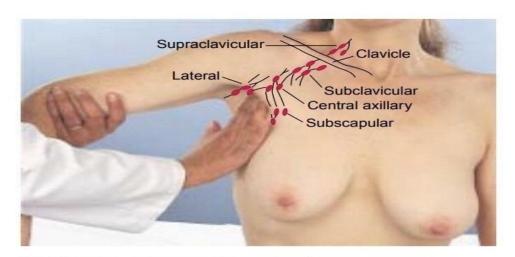


Figure 2.6: Palpation of the axillary regional lymph nodes in breast examination, (Brain Kart, 2018-2023)

2.2.1. c Diagnostic Mammography, breast Ultrasound and Magnetic resonance imaging

Mammography

Digital mammography, and tomo-mammography (a more sensitive diagnostic modality) are being introduced, which allow manipulation of the images and computer-aided diagnosis (Norman et al., 2018). Is the best tool for finding

breast cancer before it is larger than 2 centimeters (Figure 2.8) or has spread (Schattner, 2020).

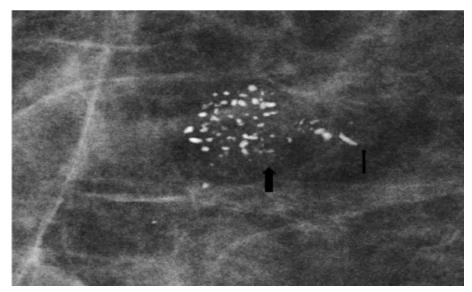


Figure 2.7: Clustered microcalcifications, (Carl, 2012)

Ultrasound (US)

Ultrasound has a valuable impact on the detectability of breast lesions and the differentiation of malignant from benign lesions. Combining 2D and 3D ABUS mammography improves diagnostic performance. The findings support 3D ABUS's improved efficiency in detecting the extent of breast cancer and assessing response to neoadjuvant chemotherapy (Vourtsis, 2019).

Magnetic resonance imaging (MRI)

Magnetic resonance (MR) imaging is an advanced modality reserved for supplemental breast cancer screening in high-risk individuals, with excellent sensitivity and specificity reported in recent literature (Vreemann et al., 2018) (Mann et al., 2019). In a meta-analysis of 44 studies, the sensitivity and specificity of diagnostic breast MRI were determined to be 90% and 72%, respectively (Michael et al., 2017). Supplemental screening with MR imaging has been associated with the detection of earlier-stage disease and improved 10-year survival (Evans et al., 2016).

The advantage of contrast-enhanced MR imaging as a functional imaging modality optimized to capture biologically more aggressive tumors that may be mammographically occult is the basis of a growing interest in expanding the role of MR imaging in breast cancer screening (figure 2.8) (Monticciolo et al., 2018).

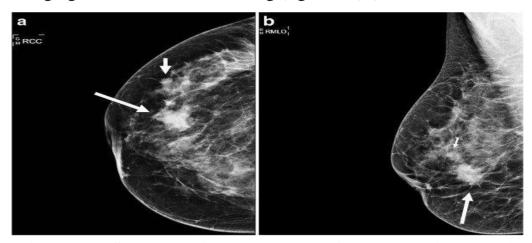


Figure 2.8: Speculated, irregular mass lesion (long white arrows) measuring 2.5x2 cm, located at mid-outer quadrant causing retraction of areola nipple, (Research Gate, 2008-2023)

2.2.2. Needle biopsy/cytology

Fine needle aspiration (FNAC) is the least invasive technique for obtaining a cellular diagnosis and is rapid and very accurate if both the operator and the cytologist are experienced (Norman et al., 2018). In the Verma et al. (2021) study, the diagnostic accuracy of FNAC versus core needle biopsy (CNB) for preoperative diagnosis of breast lumps was 94.52 vs. 94.23%.

For the preoperative pathological diagnosis of breast cancer in a developing country, FNAC is a quick, less complex, affordable, reliable, and pertinent approach. With high sensitivity and specificity, most malignant breast lesions can be reliably diagnosed by FNAC. If the initial FNAC is inadequate, CNB can be a useful second line method of pathological diagnosis in order to minimize the chance of a missed diagnosis of breast cancer (Saha, et al., 2016)

2.2.6. Pathology of breast cancer

Carcinoma develops in the lining layer (epithelial cells) of the breast in the cells lining the ducts or lobules (Figure 2.9). Carcinoma develops when normal cell changes into a carcinoma cell in the lining layer (epithelial cells) of the breast in the cells lining the ducts or lobules. It is referred to as a carcinoma in situ if it does not spread to adjacent tissue. Invasive or infiltrating carcinoma is the term used when the cancer cells have developed and separated from the ducts or lobules (invasive ductal carcinoma and invasive lobular carcinoma) (ACS, 2020).

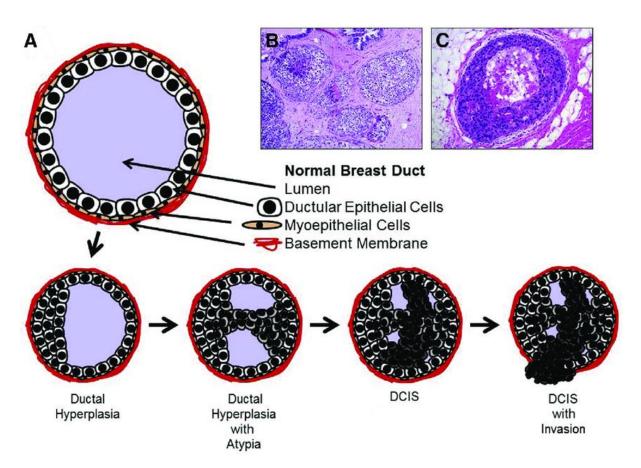


Figure 2.9: Natural history of breast ductal carcinoma in situ and progression to invasive breast cancer (William, Research Gate, 2019)

Invasive carcinoma has morphological variants, like tubular carcinoma, cribriform carcinoma, invasive lobular carcinoma, etc., that have a bearing on prognosis. In addition to morphological subtyping, the other conventional prognostic factors include histological grade, lymphovascular emboli, and lymph

node metastasis. Assessment of predictive biomarkers like the oestrogen receptor, the progesterone receptor, Her-2 neu, and the Ki67 index guides targeted therapy in breast cancer. (WHO, 2019; Wolff et al., 2018).

2.2.7. Clinical features of breast cancer

Palpable breast mass is evident in about 30% of women with breast cancer. Visible signs associated with breast cancer include dimpling, an orange-peel appearance (*peau d'orange*), erythema, edema, blistering, excoriations, sanguineous nipple discharge, and nipple retraction. Skin changes such as *peau d'orange* and blistering are strongly associated with inflammatory breast cancer and Paget's disease of the breast. Sanguineous nipple discharge is associated with papillary breast neoplasia. Ulcerations can be seen in advanced disease. Remember to rule out malignancy in patients being treated for mastitis or a breast abscess that is not improving clinically (Watkins, 2019).

2.2.8. Triple assessment

Triple assessment for a patient who presents with a breast lump or other symptoms suspicious of carcinoma, the diagnosis should be made by a combination of clinical assessment, radiological imaging, and a tissue sample taken for either cytological or histological analysis. The positive predictive value (PPV) of this combination should exceed 99.9% (Norman et al., 2018)

2.2.9. Pathologic and prognostic staging of breast cancer

In the AJCC Cancer Staging Manual, breast cancer staging integrates anatomic staging with tumor grade and biomarker data regarding hormone receptor status, oncogene expression, and gene expression profiling to assign a prognostic stage (Teichgraeber et al., 2021).

Breast cancer classification and staging systems have progressed rapidly in recent decades. Despite their limitations, these systems have incorporated in a more strategic and stratified way the most commonly evaluated histopathological factors and genomic panels to identify patients with different prognoses, whether in the analysis of overall survival or distant metastasis (da Luz et al., 2022).

2.2.9.1. The stage of breast cancer by the T, N, and M classifications, the tumor grade, and the results of ER/PR and HER2 testing.

The T category is determined by tumor size (largest mass in multicentric disease), and the categories range from Tis to T4. Tis is designated for DCIS and Paget disease. Lobular carcinoma in situ (LCIS) is not classified as category Tis and is now deemed benign (higher risk of future breast cancer) (American Society of Breast Surgeons 2016).

The subcategories of T1 disease:

- T1mi (microinvasive; tumor ≤ 1 mm in greatest dimension),
- T1a (greater than 1 mm but less than 5 mm),
- T1b (greater than 5 mm but less than 10 mm),
- T1c (> 10 mm, but \leq 20 mm)
- T2 (larger than 20 mm and no greater than 50 mm).
- T3 (greater than 50 mm).
- T4 (T4a, T4b, T4c, and T4d). Category T4a is defined by chest wall extension (Morris et al. 2000).

2.2.9.1.a. Clinical Staging of the Axillary Nodal Regions

Nodal staging begins with a physical examination of regional nodal basins, including the axillary, infraclavicular, and supraclavicular regions. Also, the US has emerged as the preferred technique for nodal assessment before therapy (Park Ko, UnPark, & Ko, UnCaudle, 2018).

The staging of axillary lymph nodes (N) is determined by the lymph node's location in relation to the pectoralis minor muscle:

- Level I lateral to the pectoralis minor muscle.
- Level II between the pectoralis minor muscle's medial and lateral margins and encompass interpectoral (Rotter) lymph nodes.
- Level III medial to the medial margin of the pectoralis minor muscle (Fornage, 2014).
- c N1 metastasizes to the movable ipsilateral level I and/or level II nodes.
- cN2 metastases to the fixed or matted ipsilateral level I and/or level II nodes or to ipsilateral internal mammary nodes in the absence of axillary metastases.
- cN3 includes ipsilateral level III node metastases with or without level I or level
 II nodes.

For staging purposes, metastatic intramammary lymph nodes are equivalent to the level I (Fornage, 2014).

- M0 (no distant metastases)
- M1 (metastatic disease present). Bone, lung, brain, and liver are the most common sites of metastasis in breast cancer (Kalli et al., 2018).
- cM0 is defined as no clinical or imaging evidence of distant metastases.
- cM1 is defined as distant metastases on the basis of clinical or imaging findings.
- pM1 is defined as distant metastases on the basis of pathologic proof. The final prognostic stage is determined by tumor grade, biomarker status (ER, PR, and HER2), genomic panels, and the anatomic TNM stage.
- Grade 1 (score between 3 and 5) represents a well-differentiated tumor.
- Grade 2 (score 6 or 7) represents a moderately differentiated tumor.
- Grade 3 (score 8 or 9) represents a poorly differentiated tumor (Schwartz, 2014).

The ER and PR receptor status and HER2 expression status of all invasive carcinomas should be determined whenever possible. Endocrine therapies such as

tamoxifen are known to slow the progression of ER- and PR-positive tumors (Kalli et al., 2018).

2.2.9.1.b. The stage of the breast cancer by the T, N, and M classifications

Stage 0: The disease that is only in the ducts of the breast tissue and has not spread to the surrounding tissue, in situ cancer (Tis, N0, M0).

Stage IA: small tumor, invasive, and has not spread to the lymph nodes (T1, N0, M0).

Stage IB: Cancer has spread to the lymph nodes, larger than 0.2 mm but less than 2 mm in size. There is either no evidence of a tumor in the breast or the tumor in the breast is 20 mm or smaller (T0 or T1, N1mi, M0).

Stage IIA: no evidence of a tumor in the breast, but the cancer has spread to 1 to 3 axillary lymph nodes. It has not spread to distant parts of the body (T0, N1, M0). The tumor is 20 mm or smaller and has spread to 1 to 3 axillary lymph nodes (T1, N1, M0). The tumor is larger than 20 mm but not larger than 50 mm and has not spread to the axillary lymph nodes (T2, N0, M0).

Stage IIB: The tumor is larger than 20 mm but not larger than 50 mm and has spread to 1 to 3 axillary lymph nodes (T2, N1, M0). The tumor is larger than 50 mm but has not spread to the axillary lymph nodes (T3, N0, M0).

Stage IIIA: The tumor spread to 4 to 9 axillary lymph nodes or to internal mammary lymph nodes. It has not spread to other parts of the body (T0, T1, T2, or T3; N2; M0). Also be a tumor larger than 50 mm that has spread to 1 to 3 axillary lymph nodes (T3, N1, M0).

Stage IIIB: spread to the chest wall or caused swelling or ulceration of the breast. It may or may not have spread to up to 9 axillary or internal mammary lymph nodes. It has not spread to other parts of the body (T4; N0, N1, or N2; M0).

Stage IIIC: A tumor of any size that has spread to 10 or more axillary lymph nodes, the internal mammary lymph nodes, and/or the lymph nodes under the collarbone. It has not spread to other parts of the body (any T, N3, M0).

Stage IV (**metastatic**): The tumor spread to other organs, such as the bones, lungs, brain, liver, distant lymph nodes, or chest wall (Cancer.Net, 2021).

2.3. Treatment of Early Breast Cancer

Breast cancer is currently treated with a multidisciplinary approach. Most patients benefit from a combination of therapies that may include surgery, medical therapy, and radiation therapy. This multidisciplinary approach has resulted in a significant reduction in breast cancer mortality (Michael, et al., 2017).

The evolution of the surgical treatment of breast cancer is governed by the principles of controlling the local disease and providing adequate pathology with minimal adverse effects (Kriby et al., 2018).

Guidelines of the European Society for Medical Oncology (ESMO) for patients with early breast cancer make the choice of therapy dependent on tumor size, feasibility of surgery, clinical phenotype, and the patient's willingness to preserve the breast (Cardoso, et al., 2019).

Also, systemic therapy for nonmetastatic breast cancer is determined by subtype: patients with hormone receptor—positive tumors receive endocrine therapy, and a minority receive chemotherapy as well; patients with ERBB2positive tumors receive ERBB2-targeted antibody or small-molecule inhibitor therapy combined with chemotherapy; and patients with triple-negative tumors receive chemotherapy alone (Waks & Winer, 2019).

2.3.1. Axillary surgery

The removal of affected lymph nodes involves sentinel lymph node biopsies and axillary lymph node dissections (Morrow, et al., 2001)

For patients with early breast cancer, axillary surgery is necessary for assessment and estimating the stage of the disease (Mátrai et al., 2022). It has a basic role in the treatment of the early stages of cancer.

Axillary surgery gives information to instruct adjuvant therapy and prevent the local recurrence of cancer (Bromham et al., 2017). SLNB has evolved as the basis of care in the management of the axilla and the prognosis of early breast cancer. A meta-analysis trial discovered SLNB precisely mapped the sentinel node in 96% of patients with an estimated false negative rate of 7.3% (Chen & Gillanders, 2021).

Recognition of sentinel lymph nodes through radioisotope or visual dye is based on the principle that primary tumors drain to one or more lymph nodes before they spread widely. The negative lymph node means that the tumor is still in its original location (Durre, 2022).

2.3.1.1 Sentinel Lymph Node Biopsy

The sentinel lymph nodes are the regional nodes that directly drain lymph from the primary tumor (Figure 2.10). No imaging modality is accurate enough to detect lymph node metastases when primary breast cancer is at an early stage, but sentinel lymph node biopsy is a highly reliable method for screening axillary nodes and for identifying metastatic (including micro-metastatic) disease in regional lymph nodes (Giammarile, et al., 2022).

The status of the axillary lymph nodes is the most prognostic factor in the management of breast cancer patients. SLNB is a standard technique for assessing the clinically and radiologically negative axilla. It was introduced for the first time in breast cancer surgery for assessment of the axilla in 1994 (Nadeem, et al., 2022)

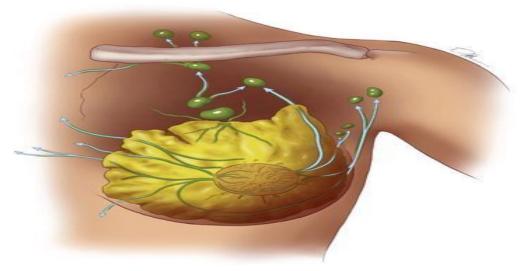


Figure 2.10: Lymphatic pathways of the breast, the direction of lymph flow. (The University of Texas MD Anderson Cancer Center, Visual Art, 2012.)

The aim of SLNB is to identify patients who are node-negative or who have limited volume axillary disease. The premise behind SLNB is that the sentinel lymph nodes the first lymph nodes to drain the cancer. if sentinel lymph nodes are identified and removed and these do not contain the metastatic disease, then the remainder of the axilla is likely to be negative, and complete axillary dissection and its sequelae can be avoided (Josef et al., 2019).

For patients with clinically suspicious axilla, an ultrasound-guided FNA may be beneficial to find out metastatic dissemination to the axilla. If the FNA is negative, then the patient should undergo an SLNB at the time of surgery with a decision about further management of the axilla, if any, pending the results of the SLNB. Breast cancer spread to ipsilateral axillary lymph nodes occurring in 15% to 30% of patients. The presence of axillary lymph node metastases has important prognostic implications and can impact medical, surgical, and radiation oncology decision-making (Michael W., et al., 2017;Thanh & William, 2017). Typically, axillary lymph nodes are involved sequentially from the low (level I) to the central (level II) to the apical (level III) lymph node groups. Women with nodenegative disease had less than a 30% risk of recurrence, compared with as much as a 75% risk for women with node-positive disease. (Catherine, 2019)

<u>Chapter two</u> <u>Literature review</u>

It is appropriate to do SLNB for all patients with node-negative (N0) operable invasive breast cancer, including DCIS patients who require a mastectomy, clinically suspicious nodes but a non-diagnostic needle biopsy, N0 but node positive on FNA or core biopsy, and N0 after new adjuvant chemotherapy, whether node negative or node-positive (Gabriel et al., 2021).

2.3.1.1.a. The technique of SLNB procedure

The patient was brought to the operating room and positioned with the ipsilateral arm abducted up to 90 degrees. The breast, anterior chest walls, and axilla are prepared and draped in the usual standard sterile fashion. Five milliliters of blue dye is injected around the tumor periphery, at the palpable edge of the biopsy cavity, or into the subareolar plexus. Breast massage is performed for 5 minutes to dilate the breast lymphatics and facilitate lymphatic drainage (Michael et al., 2017).

The SLNB procedure begins with localization of the SLN through injection of a radioactive substance and/or a blue dye (methylene, isosulfan) intradermally into the tumor, the area around it (peritumorally) (Figure 2.11), or the area around the nipple, or the subareolar plexus. Lymph vessels will carry these substances along the same path that cancer would likely take. The first lymph node(s) the dye or radioactive substance travels to will be the sentinel node(s) (Figure 2.11) (Henry et al., 2020).

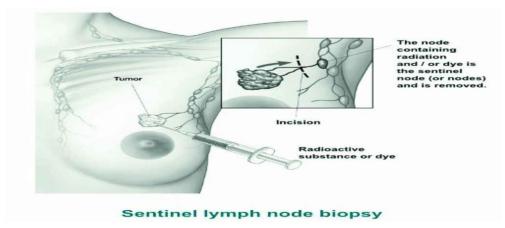


Figure 2.11: Injection of Blue dye for SLNB, (ACS, cancer.org) | 1.800.227.2345, 2021)

The blue lymphatics followed toward the axilla to identify the sentinel lymph node(s) (Figure 2.12). Successful SLN identification by blue dye is defined as the identification of any blue node or non–blue node with a blue afferent lymphatic (Gabriel et al., 2021). All blue nodes are removed (Figure 2.13, 2.14)



Figure 2.12: The blue lymphatics toward the axilla to identify the sentinel lymph node (Smart Health tower, 2021)

SLNB is best done prior to the breast operation while the lymphatics are still intact, and through a separate transverse skin line incision in the axilla. Even tumors high in the axillary tail will be further from the axilla than they appear, and one should avoid the temptation to do the entire operation through a single incision, except perhaps for mastectomy done through a single oblique incision, where SLNB is easily done through the axillary end of the incision prior to proceeding with the mastectomy (Gabriel et al., 2021).



Figure 2.13: SLN identification by blue dye, blue colored lymph node seen during the operation (Smart Health tower, 2021)



Figure 2.14: Sentinel lymph nodes removed (Smart Health tower, 2021)

A final and critical element in SLNB is the careful palpation of the axilla and the submission of any palpably suspicious nodes as SLN. Once all SLNs have been identified and removed, the clavipectoral fascia is reapproximated, and the skin is closed in two layers without drainage (Michael et al., 2017).

2.3.1.1.b. Sentinel Lymph Node Biopsy in Pregnant Women

In a 2010 study involving 12 pregnant women who underwent lymphatic mapping during the 26th week of pregnancy, 11 healthy babies were delivered, all of whom had normal weights and no abnormalities. The study supports the safety of SLNB when utilized with a low-dose lymphoscintigraphic technique in pregnant patients with breast cancer (Gentilini et al., 2010).

Also, according to a study by Prathi et al. (2011) to investigate the safety of blue dye for lymphatic mapping in pregnant women and extrapolate the estimate of maximal fetal exposure to the blue dye during the SLNB procedure, Found that the maximum dose to the fetus is 0.25 mg (5% of the injected dose). The methylene blue dye can be used for lymphatic mapping in pregnancy-associated breast cancer with minimal fetal risk.

81 pregnant women underwent surgery, while 25 (53.2%) underwent SLNB, 20 (42.6%) underwent upfront axillary lymph node dissection, and 2 (4.3%) underwent no lymph node surgery. In the first, second, and third trimesters. All patients who underwent mapping had success. There were no side effects related to SLNB, using either methylene blue or 99-technetium. SLNB in patients with breast cancer who are pregnant seems to be secure and reliable (Adrienne et al., 2014).

2.3.1.2. Axillary lymph node dissection (ALND)

Regarding axillary surgery after SLNB, according to the ACOSOG Z0011 study's recommendations, axillary lymph node dissection (ALND) was not carried out if metastases were only discovered in one or two sentinel lymph nodes (SLNs); however, ALND was carried out if metastases were discovered in three or more sentinel lymph nodes (Giuliano et al., 2011) (Jung et al. 2019). Macrometastasis (>2.0 mm) was used to determine nodal metastasis (nodepositive); nodal negativity was stated as the absence of tumor cells in lymph nodes, the presence of isolated tumor cells (0.2 mm), or the presence of micrometastasis (0.2-2 mm) (Edge et al 2009) (Galimberti et al., 2013) (Reimer et al., 2017) (Naidoo 2017) (Zhu et al., 2018) About 10% of patients experience ALND adverse effect of infection or cellulitis of the arm, chest wall, or breast. Repeated infections increase the risk of developing lymphedema (Gabriel et al., 2021).

2.3.1.2. a. Pathology

Axillary nodes have typically been examined by a single H&E-stained section, despite evidence that additional studies (serial sections and/or immunohistochemical [IHC] stains for cytokeratins) could identify missed nodal metastases in a significant fraction of patients (Tan et al., 2008). These enhanced techniques—prohibitive for the examination of an entire ALND specimen—became feasible for SLNB and promised more accurate staging and selection of treatment (Giuliano et al., 2011).

2.3.2 Breast conserving surgery (BCS)

For the majority of women with primary breast cancer, the first treatment is breast surgery with curative intent (Breast Cancer Now, 2020). BCS also called partial or segmental mastectomy, lumpectomy, wide local excision, or quadrantectomy, enables the removal of the cancerous tissue with simultaneous preservation of intact breast tissue and is often combined with plastic surgery techniques called oncoplasty. However, the use of BCS is mostly related to significantly better cosmetic outcomes, a lowered psychological burden on the patient, and a reduced number of postoperative complications (Morrow et al., 2001; Rahman, 2011).

Oncoplastic breast surgery techniques have been used to conserve the breast and perform cancer resection; that is, where the tumor, along with a margin of normal tissue, is excised, the aesthetic outcomes of these procedures are extremely important by either moving or adjusting the remaining breast tissue around (volume displacement) or bringing in tissue from elsewhere to fill the defect after breast cancer removal (volume replacement) (Nanda et al., 2021).

Breast conserving therapy (BCT) has been accepted as an appropriate treatment modality for many patients with (T1N0), IIA (T1N1 or T2N0), or IIB (T2N1). The term BCT BCS or lumpectomy is followed by radiation therapy to

<u>Chapter two</u> <u>Literature review</u>

treat any microscopic residual tumor. The national comprehensive cancer network continues to recognize BCT as being supported by the highest level of evidence in terms of its equivalency to mastectomy in early breast cancer treatment for the majority of women. For patients with clinical T1N0 disease, surgery is typically the first treatment modality (Michael et al., 2017; Michele & Jeffrey, 2021).

2.3.2. a. Ductal carcinoma in situ (DCIS)

Ductal carcinoma in situ is a non-invasive form of breast cancer. Its incidence is increasing due to the widespread use of mammographic screening (Badve & Gökmen, 2019). DCIS is commonly defined as the proliferation of malignant epithelial cells within the mammary ductal system with no evidence of invasion into the surrounding stroma on routine light microscopic examination (Figure 13).

Most patients with DCIS will present with no breast-related symptoms or findings on physical examination. More than 90% of all cases of DCIS are detected in imaging studies – commonly as microcalcifications on mammography (2.7) (Michael et al., 2017).

As in situ lesions tend to exhibit micro-calcifications more frequently than invasive carcinomas, it is natural that the incidence of detecting pre-invasive lesions has dramatically increased (up to 20%) following the routine use of mammographic screening (DeSantis et al., 2017).

Expression of ER is observed in greater than 80% of cases, and in some series, it is observed in 90–95% of cases (E5194 and Toronto cohorts; Rakovitch, 2017; Sanati, 2019). While progesterone receptor (PR) expression is observed in approximately 60% of cases (Lari, 2011).

<u>Chapter two</u> <u>Literature review</u>

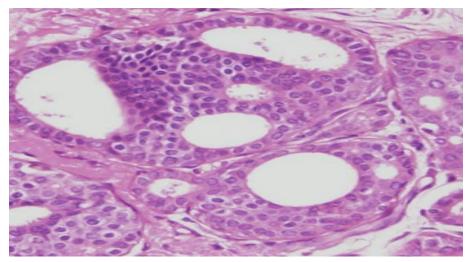


Figure 2.15: Ductal carcinoma in situ, (Deana, J. Attai, 2013)

Treatment for DCIS is BCS and mastectomy, there is no size limit for offering BCS other than the balance between the extent of the disease and breast size. Provided that clear resection margins are achieved; 2 mm margins are adequate with whole breast radiotherapy (Cardoso et al., 2019; Josef et al., 2019).

Mastectomy is curative in 98% of patients with DCIS, regardless of the tumor grade or the size of the lesion. Mastectomy should be performed if BCT is contraindicated, or based on patient preference (Michael et al., 2017). While mastectomy is highly effective, but may be overtreatment for many women particularly those with small low- and intermediate-grade lesions that may never have become symptomatic within a patient's lifetime. Most women with DCIS are suitable for a skin sparing mastectomy approach with immediate breast reconstruction. In general, it is difficult to excise lesions over 5 cm except in women with larger breasts when a mammoplasty is an option. In such women once the DCIS is excised, the breast is reshaped and made smaller, and usually the opposite breast is reduced to match. (Josef et al., 2019).

Axillary lymph node involvement in DCIS is rare, and SLNB is not indicated during breast-conserving surgery (Michael et al., 2017). But axillary

node evaluation with SLNB is reasonable in large and high-grade tumors (Cardoso et al., 2019).

There is no role for chemotherapy in DCIS. However, endocrine therapy is commonly recommended (Michael et al., 2017). Tamoxifen is recommended as systemic adjuvant therapy for ER-positive DCIS following BCS to prevent local recurrence. Also, it is recommended following mastectomy to decrease the risk of contralateral breast cancer in high-risk patients (Cardoso et al., 2019). Younger women, with more extensive high-grade DCIS with comedo necrosis that is close to margins appear at greater risk of local recurrence and so these women may benefit from radiotherapy (Josef et al., 2019)

2.3.2. b. Lobular carcinoma in situ (LCIS)

Lobular carcinoma in situ (LCIS) is a noninvasive lesion that arises from the lobules and terminal ducts of the breast. It is multifocal and has morphologic features characterized by solid proliferation of small cells, with small, round to oval nuclei, and variably distinct cell borders (Figure 2.16).

The cells lose polarity, varying in shape while maintaining a surprisingly uniform size (Hortobagyi et al., 2017) (Josef et al., 2019). The presence of microcalcification (Figure 2.7) in mammography can be a potential predictor of an upgrade. (Lee et al., 2022).

Lobular carcinoma in situ is a risk factor and a nonobligate precursor of breast carcinoma. Classic LCIS diagnosed by needle core biopsy with concordant imaging and pathologic findings does not mandate surgical excision. When LCIS is identified on core biopsy, surgical excision is performed to exclude an associated cancer. If LCIS is found on excisional biopsy, no further surgical intervention is needed. (Wen & Brogi, 2018; Josef et al., 2019).

After surgical excision patient should be monitored with interval history and physical examination every 6-12 months and annual diagnostic mammogram (NCCN, 2019).

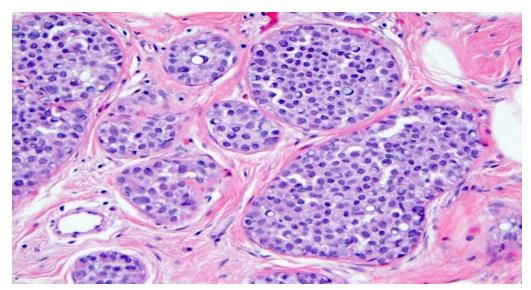


Figure 2.16: Lobular carcinoma in situ, Jasmine Vickery, Anna Biernacka, 2002-2023, PathologyOutlines.com, Inc.

2.3.2. c. Invasive ductal carcinoma (IDC)

Invasive ductal carcinoma (IDC) is characterized by an irregular nest-like or strip-like structure, most of which are surrounded by fibrous stroma or adipose tissue devoid of myoepithelial cells (Figure 2.17) (Zhao et al., 2022).

Invasive breast cancer of no special type (NST), it can develop within a benign tumor or coexist with it (Saimura et al., 2018). 10% of breast fibroadenomas were infiltrating ductal carcinoma. In a case report done by Saadallah, et al. 2019, and the carcinomatous lesion was an infiltrating ductal carcinoma adjacent to an aged fibroadenoma.

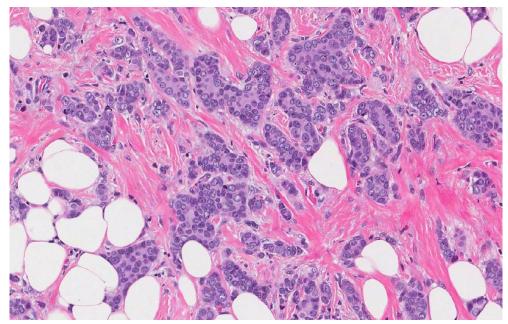


Figure 2.17: Invasive ductal carcinoma, Jason Wasserman, (2022)

2.3.2. d. Breast-conserving surgery after new adjuvant therapy

Significant numbers of patients with large and locally advanced breast cancers (clinical T2N0 or T2N1 disease) are treated with neoadjuvant chemotherapy (NAC) and then become suitable for BCS. The goal of neoadjuvant therapy is to shrink primary breast cancer prior to surgery, facilitating BCT. More patients after chemotherapy than after endocrine therapy have a diffuse pattern of response and a reduction in cellularity, but there is a little reduction in volume (Michael et al., 2017).

2.3.2. e. Inflammatory breast cancer

Inflammatory breast cancer (IBC) is a deadly and aggressive type of breast cancer (Figure 2.18) (Jagsi et al., 2022). It accounts for only 2% to 4% of all breast cancer cases and contributes to 7% to 10% of breast cancer-related mortality, which increased at an annual rate of between 1.23% and 4.35% per year. IBC is peau d'orange, characterized by edema, warmth, and erythema. The National Comprehensive Cancer Network (NCCN) guidelines and the international IBC expert guidelines recommend intensive therapy (systemic therapy, surgery, and

<u>Chapter two</u> <u>Literature review</u>

radiation therapy) for patients with primary IBC to achieve the best local control and survival outcome. IBC was treated mainly with surgery, and, with or without adjuvant radiation therapy, the 5-year survival was only 5%. (Menta et al., 2018)

The safety of SLNB has not been established for patients with IBC, and following neoadjuvant chemotherapy, ALND remains standard care. SLNB for inflammatory breast cancer only makes sense in the setting of a clinical trial including a backup ALND for performance characteristics, especially the false-negative rate (Gabriel et al., 2021).



Figure 2.18: Inflammatory breast cancer, (Vuthinun, 2016)

2.3.2. f. Paget Disease of the Breast

Mammary Paget's disease is a condition that affects the nipple-areola complex of breast carcinoma. The nipple usually has an eczematoid change, a red and ulcerative nipple's lesion, or an erythematous and crusted lesion, with or without a mass-like lesion and nipple infiltration and inversion (Figure 2.19).

<u>Chapter two</u> <u>Literature review</u>

It occurs in 0.5–5% of all cases of breast cancer, can be associated with underlying DCIS in more than 95% of cases, especially in postmenopausal women, or can also be associated with invasive breast cancer (Plutino et al., 2022).

Management options are typically surgical and include breast-conserving surgery or mastectomy in addition to oncoplastic techniques. A sentinel lymph node biopsy is performed on all patients undergoing surgery. Adjuvant chemotherapy, radiotherapy, or endocrine therapy can be used to treat concomitant invasive disease or ductal carcinoma in situ (Hudson-Phillips et al., 2023).



Figure 2.19: Paget Disease of the Breast, (Louisa, 2021)

2.3.3 Mastectomy

A mastectomy is the complete removal of the breast and is often associated with immediate breast reconstruction (Morrow et al., 2001).

2.3.3. a. Simple mastectomy and modified radical mastectomy

The surgical techniques used in mastectomy are in constant evolution because of advancements in knowledge and the needs of patients. Modified radical mastectomy (MRM) became the standard treatment for women with stage I and II

breast cancer in the 1970s. However, ALND, a part of a modified radical mastectomy, was associated with significant side effects. Hence, the simple mastectomy (SM) was developed to spare the ALND and focus on treating the local disease only. Studies showed that survival after SM with or without radiation was comparable to that after RM.

Recently, adjuvant systemic treatment has been shown to significantly improve disease-free and overall survival in patients with node-positive breast cancer, which requires nodal staging to guide therapy. SLNB was invented to provide adequate pathologic nodal status in clinically negative axillae. Today, SM coupled with SLNB has largely replaced the MRM (Kriby et al., 2018).

2.3.3. b. Nipple sparing mastectomy

In some patients, mastectomy (simple mastectomy, skin-sparing mastectomy, or nipple sparing mastectomy (NSM)) is still carried out due to tumor size relative to breast size, multicentric tumor, or patient choice (Cardoso et al. 2019).

According to the findings of a study conducted by Fu et al., the proportion of NSM has steadily increased, while the proportion of total mastectomy has begun to decline since 2013. NSM that has an esthetic effect refers to the removal of all visible breast tissue and the submission of subpapillary duct tissue for histological evaluation. That is, NSM excises the breast parenchyma to the same extent as conventional total mastectomy (Fu et al., 2022).

The 2020 National Comprehensive Cancer Network (NCCN) guidelines recommend that NSM is optional in oncology, except for the following contraindications: Paget's disease, bloody nipple discharge associated with malignant tumors, inflammatory breast cancer, and/or imaging findings suggesting that the nipple or subareolar tissue is involved in malignant lesions (NCCN, 2020).

2.3.4 Chemotherapy

Chemotherapy using a first-generation regime, such as a 6-monthly cycle of cyclophosphamide, methotrexate, and 5-fluorouracil (CMF), will achieve a 25% reduction in the risk of relapse over a 10–15-year period. A woman with a 96% chance of survival at 5 years only has a 4% chance of death over this time, and the absolute benefit from chemotherapy would be an increase in the survival rate of 1%, to 97%. It is considered in node-negative patients with high tumor grades.

Primary chemotherapy (neoadjuvant) is being used for those who require mastectomy (and almost certainly postoperative adjuvant chemotherapy) to reduce tumor volume to enable breast-conserving surgery to be performed. Patients with Her-2-positive disease will receive Herceptin as part of their management and have high complete response rates (Norman et al., 2018).

Even though chemotherapy is thought to be effective, it frequently causes hair loss, nausea, vomiting, diarrhea, mouth sores, fatigue, increased susceptibility to infections, bone marrow suppression combined with leucopenia and anemia, and easier bruising or bleeding. Other less common side effects include cardiomyopathy, neuropathy, hand-foot syndrome, and impaired mental functions. In younger women, disruptions of the menstrual cycle and fertility issues might also appear (Łukasiewicz et al., 2021).

2.3.5 Radiation Therapy

Radiation therapy after lumpectomy has been shown to reduce the odds of invasive and noninvasive recurrences in the breast but has not been associated with a survival advantage. In some patients with low risk negative disease and a widely negative resected margin it is reasonable to omit radiation therapy, particularly in settings of comorbidity, advanced age, or patient preference. Data shows that a gene expression assay such as Oncotype DX DCIS may be utilized as a useful tool

to stratify patients according to a low, intermediate, or high rate of recurrence to make a decision for post-lumpectomy radiation (Gabriel et al., 2021).

Irritation and darkening of the skin exposed to radiation, fatigue, and lymphoedema are some of the most common side effects of radiation therapy applied to breast cancer patients. Nonetheless, radiation therapy is significantly associated with the improvement of the overall survival rates of patients and a lowered risk of recurrence (Joshi et al., 2007)

2.3.6 Endocrine therapy

Endocrinal therapy aims to lower estrogen levels or prevent breast cancer cells from being stimulated by estrogen. Selective estrogen receptor modulators (SERMs) (tamoxifen, toremifene) and selective estrogen receptor degraders (SERDs) (fulvestrant) are drugs that block ERs, while aromatase inhibitors (letrozole, anastrazole, exemestane) are treatments that aim to lower estrogen levels (Tremont et al., 2017).

2.3.7. Biological therapy

Biological therapy (targeted therapy) can be provided at every stage of breast cancer therapy—before surgery as neoadjuvant therapy or after surgery as adjuvant therapy. Biological therapy is quite common in HER2-positive breast cancer patients; major drugs include trastuzumab, pertuzumab, trastuzumab deruxtecan, lapatinib, and neratinib (Maximiano et al., 2016; Ishii et al., 2019; Nguyen et al., 2021).

2.3.8. Molecular Subtyping/Biomarker Profile (ER, PR, HER2)

Immunohistochemical markers have traditionally guided treatment decisions in breast cancer. However, advancements in gene expression profiling and the availability of gene-based assays have propelled these newer tests into routine clinical practice (Gao, & Swain, 2018).

<u>Chapter two</u> <u>Literature review</u>

Luminal A subtypes express keratins and coexpress ER, are associated with low grade invasive carcinoma of no special type, and are responsive to hormone therapy (Tamoxifen). Luminal B also expresses keratins but exhibits diminished ER, especially PR expression, a histologically higher grade associated with cellular proliferation, and may overexpress the HER-2 oncogene. Less sensitive to hormone therapy, they are more likely to respond to chemotherapy. The HER-2 enriched subtype, characterized by increased expression of the HER2 oncogene and its negative status for ER and PR expression, exhibits high-grade histology, the most aggressive subtype with the highest mortality. However, antiHER-2 (trastuzumab) treatment improved the outcome (Gabriel et al., 2021).

HER2 can now be targeted using monoclonal antibodies and small molecule inhibitors. Using immunohistochemistry and image analysis, HER2 is scored 0, 1+, 2+, and 3+. Positivity is noted as 3+, whereas scores of 0 and 1+ are considered negative. A score of 2+ is considered indeterminate, and further testing for gene amplification can be performed using either FISH (fluorescence in situ hybridization) or CISH. An emerging biomarker is the Ki-67 index. The Ki-67 antigen is present in all phases of the cell cycle except for the G0/resting phase and reflects the proliferative potential of breast cancer. Ki-67 is determined by IHC and noted as a percentage, where <10% is considered a low proliferative index, 10% to 20% is considered borderline, and >20% is considered high (Michael et al., 2017).

2.4. Complications after axilla and breast surgery

Breast or axillary procedures have been linked to up to 30% of postoperative problems (wound infection, seroma formation, and hematoma), all of each can be caught early (McNeely et al., 2012; Rizvi et al., 2020).

The main surgical risks complications are Numbness around the scar and upper arm (which can be permanent), Seroma (liquid collection at the site of

operation), Infection of the arm, Mild wound dehiscence (opening up) or delayed wound healing, Shoulder stiffness, Haematoma (a collection of blood at the site of the operation), Neuralgia (pain in the nerves in the arm or axilla), poor scarring (lumpy and itchy) at the site of the surgical incision (Waks & Winer 2019)

2.4.1. Wound infections

Characterized by localized ache or soreness, localized edema, erythema, or heat, and purulent discharge (CDC, 2023).

Cellulitis of the arm, chest wall, or breast is a well-recognized but relatively infrequent side effect of ALND, affecting about 10% of patients. Cellulitis can arise de novo or following a nonsterile skin break, there is no evidence that sterile skin punctures cause cellulitis or that avoidance is preventive of either infection or lymphedema. Repeated episodes of infection may increase the risk of lymphedema, and prompt treatment with oral or IV antibiotics makes sense (Gabriel et al., 2021).

2.4.2. Seroma

Seroma develops during axillary and breast surgery as a result of persistent lymphorrhea, which results in a protracted healing period and a higher risk of infection (Radu et al., 2021).

In 3%, 10%, and up to 85% of all cases, seroma formation occurs mostly within the first few weeks after breast surgery. The latter finding suggests it could be a side effect of surgery rather than a complication. Needle aspiration of seroma liquid has an impact on the patient's wellbeing and can also significantly impact treatment by delaying adjuvant therapy (Pochert et al., 2022).

2.4.3. Hematoma

Hematoma is a collection of blood outside of blood vessels. Hematomas are typically brought on by damage to the blood vessel wall (Siamak 2022). Hematoma

rates for breast reduction procedures range from 1.0 to 9.3%. After a breast reduction, intraoperative hypotension may increase the chance of hematoma (Daar DA, et al., 2021). It's typical for wound-related issues to arise after breast surgery. Inadequate cosmesis might result from delayed wound healing (Iqbal et al., 2020).

2.4.4. Paresthesia

Paresthesia caused by intercostobrachial nerve (ICBN) division is a complication of axillary lymph node dissection (Taira et al., 2014).

The division of sensory nerves is largely responsible for the sensory sequelae of both SLNB and ALND (Gabriel et al., 2021). In the first three months following surgery, sensory morbidity diminishes; occasionally, it persists for one year (Temple et al., 2002).

2.4.5. Range of motion (ROM)

Limitation in shoulder ROM is a side effect of ALND, with two randomized trials reporting less limitation for SLNB versus ALND. These and other studies confirm that shoulder ROM improves rapidly over time, and recommend exercises to restore shoulder ROM are an essential element of postoperative care. Limitation in shoulder ROM, with SLNB showing reduced impairment in comparison to ALND in randomized trials (Gabriel et al., 2021).

2.4.6. Lymphedema

Lymphoedema (persistent swelling of the arm) (Figure 18) is tissue swelling caused by decreased lymphatic outflow and increased interstitial lymphatic fluid retention (Grada, 2017). ALND results in a mechanical obstruction that causes a lymph fluid backup and upper limb edema (Dayan et al., 2020).

This can be uncomfortable and can interfere with the use of the arm. It usually occurs less than one year following the operation but may occur later following trauma or infection in the arm (Waks & Winer, 2019).



Figure 2.20: Lymphedema after breast cancer treatment, (Stanley, 2018)

Lymphedema is diagnosed through clinical examination. Historically, lymphedema could be diagnosed with a 10% change in limb volume. Heaviness, temporary swelling, and discomfort symptoms come before swelling (Wiser et al., 2020).

The randomized trial conducted in Sweden and Denmark between 2015 and 2019 analyzed patient-reported outcomes (501 in the SLNB only group and 475 in the completion ALND group) and found that, one year after surgery, arm function and symptoms are significantly worse after completion ALND following SLNB than by SLNB alone (Matilda et al., 2022).

Lymphedema can be managed with a variety of elastic compression garments, compression pumps, bandaging, physical activity, and sophisticated physiotherapy (Markkula, 2019).

Table 2.1: Early and late post-breast and axillary surgery complications CDC, (2023), Wound Essentials, (2011). Lee, J. et al. (2021). ME Kazzam, (2022), Ducic, I et al., (2014), Arsh A. (2019)

Infection	Day 10-12	purulent	localized	localized	localized
		drainage	pain	tenderness	swelling;
Hematoma	Day 1-10	localized	localized	pain	breast
		bruise	dark		swelling
			red/black		
			color		
Seroma	Day 10-30	localized	infection	Reduced	wound
		pain		shoulder	dehiscence
				movement	
Paresthesia	Day 10-90	localized pain, changes in skin sensation	Hyperesthesia	Hypoesthesia	Localized numbness
Shoulder stiffness	Day 10-90	Shoulder	Limitshoulder		
		pain	ROM		
Lymphedema/	Day 30- 90	11-20 %	21-40 %.	41-80%	≽80%
Difference	and	Mild	Moderate	Evident	Severe
between the two	above				
extremities					

2.5. Recommendations after management of early breast cancer

The ASCO Guidelines recommend surveillance with history and physical examination every 3–6 months for the next 3 years after primary therapy, then every 6–12 months for the next 2 years, and annually thereafter. All patients should be counseled for breast self-examination, regular pelvic examination, and genetic counseling for high-risk women.

2.5.1. Recommendations for pre and post -menopausal women

- Regular annual or every 2 years mammography is recommended for women aged 50- 59 years, regular mammography may also be done for women aged 40-49 and 70-74 years.

- In women with a strong family history of breast cancer, with or without proven BRCA mutation, annual MRI and annual mammography are recommended (Cardoso et al., 2019)

2.6. Previous studies

■ Veronesi & Corso (2019), conducted an analytical study on standard and controversies in sentinel node in breast cancer (BC) patients. The study enrolled women with clinical T1–T2 invasive BC, non-palpable adenopathy, and 1–2 SNs containing metastases.

The confirmed that ALND is not indicated in positive SNBs (1-2 with metastases), in patients eligible for BCS. There is a trend towards reducing surgical treatment of the axilla in BC patients.

- Gong, J., et al. (2019) conduct a quantitative analysis of current evidence and provide important insights into internal mammary nodes (IMN) management. In the study reporting the rate of positive internal mammary lymph node sentinel lymphoma (IMN-SLNB), positivity was identified. The study concluded that mammary lymph node metastasis may be underestimated. Patients with positive axillary lymph nodes have a higher risk of internal lymph node metastasis. The metastasis of axillary lymph nodes was a major predictive factor of IMN involvement. Patients with positive axillary lymph nodes have a higher risk of internal lymph node metastasis.
- Freitas-Junior et al., (2017) conducted a randomized clinical trial study to evaluated the possibility of not draining the axilla following axillary dissection. The study included 240 breast cancer patients who underwent axillary dissection as part of conservative treatment. The study concluded

that axillary dissection can feasibly be performed without drainage. However, more needle aspirations could be required, and there could be more cases of wound dehiscence in patients who do not undergo auxiliary drainage.

- Geng et al. (2016) conducted a study aimed at evaluating the feasibility and accuracy of SLNB for initially clinically node-negative breast cancer after NAC by conducting a systematic review and meta-analysis. The researchers searched PubMed, Embase, and the Cochrane Library from January 1, 1993, to November 30, 2015, for studies on initially clinically node-negative breast cancer patients who underwent SLNB after NAC followed by axillary lymph node dissection (ALND). The study concluded that SLNB is technically feasible and accurate enough for axillary staging in initially clinically node-negative breast cancer patients after NAC.
- Kang et al. (2014) conducted a retrospective study to determine the feasibility of SLNB based on axillary anatomy in cases where SLN was not detected by conventional lymphatic mapping methods. A retrospective analysis involving 208 patients who received anatomical SLNB between January 2003 and December 2010 was performed. In conclusion, results suggest that anatomical SLNB may not replace ALND in cases where SLN is not detected by conventional lymphatic mapping methods but may be considered as a method for predicting axillary status before conducting a node dissection.

Chapter Three Patients & Methods

Chapter three Method

3. PATIENTS & METHODS

3.1. Method:

This chapter gives insight into the methods for this study under the title "The effects of Sentinel Lymph Node Biopsy in the Management of Early Breast Cancer with Negative Axillary Lymph Node in the Hospitals in Sulaimani City.

3.2. Design:

It's planned to do descriptive analytic prospective observational study of a group of patients in Sulaimani hospitals, in which patients have the blue dye method of sentinel lymph node biopsy with breast surgery during one year of study in Sulaimani surgical hospitals. The researcher wants to assess the effects of sentinel lymph node biopsy on the management of early breast cancer in the Smart Health Tower and Soma Surgical hospitals. A prepared questionnaire was used to interview the participants, and an observational checklist was used for recording post-operative problems. Any patients who underwent breast and axillary surgery and were diagnosed with early breast cancer with node-negative axillae in selected hospitals were eligible to participate in this study. The study was conducted at Smart Health Tower and Soma Surgical Hospitals. The research was carried out from March 1, 2021, to April 1, 2022.

Chapter three Method Research Design Descriptive analytic observational research design **Population** Women with stage1, stage2, and not advanced stage 3 breast cancer Setting Smart Health Tower and Soma Private Surgical Hospital in Sulaimani City Sample and sample Size Sample of 110 women with early breast cancer, 41 SLNB alone, 69 SLNB + Sampling Sampling Technique Purposive Sampling Techniqe **Tools** Sociodemographic characteristic' SLNB results Postoperative complications Interview Data collection method Observation Data analysis and interpretation Descriptive statistical analysis

Figure 3.1: Representation of Research Methodology

Chapter three Method

3.3. Administrative Arrangements and Ethical Approval

An official permit was obtained from the Smart Health Tower and Soma Surgical hospitals in order to facilitate the data collection process for conducting this study, and they gave their approval (Appendix 2).

- Approval of the faculty scientific committee on the research of the Nursing College
- The Research and Ethical Committee at the College of Medicine at the University of Sulaimani granted this study. The study protocol was presented to the Ethics Committee of the College of Medicine at Sulaimani University with regard to the confidentiality and anonymity of the study participants. The protocol was reviewed by the members of the ethics committee and approved (Appendix 1).
- Informed consent (verbal and written) (the form was read by the researcher with translation for the illiterate and some other patients) was obtained from all participants prior to their involvement in this study to gain their confidence and acceptance to participate in the current study. As well, the confidentiality of all personal information was guaranteed throughout the study to ensure the anonymity of the participants (Appendix 3).

3.4. Study Setting

The study was conducted between March 1, 2021, and April 1, 2022, in the waiting room preoperatively, in the operating theater intraoperatively, and at the clinic postoperatively in both Smart Health Tower and Soma Surgical Hospitals in Sulaimani City. They are the leading private surgical hospitals in the area. Smart Health Tower, located at Madame Mitterrand Street in Sulaymaniyah, Iraq, is one of the public and private hospitals that do breast surgery there. Every week, 3-6 SLNB surgeries were performed. Also, Soma Surgical Hospital is one of the essential private hospitals in Sulaimani for breast surgery and other surgical procedures, located in the centre of Sulaimani city.

3.5. Population and Sample

A purposive group of patients was sampled as a method for selecting samples in this study. A total of 140 cases (that were done with SLNB alone or with SLNB plus LAS) were included in the study. A researcher interviewed 140 patients who met the inclusion criteria. The following figure shows the steps that were taken to get a final group of samples. Excluded from the study were 30 cases out of 140. This is due to several reasons: the surgeon decided to change decision-making from doing SLNB to sampling alone; other reasons were that it was difficult to contact the patient after surgery or after discharge from the hospital. Furthermore, coronaviruses caused 2 patients deaths during the adjuvant therapy treatment phase.

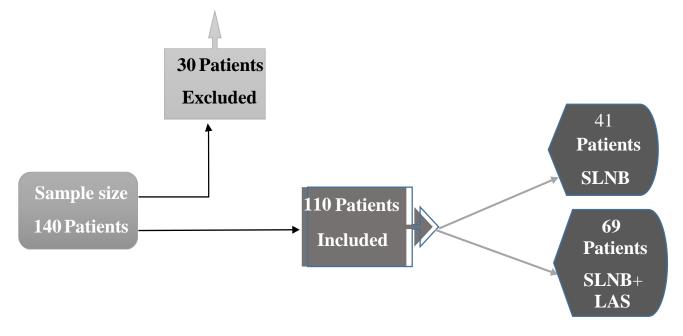


Figure 3.2: Sketching for steps for the participants refined and reached the final number of 110 in the study

3.6. Sample Size:

The sample size was detected based on the census report of the surgical hospitals in Sulaimani city (Smart Health Tower and Soma General Surgical Hospital). In the final year (2020-2021), the total number of early breast cancer surgeries that used SLNB was around 100 cases in Smart Health Tower, and 40-50

cases in Soma Hospital. The sample size was calculated and the sample size was taken based on the formula in Raosoft (Appendix 5).

3.7. Inclusion criteria:

- 1- Patients with early breast cancer (stage1, stage2)
- 2- Clinical negative axilla

3.8. Exclusion criteria:

The study excluded:

- 1- Patients with locally advanced (stage3) and Metastatic (stage4) of breast cancer
- 2- Recurrence of breast cancer
- 3- Male patient with breast cancer

3.7. Data Collection/ Duration of the study:

The researcher compiled the data over a period of 13 months, from March 1, 2021, to April 1, 2022. The present study was carried out through the following (3) phases:

Preoperative Phase:

The patients were selected in their waiting rooms for surgery according to eligibility criteria. The researchers explained the aim and approach of the study to every patient, and then informed oral and written consents were obtained from all the eligible ones to participate in the study. The data was gathered through direct interviews and recorded in the prepared questionnaire form (Appendix 6). Each form was coded, and each woman was questioned individually and assured of confidentiality by the researchers. Regarding patient investigations, the researcher collects them from the patient's file. A questionnaire took an average of 30 minutes to complete for each woman.

Intraoperative Phase:

A total of 140 women who met the inclusion criteria underwent surgical treatment for breast cancer. Axillary surgery removes sentinel nodes for biopsy and staging of the axilla and resection of breast tumors through BCS or mastectomy (simple and modified radical mastectomy). Arm circumferences were measured with a manual tape measure, 10 cm above and below the elbow on the operated arm. Local breast examination (quadrant of the breast where the mass was located, nodal status of the axilla). The procedure of SLNB, the site and route of blue dye injection, the number of sentinel lymph nodes visualized and removed, the number of lymph nodes not visualized but removed, and the type of breast surgery were all recorded by the researcher. The average time required for each surgery was 45 minutes to complete a questionnaire.

Postoperative Phase:

The early post-operative complications (wound infection, hematoma, and seroma) were recorded in the observational check list 10–12 days after surgery. Later, after 1 to 3 months of surgery, the researcher recorded in the observational check list the late post-operative complications (paresthesias/numbness, reduced range of motion in the upper extremities, and lymphedema).

3.8. The study instrument

A questionnaire was constructed by the researcher of this study to measure the variables underlying the present study mainly to evaluate the effects of sentinel lymph node biopsy in the management of early breast cancer with negative axillary lymph node, and to assess complications and arm morbidity post-axillary and breast surgery when treating early breast cancer.

3.9. The questionnaire includes the seven following parts

Part One: Socio- demographic features

This part includes age, marital status, and ethnic group, level of education, occupation, address, and living status.

Part Two: History of patient

This part includes the present complaint, history of the present illness, general health, menstrual history, obstetric history, psychiatric, endocrine system, past medical history, health maintenance, previous breast disease, drug history, and family history of breast cancer, socioeconomic status, and dietary habits. Also, includes general appearance, nutritional status, upper limb (arm circumference)

Part Three: Examination/ Local examination of the breast

This part includes breast size, breast shape, visible swelling of breast, breast consistency, temperature warmth of breast, mass site, mass size, and local examination of the axilla.

Part four: Investigations

This part contains information about imaging modalities used for detecting tumors or abnormalities, finding and pinpointing cancers in the breast, evaluating axillary nodal status in newly diagnosed breast cancer, identifying metastatic disease in axillary LNs, and comparing normal and suspicious nodes, including ultrasonography (BIRAD), mammography (BIRAD), and MRI (BIRAD). This section also includes needle core biopsy, fine needle aspiration, and excisional biopsy for definitive cancer diagnosis. Also, this part contains the histological type and grade of breast cancer tumors. Chest, abdomen, and bone scan are also included.

Part five: Surgical and non-surgical treatments

This part includes types of breast surgery, axillary surgery, and systemic therapy

Part six: Surgical technique for sentinel lymph node biopsy

This section contains information on the type of anesthesia used for the SLNB procedure, as well as the location and route of the blue dye injections. The type of incision and number of visualized and non-visualized lymph nodes were recorded. The results of SLNB pathology and SLNB metastasis classification are also included. This section goes over complete axillary dissection after the results of a sentinel LN biopsy and pathology with the count of LN removed.

Under general anesthesia, sentinel lymph node biopsy procedures were carried out on all 140 patients. It used methylene blue (MB), as a tracer dye. When in solution, the dark green crystalline component MB becomes dark blue. Methylene blue 5 ml (0.3mg), was injected into the breast functional tissues around the breast tumor (peritumeral) and subareolar region (Teal et al., 2005). Breast massage is performed for 5 minutes. SLNB is done through a small 1.5-2 cm transverse skin line incision in the lower axilla. Dissection started and SLN was identified either by finding blue lymph nodes, blue lymphatics or by careful palpation of the area for palpable lymph nodes not visualized by the dye. The wound is completely closed, and no drain has been inserted.

A single oblique incision is used for the majority of the mastectomy, and SLNB can be completed quickly through the axillary end of the incision before starting the mastectomy.

<u>Part seven:</u> Structured Observation record of postoperative complications It includes wound infection, hematoma, seroma, numbness, arm swelling

3.10. Validity and Reliability

3.10.1. Validity

The term "validity" refers to the ability to "measure what is intended to be measured." (Solans-Domènech, 2019). The face validity of the current study questionnaire was determined with the help of a panel of 11 different specialists in the field of the current study (Appendix 7). The experts were asked to review the questionnaire and observational data list for content clarity, relevance, and adequacy to achieve the study objectives. The outcome indicated that the experts agreed on the tool items. Except for a few changes, the investigator took into consideration their responses and suggestions, and some changes have been made to the tools.

3.10.2. Pilot Study

The pilot study was conducted in the Smart Health Tower for a period of 1 month, from 1.03.2021 to 1.04.2021. The investigator gave a self-introduction. Women who met the inclusion criteria were selected, and sociodemographic variables were assessed by the structured interview method. After the interview, written consent was obtained from the patient. Samples were selected by purposive sampling technique. Group ten women together for routine care. The researcher includes the pilot study:

- 1. To help the researcher develop auditing, observation, and interviewing skills, ensure that the tools used are clear, easy, and simple to use.
- 2. It also provided an opportunity to identify barriers that may be encountered during the study process.
- 3. To estimate the amount of time required for each patient Through the pilot study, the instrument was reliable for proceeding with the main study.

3.10.3. Reliability

The reliability of an instrument is the degree of consistency with which it measures the attribute, and it is supposed to measure over a given period. The reliability value was (r 0.820) Cronbach's alpha (statistically adequate) Appendix (4). Hence, the tool was reliable and used in this study.

3.11. Statistical analysis

Data analysis involves the translation of information collected during a research project into an interpretable and managerial form. It involves using statistical procedures to give the organization and meaning to the data. The data obtained were analyzed using descriptive and inferential statistics. After collecting the data and prior to data entry and analysis, the study questions were coded. Data entry was performed via an excel spreadsheet, and then the statistical analysis was performed by the SPSS program, version 21 (IBM SPSS Statistical Package for the Social Sciences). The statistical procedure that was applied was as follows:

3.11.1- Descriptive statistics

- **A.** Frequencies (f) and Percentage (%) of the socio demographic variables.
- **B.** Mean (\bar{x}) and Standard Deviation (SD) of the age group with early breast cancer

3.11.2- Inferential statistics:

- **A. Chi-square test:** To determine the frequency distinction between the two groups of SLNB and ALND, the Chi-square test (correlation test) was used to determine the hypothesis and compare the tumor size and the number of axillary lymph node involvement.
- **B. Fisher's exact test:** Fisher's exact test is used to compare the categorical data between different groups of patients (i.e., based on operation type) with concerning to complications.

C. **P value:** The level of statistical significance was considered $p \le 0.05$ and any significant value of three decimal digits was considered as < 0.001. While the p > 0.05 was considered not significant and highly significant at p value ≤ 0.000 .

3.12. Limitations of the study

As a result, the study's topic was not a common topic that had not been done before in our region, was novel for advancing current knowledge in this field, and challenging for the researcher, who encountered the following barriers and difficulties:

- 1. Transportation was a problem for the researcher, especially at night and early morning.
- 2. Lack of facilities for meeting the patient after discharge from the hospital and recording later complications, especially for those who lived outside Sulaimani Governorate. Because of the limited time of the researcher and the difficulty of the researcher's travel outside of the city.
- 3. This study had a small sample size because many major surgical hospitals at the time refused to conduct research on their patients and record information about breast and axillary surgery at their hospitals, preventing the research from drawing generalizations from its findings.

<u>Chapter four</u> Results

4. Results

 $\begin{tabular}{ll} \textbf{Table 4.1. Distribution of the study samples according to socio-demographic characteristics} \\ \end{tabular}$

Sociodemographic		Frequency	0/0
Age	Mean ± SD	46.9±9.7	
	25 - 45 Years	51	46.4%
	46 - 65 Years	54	49.1%
	66 - 77 Years	5	4.5%
Blood group	A	42	38.18%
	AB	6	5.46%
	В	26	23.64%
	0	36	32.72%
Marital status	Married	95	86.37%
	Unmarried	7	6.36%
	Widow or divorce	8	7.27%
Parity	Multiparous	93	84.55%
	Nulliparous	17	15.46%
Occupation	Unemployed	4	3.64%
-	Housewife	78	70.91%
	Teacher	15	13.64%
	Worker	2	1.82%
	Employee	7	6.36%
	Retired	2	1.82%
	Others	2	1.82%
Education	Illiterate	39	35.45%
	Able to read	36	32.73%
	and write		
	Intermediate	9	8.18%
	Secondary	8	7.27%
	Institute	10	9.09%
	College graduate	8	7.27%
Living status	Moderate	81	73.6%
	Low	29	26.4%
Address	Governorate	63	57.3%
	Qadha	34	30.9%
	Nahya	11	10.0%
	Village	2	1.8%
Total		110	100.0%

The 110 patients were all women. Their age ranged from 25 to 77 years (mean 46.9 ± 9.7). They were married 95 patients (86.37%), multiparous 93 patients (84.55%), housewives 78 patients (70.91%), illiterate 39 patients (35.45%), able to read and write 36 patients (32.73%), of moderate socioeconomic status 81 patients (73.6%), and living in Sulaimaniyah governorate: 63 patients (57.3%) (Table 4.1).

Table 4.2. Distribution of the study samples according to social and personal history

Social and personal		Frequency	0/0
history			
Smoking	Yes	7	6.4%
	No	103	93.6%
Alcohol	Yes	1	0.9%
	No	109	99.1%
Exercise	Yes	3	2.7%
	No	107	97.3%
Dietary habit	Non- vegetarian	32	29.091%
	Semi- vegetarian	76	69.091%
	Vegetarian	2	1.818%
Body Mass Index	Mean ± SD 30	0.12 ± 5.12	
	Normal (< 25)	13	11.818%
	Overweight (25 - 29.99)	43	39.091%
	Obese (≥30)	54	49.091%
Total		110	100.0%

Table 4.2 Showed that most patients were nonsmokers: 103 patients (93.6%), nonalcoholic: 109 patients (99.1%), practicing regular exercise: 3 patients (2.7%). Dietary habits: vegetarian in 2 patients (1.81%). Their BMI (mean 30.12 ± 5.12) was as follows: 13 patients (11.818%) had normal weight, 43 patients (39.09%) were overweight, and 54 patients (49.09%) were obese.

Table 4.3. Distribution of the study samples according to patients' complaints and present illness histories

Patient complaint of presen	nt illness	Frequency	0/0
Mass	Yes	100	90.9%
	No	10	9.1%
Pain and mass	Yes	44	40.0%
	No	66	60.0%
Pain without mass	yes	4	3.6%
Nipple blood discharge	Yes	15	13.6%
	No	95	86.4%
Nipple retraction	Yes	15	13.6%
	No	95	86.4%
Nipple ulceration	Yes	9	8.2%
	No	101	91.8%
Breast enlargement	Yes	18	16.4%
	No	92	83.6%
Breast asymmetry	Yes	29	26.4%
	No	81	73.6%
Skin changes	Yes	4	3.6%
	No	106	96.4%
Duration of patient complaint	< 1 month	21	19.1%
	1 - 3 months	59	53.63%
	4 - 6 months	17	15.5%
	> 6 months	13	11.8%
Total		110	100.0%

Table 4.3 showed that most patients (100 patients, 90.9%) presented with a chief complaint of breast mass; 44 patients (40.0%) presented mass with breast pain, only 4 patients (3.6%) had pain alone; 15 patients had nipple discharge (13.6%); 15 patients had nipple retraction (13.6%); and 9 patients had nipple ulceration (8.2%). 18 patients had breast enlargement (16.4%), 29 patients had breast asymmetry (26.4%), and skin changes occurred in 4 patients (3.6%). The duration of the chief complaint ranged from less than 1 month to more than 6 months.

Table 4.4 Distribution of the study samples according to patients' past medical histories

Past history		Frequency	%
Weight loss	Yes	33	30.0%
	No	77	70.0%
Diabetes Mellitus (DM)	Yes	10	9.1%
	No	100	90.9%
Self -breast examination	Yes	23	20.9%
	No	87	79.1%
Mammography	Yes	13	11.8%
	No	97	88.2%
Previous breast disease	None	76	69.091%
	Mastalgia	17	15.45%
	Breast mass	6	5.455%
	Breast abscess	2	1.818%
	Nipple discharge	5	4.545%
	Nipple retraction	1	0.909%
	Nipple ulcer	1	0.909%
	mastectomy	1	0.909%
	Breast mass, adenoma	1	0.909%
Contraceptive (CP) pills	Yes	39	35.5%
	No	71	64.5%
CP duration	None	71	64.546%
	< 1 year	13	11.818%
	1 - 3 Years	14	12.727%
	4 - 5 Years	4	3.636%
	> 5 years	8	7.273%
Family history of breast	Yes	35	31.8%
cancer	No	75	68.2%
Family history of ovarian	Yes	11	10.0%
cancer	No	99	90.0%
Total		110	100.0%

Table 4.4 showed that 33 patients (30.0%) lost weight, 10 patients (9.1%) had diabetes mellitus, 23 patients (20.9%) practiced self-breast examination, and 13 patients (11.8%) had mammography screening irregularly every 1-2 years. Past history of breast diseases: 17 patients (15.45%) had history of mastalgia, 6 patients (5.5%) had history of breast mass, 2 patients (1.8%) had history of breast abscess, 5

patients (4.5%) had nipple discharge, 1 patient had nipple ulcers, and the other had nipple retraction. Past history of breast operations included: 1 patient (0.9%) had an operation for removal of a painful adenoma, 1 patient (0.9%) underwent a left mastectomy, and 39 patients (35.5%) were taking oral contraceptive pills for durations ranging from less than 1 month to more than 5 years. 35 patients (31.8%) have a history of breast cancer in their family; 11 patients (10.0%) have a history of ovarian cancer in their family.

Table 4.5. Distribution of the study samples according to patients' breast cancer characteristics

Breast Characteristics		Frequency	0/0
Breast size	Normal	94	85.5%
	Small	3	2.7%
	Large	13	11.8%
Affected breast size	Normal	59	53.636%
	Small	9	8.182%
	Large	42	38.182%
Tethering- dimpling	Yes	3	2.7%
	No	107	97.3%
Warmth	Yes	20	18.2%
	No	90	81.8%
Mass site	Upper outer	59	53.636%
	Upper inner	30	27.273%
	Lower outer	10	9.091%
	Lower inner	11	10.0%
Total		110	100.0%

Table 4.5 showed that the majority of patients (85.5%) had normal breast size. In 42 patients (38.18%), the affected breast with cancer was larger than the other breasts. 20 patients (18.2%) felt warmth in their affected breast. In terms of mass location, 53.63% of the patients had mass in the upper outer site of the breast, 30 patients (27.27%) had mass in the upper inner site, 10 patients (9.091%) had mass in the lower outer site, and 11 patients (10.0%) had mass in the lower inner site.

Table 4.6. Distribution of the study samples according to patients' ultrasound, mammography, and MRI findings of the breast and axilla

Imaging		Frequency	0/0
Ultrasoundfindings	Normal	2	1.818%
	Fibrocystic changes	4	3.636%
	Ductectasia	5	4.546%
	Solid mass	79	71.818%
	Fibrocystic changes, Abscess	1	0.909%
	Fibrocystic changes, Ductectasia	3	2.727%
	Fibrocystic changes, Solid mass	9	8.182%
	Ductectasia, Breast cyst	2	1.818%
	Ductectasia, Solid mass	5	4.546%
Suspicious axillary			
LN	Yes	41	37.3%
	No	69	62.7%
N0. of S. axillary LN			60 7 0/
	None	69	62.7%
	One Node	21	19.1%
DIDADGD IIG	2 - 4 Nodes	20	18.2%
BIRADS By US	1	1	0.909%
	2	6	5.455%
	3	3 32	2.727%
	4 5	29	29.091% 26.363%
	6	39	20.303% 35.455%
	•	39	33.433%
	Multicentric	15	13.636%
Tumor by US	Unifocal	68	61.818%
	Multifocal	23	20.909%
	Unifocal, Bilateral	4	3.636%
BIRADSByMammog	1	2	1.8%
·	2	2	1.8%
	3	4	3.6%
	4	15	13.6%
	5	30	27.3%
	6	18	16.4%
	Not performed	39	35.5%
BIRADS By MRI	2	1	0.9%
	3	2	1.8%
	4	5	4.5%
	5	20	18.2%
	6	28	25.5%
	Not performed	54	49.1%
Total		110	100.0%

Table 4.6 showed that the majority of patients (71.81%) had solid mass on ultrasound imaging; also, 9 patients (8.18%) had solid mass with fibrocystic change, and 5 patients (4.54%) had solid mass with ductectasia on ultrasound imaging. 4 patients (3.63%) had fibrocystic change, 3 patients (2.72%) had fibrocystic change with ductectasia, and 1 patient had it with an abscess. 5 patients (4.54%) had ductectasia, and 2 patients (1.81%) had it with a breast abscess. An ultrasound imaging study also found that 2 patients (1.81%) had normal breasts.

Ultrasound imaging found that 41 patients (37.3%) had suspiciously enlarged axillary lymph nodes ranging from 1 to 4 nodes.

Regarding tumor focality, 68 patients (61.81%) had unifocal tumors, 23 patients (20.90%) were multifocal, 15 patients (13.63%) were multicentric, and 4 patients (3.63%) had unifocal, bilateral tumors.

Breast imaging reporting BIRAD on US patients reveals that 39 (35.45%) had BIRAD 6, 26.36% had BIRAD 5, 29.09% had BIRAD 4, 2.72% had BIRAD 3, 5.45% had BIRAD 2, and 1 patient had BIRAD 1.

Table 4.7. Distribution of the study samples according to patients' histological results of a breast core biopsy

Breast core biopsy		Frequency	0/0
In situ carcinoma	Ductal	40	36.4%
	Lobular	4	3.6%
	Ductal &lobular	1	0.9%
	None	65	59.1%
Invasive carcinoma	Ductal	86	78.2%
	Lobular	2	1.8%
	Ductal &lobular	4	3.6%
	None	18	16.4%
Tumor grade	G1	9	8.2%
	G2	49	44.5%
	G3	40	36.4%
	None	12	10.9%
L. vascular invasion	Yes	23	20.9%
	No	87	79.1%
Hormone receptor	None	13	11.81%
	ER	23	20.90%
	PR	4	3.636%
	HER2	12	10.90%
	ER, PR	49	44.54%
	ER, PR, HER2	6	5.455%
	ER, HER2	3	2.727%
Total		110	100.0%

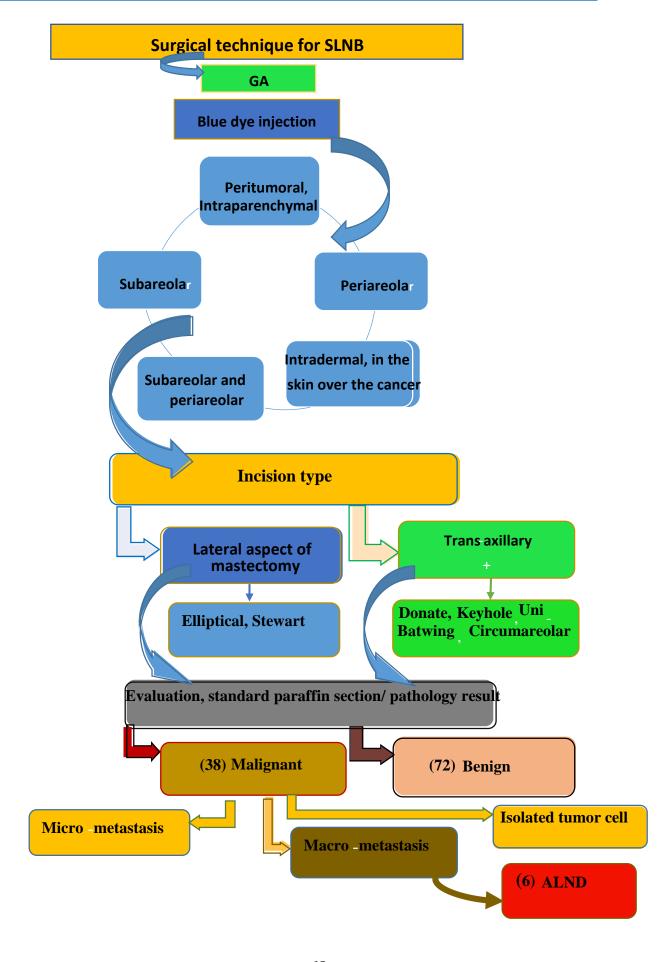
Table 4.7 showed that 40 patients (36.4%) had ductal carcinoma in situ, another 4 patients (3.6%) had lobular carcinoma in situ, and 1 patient had both ductal and lobular carcinoma in situ. Also, the showed that the majority of patients (78.2%) had invasive ductal carcinoma, another 2 patients (1.8%) had invasive lobular carcinoma, and 4 patients (3.6%) had invasive ductal and lobular carcinoma. Regarding tumor grade, 49 patients (44.5%) were grade 2, 40 patients (36.4%) were grade 3, and 9 patients (8.2%) were grade 1. Most patients did not have lymphatic vascular invasion, but 23 patients (20.9%) did. 49 (44.54%) of the patients had

positive ER and PR receptors, 6 patients (5.45%) had ER, PR, and HER2 positive hormone receptors, and 3 patients (2.72%) had both ER and HER2 receptors. While 23 patients (20.90%) have ER, 12 patients (10.90%) have HER2, and 4 patients (3.63%) have PR positive hormone receptors.

Table 4.8. The identification rates of sentinel nodes using blue dye for SLNB and SLNB+ Lower axillary sampling (LAS)

Procedure (SLNB&LAS)	Frequency	Identification rate %
SLNB n=41	40	97.56%
SLNB+ LAS n=110	101	91.8%

This table showed that the identification rate of the SLNB procedure was 97.56%, while, the identification rate of the SLNB plus LAS procedure was 91.8%.



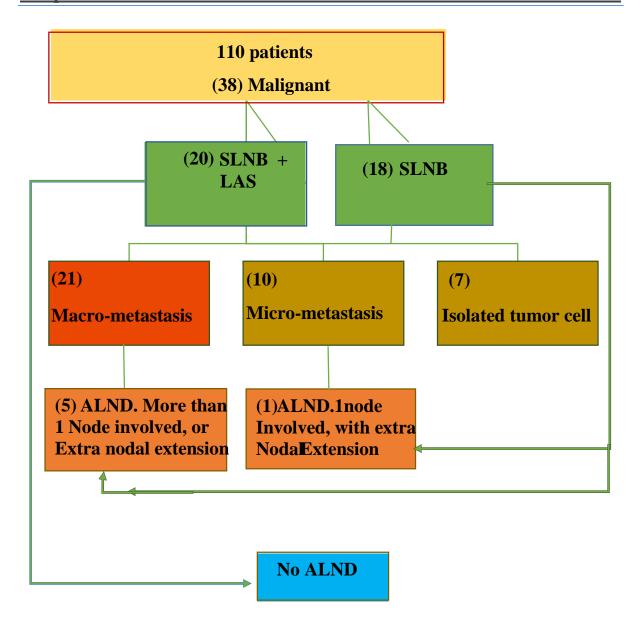


Figure 4.1: Sketching diagram on surgical technique and pathological results of the SLNB

Table 4.9. Types of breast surgery and their relationships to postoperative complications

Complications / T	ype	Breast conservative surgery	Simple mastectomy	Modified radical mastecto my(MRM	Total	P value
Wound infection	Yes No	14 (19.2%) 59 (80.8%)	5 (29.4%) 12	1 (5.3%) 18 (94.7%)	20 (18.3%) 89 (81.7%)	0.17
Seroma	Yes No	19 (26.0%) 54 (74.0%)	3 (17.6%) 14 (82.4%)	7 (36.8%) 12 (63.2%)	29 (26.6%) 80 (73.4%)	0.42
Hematoma	Yes No	6 (8.2%) 67 (91.8%)	2 (11.8%) 15 (88.2%)	2 (10.5%) 17 (89.5%)	10 (9.2%) 99 (90.8%)	0.88
Paresthesia's	Yes No	11 (15.1%) 62 (84.9%)	1 (5.9%) 16 (94.1%)	5 (26.3%) 14 (73.7%)	17 (15.6%) 92 (84.4%)	0.24
Decrease ROM	Yes No	16 (21.9%) 57 (71.8%)	5 (29.4%) 12	5 (26.3%) 14 (73.7%)	26 (23.9%) 83 (76.1%)	0.78
Lymphedema	Yes No	3 (4.1%) 71 (95.9%)	0 (0%) 17 (100%)	1 (5.3%) 18 (94.7%)	4 (3.7%) 105 (96.4%)	0.66
Total		73 (100%)	17 (100%)	19 (100%)	110 (100%)	

^{*}By Fisher's exact test.

Table 4.9 shows that 73 patients who underwent BCS had 14 (19.2%) post-operative wound infections, 19 (26.0%) seromas, 6 (8.2%) hematomas, 11 (15.1%) paresthesias, 16 (21.9%) decreasing ROMs, and 3 (4.1%) cases of lymphedema.

The table also reveals that out of 17 patients who underwent simple mastectomy surgery, 5 patients (29.4%) developed post-operative wound infections; 3 patients (17.6%) developed seroma; 2 patients (11.8%) developed hematomas; 1 patient (5.9%) experienced paresthesia; and 5 patients (29.4%) had decreased range of motion (ROM).

The data also reveals that of the 19 patients who underwent modified radical mastectomy (MRM), 5.3% had post-operative wound infections, 36.8% had

seromas, and 10.5% had hematomas. Five patients (26.3%) reported paresthesia, five (26.3%) had decreased range of motion, and one (5.3%) had lymphedema.

Table 4.10. Distribution of the study samples according to the patients' histopathology results for the tumor size and axillary involvement of the disease and it is association

		Results/ patholo		
	Benign	Malignant	Total	P value
Tumor size				
T1 (< 2 cm)	22	11	33	0.52
T2 (2 - 5 cm)	46	24	70	
T3 (> 5 cm)	4	3	7	
Total	72 (65.45%)	38 (34.54%)	110 (100%)	

^{*}By Fisher's exact test

The majority of patients' tumor sizes ranged from 2 to 5 cm, according to Table 4.10, with 33 patients having tumor sizes less than 2 cm and 7 patients having tumor sizes greater than 5 cm. Also, the table showed that the majority of patients had benign axillary lymph nodes, while in 38 patients, their axillary lymph nodes were involved with the disease

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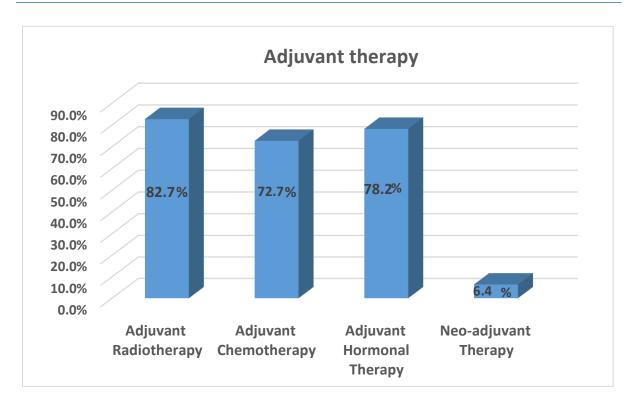


Figure 4.2.: The value of the study samples' adjuvant therapy and its comparison with the value of neoadjuvant therapy

Figure 4.2 shows the distribution of the study samples according to patients' non-surgical treatments (systemic therapy), adjuvant therapy, and neo-adjuvant therapy. It showed that of the majority of patients taking adjuvant systemic therapy, 82.7 percent had taken adjuvant radiotherapy, 72.7 percent had taken adjuvant chemotherapy, 78.2% had taken adjuvant endocrine (hormonal) therapy, and 6.4% had taken neo-adjuvant chemotherapy.

Table 4.11. Distribution of the study samples according to patients' post-operative complications

Complications	·	Frequency	<u>%</u>
Post-operative pain	Yes	3	2.7%
	No	107	97.3%
Wound infection	Yes	21	19.1%
	No	89	80.9%
Seroma	Yes	30	27.3%
	No	80	72.7%
Hematoma	Yes	11	10.0%
	No	99	90.0%
Paresthesia's	Yes	17	15.5%
	No	93	84.5%
Decrease ROM	Yes	27	24.5%
	No	83	75.5%
Lymphedema	Yes	4	3.6%
	No	106	96.4%
Total		110	100.0%

Table 4.11 showed that 3 patients (2.7%) had post-operative pain, 21 patients (19.1%) had wound infection, 30 patients (27.3%) had seroma, 11 patients (10.0%) had hematoma, 17 patients (15.5%) had paresthesia, 27 patients (24.5%) had decreased range of motion, and 4 patients (3.6%) had lymphedema.

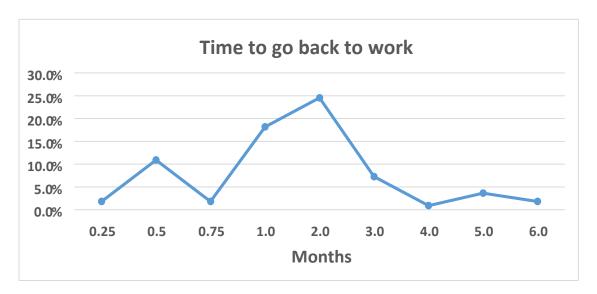


Figure 4.3.: Distribution of the study samples' time to go back to their daily normal activities or work

Figure 4.3 line graphs show that after breast and axillary surgery, 2% of patients return to work after one week, 10% do so after two weeks, 2% do so after three weeks, nearly 20% do so after one month, and 25% do so after two months. At three months, five months, and six months, 7%, 4%, and 2%, respectively, return to their regular daily activities or jobs.

Table 4.12. Distribution of the study samples according to patients' post-operative Complications associated with the SLNB alone, SLNB plus LAS, and ALND groups

Complications			SLNB	&		
/ Type of LN		SLNB	LAS	ALND	Total	P value
Wound	Yes	5 (13.9%)	14 (20.6%)	2 (33.3%)	21 (19.1%)	0.47
infection						
	No	31 (86.1%)	54 (79.4%)	4 (66.7%)	89 (80.9%)	
Seroma	Yes	8 (22.2%)	18 (26.5%)	4 (66.7%)	30 (27.3%)	0.08
	No	28 (78.8%)	50 (73.5%)	2 (33.3%)	80 (72.7%)	
Hematoma	Yes	3 (8.3%)	6 (8.8%)	2 (33.3%)	11 (10.0%)	0.15
	No	33 (91.7%)	62 (91.2%)	4 (66.7%)	99 (90.0%)	
Paresthesia's	Yes	4 (11.1%)	12 (17.6%)	1 (16.7%)	17 (15.5%)	0.68
	No	32 (88.9%)	6(82.4%)	5 (83.3%)	93 (84.5%)	
Decrease ROM	Yes	10 (27.8%)	13 (19.1%)	4 (66.7%)	27 (24.5%)	0.03
	No	26 (72.2%)	55 (80.9%)	2 (33.3%)	83 (75.5%)	
Lymphedema	Yes	1 (2.8%)	1 (1.5%)	2 (33.3%)	4 (3.6%)	< 0.001
	No	35 (97.2%)	67 (98.5%)	4 (66.7%)	106 (96.4%)	
Total		36 (100%)	68 (100%)	6 (100%)	110 (100%)	

^{*}By Fisher's exact test.

Table 4.12 showed that 36 patients who underwent SLNB and breast surgery. 5 patients (13.9%) had post-operative wound infections, 8 (22.2%) seromas, 3 (8.3%) hematomas, 4 (11.1%) paresthesia, 10 (27.8%) decreasing ROMs, and 1 (2.8%) cases of lymphedema. 14 patients (20.6%) developed post-operative wound infections after SLNB with LAS and breast surgery; 18 patients (26.5%) developed seroma; 6 patients (8.8%) developed hematomas; 12 patients (17.6%) experienced paresthesia; and 13 patients (19.1%) had decreased range of motion (ROM); there was 1 (1.5%) case of lymphedema. The data also reveals that of the 6 patients who underwent ALND, 2 (33.3%) had post-operative wound infections, 4 (66.7%) had seromas, and 2 (33.3%) had hematomas. 1 patient (16.7%) reported paresthesia; 4 (66.7%) had decreased range of motion; and 2 (33.3%) had lymphedema.

5- Discussion

A developed questionnaire and an observational check list were utilized in this study to discuss the effects of sentinel lymph node biopsy in the treatment of early breast cancer with negative axillary nodes and to assess indicators of post-surgical problems. Finding significant answers to the research questions is the main goal of this chapter; to do this, the data must be processed and examined in a systematic and consistent way. The researcher may discuss this pattern and interpret the findings of this study.

It is crucial to stage and manage the axilla in breast cancer patients, especially in the early stages of the disease, using a less intrusive treatment that causes less anatomical damage. Treatment for breast cancer needs a methodical timetable for the addition of treatments over an extended period of time. The medical team, including the surgeon, should be aware of each step of this process as it is carried out in accordance with national guidelines for treating breast cancer patients.

Women with breast cancer require more physical and psychological support during therapy than other patients because they fear the disease may return, most of them have a weakened immune system, and the therapy itself affects body organs, making the patient more susceptible to illnesses. Hence, it is crucial to assess the surgical approach and techniques employed to remove the tumor and any involved nodes with the least amount of invasion. The patient will benefit more by commencing adjuvant therapy on schedule, finishing it as directed, and recovering from surgery with fewer or no difficulties.

5.1 Patients socio-demographic features:

One hundred and ten women were participating in this research. All women who were preparing for surgery as part of first-line treatment for breast cancer and had early breast cancer with clinically negative axillary lymph nodes were included in this study. Of them, 41 patients underwent breast surgery using only SLNB. Others had breast surgeries that included SLNB plus axillary sampling. Blue dye was used for the visualization of axillary lymph nodes for all 110 participants.

The analysis of the results identified that the participant's age ranged from 25 to 77 years (mean 46.9 ± 9.7). Moreover, most of them were married and housewives. The baseline characteristics of the women in this study were consistent with the retrospective study findings by Huang (2021). They discovered that 5788 of the 6,304 additional breast cancer instances were in people aged 45 and older. Furthermore, Baset et al.'s (2021) presented data indicating that the average age of Afghan women with breast cancer was 45.8, and the mean age was 45 in India "between" 2015 and 2017.

Regarding blood types, 38.18% of women have group A, 32.72% have group O, and the remaining women have group B or AB types. Similarly a retrospective study, revealed that from a total of 6304 new cases of breast cancer , 5788 were at age 45 and above, were in group A, and 516 were above age 70 were in group B. (Huang et al.,2021).

Regarding illiteracy among breast cancer women in the present study, illiteracy was 35.45%, but a study done by Balekouzou et al. (2017) revealed that breast cancer and illiteracy were found to be significantly related in Bangui, Central Africa (p 0.001).

Additionally, there was a statistically significant link between education level and breast cancer (P 0.001). Breast cancer risk was discovered to be 1.9 times higher among the illiterate population (OR = 1.9, 95%CI: 1.28–2.83). (Baset et al., 2021). According to Bellanger (2018), the mortality rate from breast cancer is disproportionately greater for women in developing nations, and breast cancer cases rise with income at any age.

The researcher thinks that since breast cancer is more prevalent among western-educated women than in undeveloped countries, there is no direct correlation between illiteracy and the occurrence of breast cancer in women.

The majority of participants had moderate or low socioeconomic status. The researcher thinks that this is because, compared to other hospitals, the two facilities we chose for our research sampling were better suited to serving middle-class and low-income patients who needed breast surgery.

5.2 Social and personal history of the study participants

In terms of lifestyle, regular exercise, and a healthy diet, the current study found that the majority of participants did not exercise regularly and only two were vegetarians, which concurs with the results of studies done by Aunes et al., (2012) Wu et al., (2013) Arthur et al., (2020) and bolsters the idea that leading a generally healthy lifestyle may lessen the effect of genetic variables on the chance of developing invasive breast cancer.

By lowering the reabsorption of estrogen and androgens in the colon, the ideal amount of physical activity is expected to reduce risk by 3% for every additional 180 minutes of moderate-intensity exercise per week, with a 5% risk reduction for every additional 10 g of fiber per day. Moreover an Indian case—control study found that diet is one of the major risk factors for breast cancer, and

concluded that adequate exercise and weight control are the most effective lifestyle changes that can reduce the risk of developing breast cancer. (Antony et al., 2018)

Additionally, the researcher supports the findings on the links between increased physical activity, a vegetarian or fiber-rich diet, and a reduction in breast cancer incidence in this area. Given the results of the current study, it is evident that the culture in our community is almost nonexistent when it comes to engaging in daily or weekly regular exercise and adhering to a healthy diet.

The current investigation discovered that the majority of patients weren't smokers, and almost all of them weren't alcoholics. Breast cancer risk is predicted to rise by 2% to 12% with every additional 10 g of alcohol used each day (one unit, such as 284 mL of 4% strength beer or cider, 25 mL of 40% strength spirits, or 80 mL of 12% strength wine) (Scoccianti et al., 2014).

Investigations into epidemiological studies have revealed inconsistent findings in relation to the association between smoking and breast cancer. In fact, some findings even imply that smoking may offer protection against the development of breast cancer (Chaturvedi, 2003). According to Jones et al., 2017 study, smoking was found to be connected with a slight but statistically significant greater likelihood of developing breast cancer, especially in female smokers who started when they were young or in their premenopausal years. Smoking increases the risk of breast cancer in women who have a family history of the condition.

5.3 Complaints and present illness histories of the study participants

According to this study (Table 4), the majority of women who were recommended for breast cancer surgery had a mass (90.9%), while 40.0% reported experiencing breast pain along with a lump, and only 3.6% expressed

breast pain. The most frequent symptoms that women with breast cancer present with are breast lumps (Koo, 2017). According to a study done in Mexico, lumps (71.7% of cases) were the most prevalent symptom among women who came with breast complaints to PHC clinics (González-Pérez, 2013).

Also, a prospective study in the UK presented that among women who were visiting a breast cancer diagnostic clinic, 5% of women had breast cancer, as indicated by lumps, nipple discomfort, and other symptoms, while 0.4% had breast pain (Dave et al., 2022).

Regarding nipple discharge, 13.6 percent of the participants in the current study reported bloody nipple discharge. Similar findings were found in a study conducted by Al Nemer and Kussaibi (2020). It was further noted that bloody nipple discharge revealed a strong correlation with malignancy (p 0.001), although the association was statistically insignificant for elderly age (p = 0.062), indicating that there is a low likelihood of breast cancer in those who come with nipple discharge.

5.4 Past medical histories of the study participants

The majority of patients were overweight or obese, according to the current study. This is in line with other research that found a connection between obesity and the occurrence of estrogen receptor-positive breast cancer in postmenopausal women. The local synthesis of estrogens in the breast adipose tissue is thought to play a significant role in the initiation and progression of breast cancer, as well as in mediating resistance to endocrine therapy (Bhardwaj et al., 2019; Brown, 2021).

Moreover the American Association for Cancer Research reports that individuals with high body fat and low exercise levels have breast inflammation, higher breast aromatase expression, and levels of circulating metabo-

inflammatory factors that have been associated with increased breast cancer risk (Iyengar et al., 2021).

In the assessment of risk factors for breast cancer among patients, the presented study found an association between using oral contraceptives (OC), being obese, and having a family history of breast cancer and the risk of breast cancer. This is in line with a meta-analysis of 42 case-control studies conducted between 2009 and 2020 that found a statistically significant link between OC and an elevated risk of breast cancer (OR = 1.15, 95% CI: 1.01 to 1.31, p = 0.0358). It was also found that the risk was significantly higher in individuals who had a family history of breast cancer (Barańska, 2021).

Moreover the German guideline "Peri- and Postmenopause-Diagnostics and Therapy" (2020) provides recommendations that include the most recent evidence as well as the Women's Health Initiative (WHI) study results from 2002 and 2004. These results led to reduced prescription patterns due to a high risk of cardiovascular diseases as well as an increased risk for breast cancer if hormonal replacement therapy had been administered (Henes et al., 2020).

Mørch, 2017, found in the study, women who currently or recently used the progestin-only intrauterine system had a higher risk of breast cancer than women who had never used hormonal contraceptives. It revealed that among 1.8 million women who had followed hormonal contraceptives on average for 10.9 years, 11,517 cases of breast cancer occurred. As compared with women who had never used hormonal contraception. The risk of breast cancer was still higher among women who had used hormonal contraceptives for 5 years or more than among women who had not used hormonal contraceptives.

Park, 2017, did not find any interactions between the presence of a strong family history of breast cancer and the association between obesity-metabolic phenotypes and breast cancer risk.

5.5 Breast characteristics of patients' participants

The majority of participants had breasts that were of a normal size in terms of breast characteristics. In about 35.5% of them, the cancer-affected breast was larger than the unaffected breast; some of them had warmth in the cancer-affected breast, and a small percentage reported tethering there. Also, an overview of early breast cancer is given in an article by Watkins (2019), including clinical characteristics, apparent symptoms, dimpling or tethering, skin alteration, an orange-peel look, nipple discharge, and nipple retraction as visible signs for breast cancer in the early stage.

However, in half of the patients' participants, the mass was found in the upper outside quadrant of the breast, and in the upper inner, lower outer, and lower inner of the breast for the remaining participants. Likewise, in a study involving 203 females, (Gharekhanloo et al., 2018) found that the upper outer quadrant (UOQ) was the most typical site for both benign and malignant breast tumors found on ultrasound, According to a study by (AlShamlan et al., 2021) overlapping lesions were the most frequent location of breast masses, followed by the UOQ.

5. 6 Screening and imaging findings of the participants

In pertaining to breast cancer screening, this study's findings showed that ultrasonography was performed for all patients, and mammography with MRI was performed for most of them. The screening results showed a suspicious mass, an irregular shape, high intensity with obscured indistinct irregular margins. The majority of patients had masses and lumpiness in the breast's upper outer quadrant (UOQ).

Previous studies confirmed that the ultrasound (US) detected early breast cancer and lumpiness in most women who were visiting a diagnostic and treatment clinic for breast cancer. The percentage of invasive carcinomas found in the US that are node negative exceeded 80% in 15 of 19 studies and 90% in eight of 19 investigations, according to (Berg, 2012).

A retrospective database review between "2003-2011", revealed that most breast cancers (81%) were detected at the US screening (Bae, 2014). This study, which was supported by a cross-sectional study carried out in Saudi Arabia (2017–2019), discovered that women who reported breast lumps had a higher likelihood of having a breast mass revealed on ultrasound (AlShamlan, 2021).

Also, in a multicenter retrospective investigation with a 7-year follow-up of 501 women with US-found cancer, (Kim et al. 2017) revealed that excellent results for malignancies detected at supplemental screening in the US had been recorded. They had 98% 5-year disease-free survival.

In a study involving 203 females, (Gharekhanloo et al., 2018), found that the upper outer quadrant was the most typical site for both benign and malignant breast tumors found on ultrasound. Regarding the invasiveness of cancer, when used in conjunction with mammography, breast ultrasonography finds extra early-stage, invasive breast cancers (Vourtsis, 2019).

In connection with our community's screening or imaging program, the city of Sulaimani has a screening program for women that monitors and diagnoses early breast cancer. In the city of Sulaimani, there is a breast treatment clinic that serves as a primary resource for those who are at risk for breast cancer, have a family history of the disease, are premenopausal or postmenopausal, have breast pain or a tumor in their breast, or are otherwise experiencing these risk factors. The method of operation in this breast cancer treatment facility is to create a file for them for the screening monitoring program (US, mammography) based on the

patient's status, their breast condition, or if they have just been diagnosed with breast cancer.

5.7 Patients' histological results of a breast core biopsy

The histopathology type of the presented study (Table 9) showed that the majority of patients had invasive ductal carcinoma, with tumor grades 2 and 3. Regarding hormone receptors, the majority of them in the current study were ER+, then PR+, a near quarter were HER-2 type, and half of a quarter were triplenegative receptors.

Similarly, an Azizun-Nisa, et al. study revealed that the majority of cases were grade 2, with ER+, PR+. Also a retrospective study done by Han, S et al (2021), revealed that more DCIS patients had estrogen receptor (ER) positivity (P = 0.033) and PR positivity (P = 0.017).

In an overview of early breast cancer article by Watkins (2019), up to 80% of participants were invasive ductal carcinoma. Estrogen receptor (ER) positivity breast cancer are more common among all nation in United States ethnicity, 70% of patients with IDC are hormone receptor positive with HER-2 negative.

5.8 Surgical techniques for the SLNB procedure

Under general anesthesia, sentinel lymph node biopsy procedures were carried out on all 110 patients. It used methylene blue (MB), as tracer dye. When in solution, the dark green crystalline component MB becomes dark blue (Masannat et al. 2006). Methylene blue 5 ml (0.3mg), was injected into the breast functional tissues around the breast tumor (peritumeral) and subareolar region (Teal al., 2005). Breast massage is performed for 5 minutes. SLNB is done through a small 1.5-2 cm transverse skin line incision in the lower axilla.

Dissection started and SLN was identified either by finding blue lymph nodes, blue lymphatics or by careful palpation of the area for palpable lymph

nodes not visualized by the dye. The wound is completely closed, no drain has been inserted. Prior to the breast procedure, the SLNB is performed for all patients, surgery for the breast tumor is done (either mastectomy or breast conservation surgery). A single oblique incision is used for the majority of the mastectomy, and SLNB can be completed quickly through the axillary end of the incision before starting the mastectomy. SLNB, and the tumor with resection margins were sent for histological diagnosis and other pathological findings.

Regarding axillary surgery after SLNB, according to the ACOSOG Z0011 study's recommendations, axillary lymph node dissection (ALND) was not carried out if metastases were only discovered in one or two sentinel lymph nodes (SLNs); however, ALND was carried out if metastases were discovered in three or more sentinel lymph nodes (Giuliano et al., 2011) (Jung et al. 2019).

Macrometastasis (>2.0 mm) was used to determine nodal metastasis (nodepositive); nodal negativity was stated as the absence of tumor cells in lymph nodes, the presence of isolated tumor cells (0.2 mm), or the presence of micrometastasis (0.2-2 mm). (Edge et al 2009) (Galimberti et al., 2013) (Reimer et al., 2017) (Naidoo 2017) (Zhu et al., 2018)

As a tracer for SLNB, Methylene Blue (MB) alone was used in the presented study; the identification rate (IR) was 97.56% in those with SLNB alone and was 91.8% for those with SLNB plus LAS (Table 10). Similarly, SLN identification rates were 97.4% (MB) in an Indian randomized control trial study. The findings suggested using MB for SLNB as the preferred technique in low-resource settings (Seenu et al., 2019).

When MB was utilized alone, the IR in a meta-analysis from "2000 to 2017" was 91%. These rates adhere to the suggested norms for SLNB, according to the American Society of Breast Surgeons (ASBrS) (Li et al., 2018). MB is a safe tracer that can be used in clinical practice where access to other tracers is limited (Guo et al., 2018). This is the most common tracer and has been widely used, either alone or in combination with other tracers (Liu et al., 2021).

5.9 Breast surgery types and their relationship to long-term complications

The most common surgery choices for the patients' participants in this study were BCS, simple mastectomy, and MRM, which were the second choices for breast surgeries. Regarding post-surgery problems that related to the types of breast surgeries, there was no significant relationship between each type of complication (infection, seroma, paresthesia, shoulder stiffness, arm swelling) and both types of surgeries (p > 0.05).

The majority of participants in this study underwent oncoplastic BCS and, in some cases, mastectomy (Figure 21). Perform a mastectomy due to multicentric and multifocal tumor focality, small breast size, or the patient's preference. They are fearful of cancer recurrence (Hassan et al., 2019).

Similarly, a retrospective study in India reported that, for women who presented with early breast cancer, the rate of BCS increased. According to a Masannat et al. (2006) study, breast conservation is safe for patients with multifocal and multicentric breast cancer (when it is physically possible and as long as it is possible to have good cosmetic outcomes).

Furthermore, despite the fact that the Kadam et al. (2022) study found that 68 MRM were performed on female breasts out of 86 breast surgeries, patients chose to have MRM because they were afraid their cancer might return. There is

no significant relationship between the type of breast surgery and postoperative complications (p > 0.05).

Numerous analytical investigations have suggested an association between BCS and mastectomy in breast cancer surgery, although these studies have produced conflicting findings (Javed et al., 2021). A retrospective study concluded that (75%) of BCS have favorable outcomes. Additionally, the findings of a cohort analysis showed that BCS was strongly connected with favorable prognostic aspects, but they also came to the conclusion that the proportion of Asian nations with a high mastectomy rate remained.

Also in other cohort studies in Asian settings, a study showed that, among 2245 women overall, 63% had mastectomy, 36% had BCS, and the median tumor size at presentation was 2·0 cm (Sinnadurai et al., 2018).

Analysis was done on the 2009–2012 National Surgical Quality Improvement Program database. 3339 patients were in the SM group and 6682 were in the BCS group. When treating early stage breast cancer, both BCS and SM options have low early postoperative complication rates, while BCS has fewer issues with bleeding, wound problems, and infections (Chatterjee et al., 2015)

5.10 Patients' histopathology results for the tumor and axillary involvement of the disease

The majority of the patients in the current study had no axillary lymph node involvement, according to the histopathology results of their axillary lymph nodes. The findings revealed that statistically there is no relationship between the lymph node involvement in the remaining patients and the size of the breast tumor (P value = 0.52).

Similarly, a cohort study of 453 patients with stage I-II breast cancer revealed that 22% (n = 113) were node positive, there were no associations to predict nodal involvement, and subtype had no significant association with the number of metastatic lymph nodes (Jones et al., 2013). The incidence of lymph node metastasis differs according to molecular subtype. Luminal types have a higher incidence of nodal metastasis than HER2 and TNBC (Min et al., 2021).

Regarding tumor size and surgical treatment of breast cancer, similarly to our study, Bleicher et al., (2016) and Mazor, (2019), reported in a surveillance and epidemiology study using a large national data set, the National Cancer Database, that BCT is safe for patients in the Medicare population with tumors measuring >5 cm, as demonstrated by overall survival and disease-specific surveillance rates that are similar to those for mastectomy, confirming that tumor size should not be an absolute BCT exclusion.

In contrast with our study, Port et al., (2010) in a retrospective study, found an increase in tumor size (more lymph nodes were removed for T2 tumors than for T1 tumors: 6.3 vs. 4.3; P .0001) and concluded that the total number of lymph nodes removed increased with tumor size and younger patient age.

Moreover, Neto et al., (2017) in a retrospective cross-sectional study, concluded that angiolymphatic invasion, tumor size (T3/T4) (p = 0.027), and Ki67 > 14 were factors predictive of axillary metastasis involvement in addition to the sentinel lymph node.

5. 11 Patients' non-surgical treatments (systemic therapy)

The majority of patients in the current study are taking adjuvant systemic therapy (adjuvant radiotherapy, adjuvant chemotherapy, and adjuvant endocrine therapy). Also, a few patients had taken neo-adjuvant chemotherapy.

Adjuvant and neo-adjuvant treatment options are recommended for earlystage invasive breast cancer, intended to reduce the risks of cancer

recurrence or death. Included chemotherapy (Neo-adjuvant platinum-based, adjuvant capecitabine), anti-HER2 therapy (trastuzumab), other targeted therapy, endocrine therapy (tamoxifen), bisphosphonates (postmenopausal women), and radiotherapy (Kerr et al 2022).

The findings of this study demonstrate that not all patients received chemotherapy or radiotherapy after breast surgery. The decision to administer adjuvant chemotherapy and radiotherapy is based on the pathological results of the SLNB, Ki67 markers, FISH (fluorescence in situ hybridization) and oncotype DX tests, and IHC for ER, PR, and HER2 positive patients undergoing BCS or mastectomy, according to the protocols of Hewa Oncology Hospital and Zhiyanawa Radiation Oncology Hospital.

5.12 Complications following breast and axillary surgery

The present study results revealed that some participants had one or more complications post-operatively. Also, the current study showed that patients who had SLNB plus LAS had a higher rate of complications (infection, seroma, hematoma, and paresthesia) than those who had SLNB alone (Table 15).

Statistically, there is a significant association between decreased range of motion and axillary surgery (p = 0.03) and a highly significant association between lymphedema and ALND (p 0.001).

The current study's findings were consistent with a prospective study that found that only a small percentage of patients (4%), and 6% with ALND, were at high risk of lymphedema (Rafn et al., 2022).

After ALND, most patients develop lymphedema months or years later; 80% of them develop some degree of fibrofatty accumulation, and one-third of patients have more fat than fluid in their limb (Dayan et al., 2020).

In a study (Soyder et al., 2014), lymphedema development was found in 7 (6.9%) out of 101 cases constituting the study group. Lymphedema lasted within 3 months of surgery. At that time, they had physiotherapy for their arms (Gillespie et al., 2018). It might be difficult to manage lymphedema with physiotherapy, massage, and lifetime compression. Despite complete compliance, lymphedema frequently worsens. A third of patients experience cellulitis, which can spread quickly and cause sepsis (Wiser et al., 2020).

Seroma is the most frequent postoperative complication following mastectomy and axillary surgery (incidence of 3% to 85%). Infection risk is increased by prolonged drainage from seromas (Srivastava, 2012; Onesti, 2017). A clinical trials registry in India (Prajapati et al., 2021) found that 9% of patients in the study's control group had seroma, compared with 42% in the ALND group, with paresthesia and seroma being the most common.

In a meta-analysis, the overall incidence of seroma was 24.2% (411 of 1698), with 25.2% (232 of 920) in the test groups and 23.0% (179 of 778) in the control groups, regardless of the methods used to avoid seroma, it causes discomfort for patients and can delay local healing and the start of adjuvant therapy. Although there is no agreement on the ideal drainage time, wound drainage is the most efficient method of preventing seroma (Adrien et al. 2022).

With rates ranging from 2% to 50%, complications following breast cancer surgery are rare, although they are allegedly more frequent when rapid breast reconstruction and axillary surgery are combined. According to a breakdown of operation types, morbidity rates after mastectomy ranged from 5% to 50%, and those following lumpectomy with or without reconstruction ranged from 3% to 35%. Seroma, infection, lymphedema, nerve damage, and shoulder/arm morbidity are postoperative complications connected to axillary surgery that may be complicated by the type of breast surgery done. To minimize complications,

preoperative preparation, risk factor mitigation for the patient, preventive usage, and excellent surgical technique are essential (AlHilli & Wilkerson, 2021).

5.13 Time to go back to work after surgery

The current study shows that not all patients return to their normal daily activities or work after breast and axillary surgery in the same time span, with healing times ranging from one week to six months. According to the line chart in figure 23, many patients return to their regular jobs between one and two months after surgery.

The full recovery following a mastectomy takes time. The American Cancer Society states that most women can resume their regular activities in around 4 weeks. For other people, recuperation may take months and be more prolonged. This may occur if patients undergo a more involved treatment, like a radical mastectomy, or if breast reconstruction is done concurrently with mastectomy (Catherine, 2021).

After BCS, and returning home, the majority of women should be able to function, and they can frequently resume their normal activities in 2 weeks. Depending on how involved their surgery was, some women could require assistance at home (ACS, 2021).

At the end of the discussion, the researcher thought that after the study, participants' assessments of the factors that increased their risk of breast cancer varied from one another, as did the increase in breast cancer risks in our community. The researcher emphasized that the main contributing factors to the rising incidence of breast cancer among women in the Kurdistan region are "genetic and family history, use of the contraceptive pill and hormone therapy, inability to breastfeed their child, stress, worry, or effort, and long hours at work." Particularly among individuals who have a history of protracted stress, anxiety, and depression brought on by various types of unresolved family issues? This

caused them to lose immunity, which in turn caused an increase in breast cancer risk. Which is supported by Wang et al. (2020), who found that anxiety and depression raise the chance of developing breast cancer.

Additionally, as stated under the study's limitations, the researcher encountered numerous challenges when deciding on the sample size and study location. The researcher was forced to conduct research at private hospitals due to the extremely low number of SLNB procedures for early breast cancer patients performed in governorate surgical facilities. Also, not all private surgical hospitals that performed SLNB procedures at that time permitted the researcher to conduct her research in their hospitals. Therefore, it will not be estimated to collect a sufficient number of patients who perform the SLNB operation; this will make the researcher take those patients who did SLNB plus sampling also.

Despite these challenges, the research has several positive aspects. For one thing, it is a novel study because it is the first to conduct research on SLNB in the Kurdistan area and Iraq. Second, the current study's findings are in line with international research on the SLNB method in early breast cancer. Third, many of the participants continue to speak by phone with the researcher two years or more after the study was completed in order to get support and ask any questions about their health. Fortunately, the majority of patients go on to lead normal lives after finishing systemic therapy.

Chapter Six Conclusions and Recommendations

6. Conclusions and Recommendations

6.1 Conclusions:

In summary, based on the discussion and interpretations of the study findings, SLNB results were positive for metastasis in 38 patients on histopathology, resulting in a positivity rate of 34.54%. Only a small proportion of those who had SLNB alone and had several positive nodes or one positive node with additional nodal extension underwent ALND.

Pre- and post-menopausal women are at increased risk of breast cancer. Other risk factors such as hormone and CP use, genetic and family history, and obesity with limited physical exercise.

On the other hand, breast lumps were the most frequent symptoms that women with breast cancer present and that invasive ductal carcinoma with luminal-A (ER and PR positive) is the most common subtype of early breast cancer.

In addition, while SLNB with Methylene Blue Injection is one of the most effective methods for determining axillary lymph node involvement with a minimum invasion, several complications following surgery still harm patients, including infection, seroma formation, hematoma, shoulder stiffness, and arm swelling, which are delaying adjuvant therapy, and this was supported by regression analysis.

Finally, the most important findings of this study are that they show statistically significant associations between decreased range of motion and axillary surgery (p = 0.03). A highly significant association between lymphedema and ALND (p < 0.001). This protective effect was supported by regression analysis and the Chi-square test.

6.2 Recommendations:

In light of the study's deduced conclusions, the recommendations are as follows:

- ➤ It has been demonstrated that sentinel lymph node biopsy has a beneficial effect and is useful in the managing of patients with early breast cancer. As a result, it is critical for clinician, surgeon, nurses to update SLNB techniques and procedures for staging axilla in patients with clinically positive axillary nodes.
- ➤ Not all women in the world, especially those in developing nations, have the opportunity for an early diagnosis of breast cancer and SLNB; hence, it is important for WHO to assist those nations by providing all necessities for doing this operation.
- ➤ The Ministry of Health improves the Breast Treatment Clinic and provide counseling for breast disease for women in Sulaimani City, Kurdistan, Iraq. By altering health systems to make it easier for all women to access the clinic, such as by having two shifts for employees and opening the clinic in the morning and evening with the same qualifications as medical care and screening programs.
- ➤ The teaching hospital in the Kurdistan region needs to provide the equipment and materials required to perform SLNB surgery on breast cancer patients. Women from lower economic backgrounds do not have access to private institutions for breast cancer screening and surgery.

- ➤ To minimize complications after breast and axillary surgery, it is important to plan ahead to reduce the risk for the patient, use preventative measures, and employ excellent surgical technique.
- ➤ In line with the national guidelines for annual screening for women at risk for breast cancer, nursing managers and medical teams should set up an educational program and offer advice.
- ➤ The research can serve as a source of information for future studies that wish to raise public awareness of breast cancer risk factors
- ➤ Utilizing various forms of mass media to raise awareness among the community regarding early detection and management of breast cancer

6.3 Recommendation for Further Research

- A similar study can be conducted with a larger sample size.
- Another study can be conducted to identify another dependable method for the SLNB procedure for the treatment of early breast cancer.

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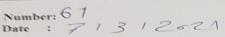
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Appendix 1: Ethical Approval

Ministry of Higher Education and Scientific Research University of Sulaimani College of Medicine Ethics committee

وهزارهتى خويندنى بالأو تويزينهومى زانستى سهر كايهتى زانكوى سليمانى كوليجى يزيشكى ليژندي ناكار



The Ethics Committee of the College of Medicine

We the members of the ethical committee approved the research project below in the meeting (No: 10) on the date (7/3/2571).

Title of the research project:

"The Role of Sentinel Lymph Node Biopsy in the Management of Breast Cancer in Sulaimani Hospitals, Iraq

Name and tile of the participants:

- 1- Assist. Lecturer/ Kwestan Mohammed Rahim/ department of Adult Nursing/ College of Nursing/University of Sulaimani
- 2- Assist Professor Dr. Nizar Mohammed Tawfeeq / department of Surgery/ College of Medicine/University of Sulaimani

Place of research study: Sulaimani Hospitals.

Members of Ethical committee of the College of Medicine

Ass. Prof. Dr Nizar Mohammed Tawfeeq Head of the committee

Lec. .Dr. Kazhan Ali Towfiq Member

Ass.Prof.Dr.Anwer Aboubaker kareem Jaff

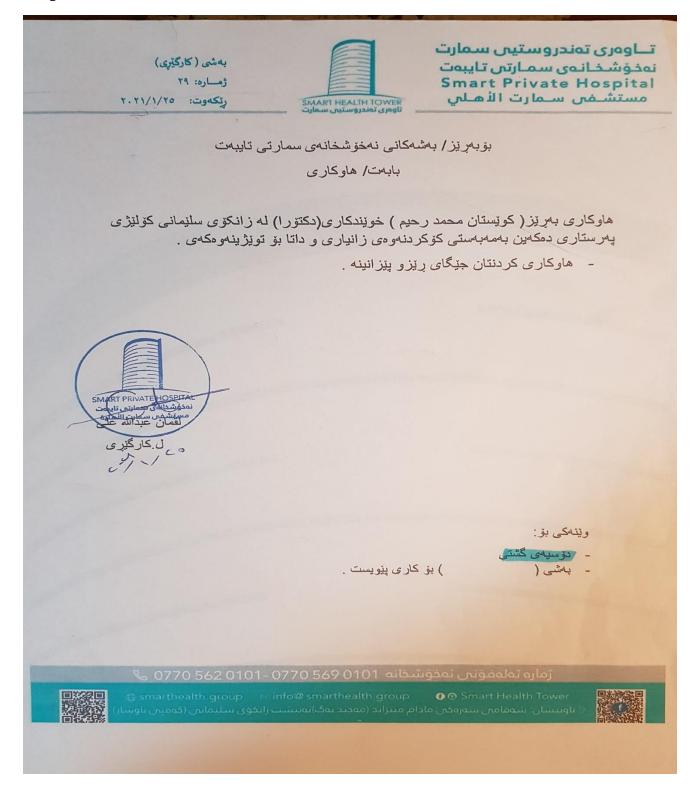
Ass.Prof Dr. Nawzad Rashed Abdulrahman Member

Dr. Ali Mohammed Kareem Jabari Member

Ass. Prof. Dr. Kamaran Awrahman Majid Member

Dr. Hadeel Abdulelah Ibrahim Saeed Member

Appendix 2: Formal Permission of Smart Health Tower, and Soma General Surgical Hospitals





نەخۆشخانەى سۆماى تاييەت SOMA PRIVATE HOSPITAL مستشفدى سوما الأهلپ

ریکهوت: ۱۸ / ۲ / ۲۰۲۱

ژماره: ٤٩

بۆ بەرپۆر/ بەشەكانى نەخۆشخانەى سۆماى تايبەت بابەت / ھاوكارى

هاوکاری به پیز (کویستان محمد رحیم) خویندکاری (دکتوّرا) نه زانکوّی سلیّمانی کوّنیّری پهرستاری دهکهین به مهبهستی کوّکردنهوهی زانیاری و داتا بوّ تویّرینهوهکهی.

هاوکاری کردنتان جیگای ریز و پیزانینه

لهگهل ريزدا ...



رەنىچ ئىازاد عثىمان بەريىوەبەرى كاركىيرى

c. soma.nospital@notmail.com T. +964 (0)53 320 5050 +964 (0)771 152 400 , nlog culos saudiou , carioù , notocur , nutică , nitoù L

Appendix 3: Consent Form

PARTICIPANT INFORMATION SHEET

Consent form for participant

You are being invited to participate in a research database which AL Kwestan Mohammed Rahim is creating.

I am Kwestan, working in Sulaimani university/ college of nursing. I am doing management outcomes research on {The role of sentinel lymph nodes biopsy in the management of breast cancer} which is very common in this country and in this region. By participating, you may assist us in finding out more about disease and treatment. I am going to give you information and invite you to be part of this research

Procedure:

- -Agreement to the collection of your personal health information from your medical chart, and through asking some questions to you directly involves, an interview, a questionnaire.
- We will not be sharing information about you to anyone outside of the research team. The information that we collect from this research project will be kept private. Any information about you will have a number on it instead of your name.

Consent statement

I have read the preceding information thoroughly. I have had the opportunity to ask questions, and all of my questions have been answered to my satisfaction. I agree to have my personal health information included in this database. I consent voluntarily to participate as a participant in this research.

0608,3 Name of Participant:

Signature of Participant:

Date: 2021 / 9 / 26

Consent form administered and explained in person by:

Name and title: AL. Kwestan Mohammed Rahim/ Adult nursing

Date: 2021 / 9 / 26 Signature:

Appendix 4: Reliability formula

Reliability Statistics

Cronbach's	
Alpha	N of Items
.820	60

Appendix 5: Sample size formula

Calculate sample size:

The sample size n and margin of error E are given by x

$$=Z(^{c}/_{100})^{2}r(100-r)$$

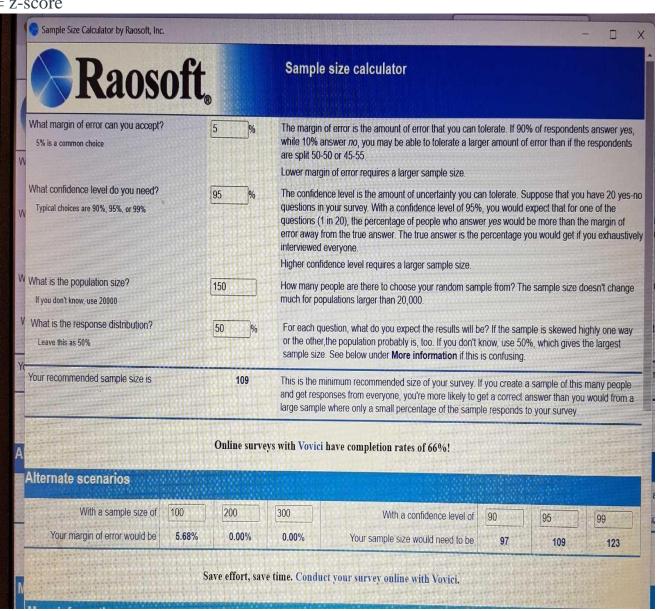
n = N x/((N-1)E2 + x)

 $E = \mathbf{Sqrt}[(N-n)x/n(N-1)]$

N = population size

e = Margin of error (percentage in decimal form) • z





Appendix 6: English version of the questionnaire

The effects of Sentinel Lymph Node Biopsy in the Management of Early Breast Cancer with Negative Axillary Lymph Node in Hospitals in Sulaimani City

Part I. SOCIODEMOGRAPHIC FEATURES

Identification Data	:	
Serial No:		
Patient Record No:		-
Patient Name:		
Age:		
Blood group:		
Marital status: Married Divorced	UnmarriedWidow	
Occupation: Unemployed Teacher Employee	HousewifeFarmerRetired	StudentWorkerOthers
Education: Illiterate Secondary school Doctorate	Primary school Institute graduate	◯Intermediate Sch. ◯ College graduate
Address: Governorate Village	Qadha	Nahya
Living status: ① Homeowner	Renter	

Part II. HISTORY OF PATIENT

The present complaint: Mass Nipple retraction Breast asymmetry	PainNipple ulcerationSkin changes	Nipple dischargeBreast enlargementAxilla-mass
Duration		
History of the Present Illnes	s/ Details of the present com	ıplaint:
Nipple discharge- color (Characteristics) Serous Milky Review of Systems: General health (Energy): 1 Tiredness 2 Malaise 3 Loss of energy Menstrual history:	Tracter):	Purulent No discharge No No No No No No No
Date of menarche: Date of menopause:		
Obstetric history:		
No. of pregnancies: Parity- Para	Gravidy- gravida(o	death)
Psychiatric: Nervousness	Depression	Anxiety
Endocrine system (Metaboli	sm):	
Hypothyroidism	Hyperthyroidisr	n

Past History:		
Past medical history:		
() НТ	Heart diseases	Diabetes
Health maintenance:		
Self -breast examination Screening mammography	Yes Yes	◯ No ◯ No
Previous breast disease: Mastalgia Nipple discharge	Breast mass	C Breast trauma
Drug History: Contraceptive pills	Postmenopausa	ıl estrogen replacement
Family History: () Family history of breast car	ncer	
Tamily history of ovarian c	ancer	
Social & Personal History: So status:	ocioeconomic	
C Low class	Middle class	High class
Personal habits and lifestyle:		
Smoking	Yes	🗘 No
Alcohol	Yes	O No
Exercise	Yes	🗘 No
C Light Exercise	Moderate Exercise	C Heavy Exercise

Dietary habits:				
Non vegetarian(r	ed meat, poul	try, fish, milk, egg	g,) more than once	a week
Semi vegetarian(red meat, pou	ltry, fish, milk, eg	gg,) less than once	a week
Vegetarian (no r				
Upper limb: Arm circumference		swelling	() dilated ve	eins
Part III. LOCAL EX	XAMINATIO	ON OF THE BRI	EAST	
•				
Breast size: Normal	Q Underdev	veloped- small	Overdeve	eloped- large
Bra size: () A (75),	○ B (80),	C (85),	\(\times\) D (90),	
Breast asymmetry:	(breast) is sma	ller than (bre	east
Breast shape (Right Normal):	Abnormal- t	uberous breast	
Breast shape (Left): Normal		🗘 Abnormal- tı	iberous breast	
Any visible swelling visible swelling (Lef		Yes Yes	O No	Any
Skin: (Right or left)		Redness Peau de orange	~	d veins tion

Appendices				
		Thickening Tethering-dimpling-J Fixation	-	Nodules (Satellite) ring CScars
Sinuses Fi	istula	~		•
Palpation (R, L): Breast consistency:		Soft Nodular		Firm Lumpy
Temperature warmth (R, L):		Yes		No
Mass site: Upper outer quadrant Lower outer quadrant		Upper inner quadran Lower inner quadra		
Mass: size (Tumor size) cm				
LOCAL EXAMINATION OF	TH	IE AXILLA		
Inspection: Swelling		Ulceration		Sinuses
Palpation: Clinical axillary node status:				
Axillary LN:		Positive		Negative
Part IV. INVESTIGATIONS Ultrasonography	5			
Normal		Fibrocystic changes		Mastitis/Abscess

Appendices		
O Ductectasia	Breast cysts	Solid mass
Axillary LN: Negative	Positive	No. of LN
BIRAD US: (Breast Imaging Rep	porting and Database)	
Negative	tenign findings	probably benign findings
Suspicious abnormality	highly suggestive	e of malignancy
Tumor (right or left): Unicentric Multifocal	Multicentric Bilateral tumo	C Unifocal or
Mammography		
BIRAD mammography: Negative suspicious abnormality	benign findingshighly suggestive	* *
MRI		
BIRAD MRI: Negative	benign findings	probably benign findings
BREAST CORE BIOPSY		
Histological type Result:		
Insitu carcinoma:	Ductal	Lobular

Appendices		
Invasive carcinoma:	Ductal	C Lobular
Tumor Grade (differentiation G1):	G 3
Lymph vascular invasion:	Yes	◯ No
Hormone receptor status: ER	○ PR	CHER2
Triple negative		
FINE NEEDLE ASPIRATI Result:	_	Positive
Part V. TREATMENT		
SURGICAL TREATMENT	•	
Breast surgery:		
DBCS	Simple mastectomy	Modified radical mastectomy
Axillary surgery: SLNB No. of LN removed	level of LN removed.	
ALND: Level I	II	III
NONSURGICAL TREATM	IENT	
Adjuvant radiotherapy		Adjuvant chemotherapy

Appendices			
Adjuvant hormonal therapy Immunotherapy		Neoadjuvant th	nerapies
Part VI. SENTINEL LYMP	H NODE BIOPS	SY	
Surgical technique			
C General Anesthesia	IV Sedation	n QLoc	eal Anesthesia
Methods:			
Radioactive technetium 99 Blue dye 1% isosulfan blu Blue dye methylene blue			blue)
Administration of Antihistami	ne 🗘 Yes		No
Site of injection:			
peritumoral in the parench Intradermal in the skin ov Subareolar Periareolar			
Routes of injection:			
Intradermal (placed in the quadrant near the nipple areola Intraparenchymal (admini Subareolar (at the upper, obelow the complex	ar border for nonp stered in a peritur	palpable tumors) moral fashion)	
Incision type:		••••	

Appendices Identification of sentinel nodes: No. of sentinel LN removed: No. of LN detected per patient 23 >3 No. of sentinel LN visualized and removed 23 1 >3 No. of LN has not visualized but removed 1 23 >3 Total no. of LN removed 1 23 >3 Lymph nodes characteristics Result of SLNB pathology: Benign Malignant

Histopathological classification of SN defines three distinct subtypes:

AXILLARY LYMPH NODE DISSECTION

micrometastatic foci (≤2 mm) isolated tumor cells.

SLN metastasis classification

macrometastases (>2 mm)

Complete axillary dissection after the result of sentinel LN biopsy after the result of pathology

No. of LN removed-----
Closure of wound Yes No
Drain Yes No
Result of ALND group pathology-----

Postoperative care ALND group

Postoperative pain management Suture removal Drain removal if inserted Time to go back to usual activities

Part VII. Postoperative Complications

Allergic reaction/anaphylaxis after receiving blue dye for lymphatic mapping

Yes No

Axillary wound infection

Yes No

Axillary seroma

Yes No

Axillary hematoma

Yes No

Axillary paresthesias / numbness

Decreased upper extremity range of motion

Yes No

Upper extremity lymphedema

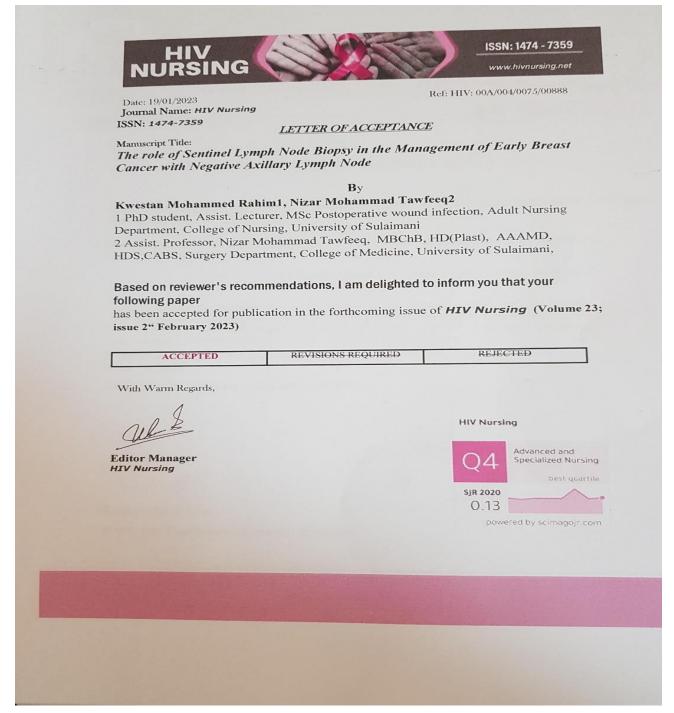
Yes No

Infection	Day 10-12	purulent drainage	localized pain	localized tenderness	localized swelling
Hematoma	Day 1-10	localized bruise	localized dark red/black color	pain	breast swelling
Seroma	Day 10-30	localized pain	infection	Reduced shoulder movement	wound dehiscence
Paresthesia	Day 10-90	localized pain, changes in skin sensation	Hyperesthesia	Hypoesthesia	Localized numbness
Shoulder stiffness	Day 10-90	Shoulder pain	Limit shoulder ROM		
Lymphedema/ Difference between the two extremities	Day 30- 90 and above	11-20 % Mild	21-40 %. Moderate	41-80% Evident	> 80% Severe

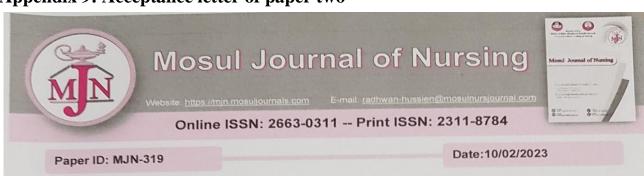
Appendix 7: List of Expertise

No	Name of the Experts	Scientific Title	Place of Job	Years of Experience
1	Dr. Tahir Hawrami	Professor	Sulaimani Medical University/ College of Medicine	43
2	Dr. Seerwan Shareef	Professor	Sulaimani Medical University/ College of Medicine	43
3	Dr. Zhyian Salah Ramzi	Professor	University of Sulaimani/ College of Medicine	29
4	Dr. Mezjda Ismail Mohammed	Assistant Professor	Sulaimani Medical University/ College of Medicine	43
5	Dr. Atiya Kareem Mohammed	Assistant Professor	University of Sulaimani/ College of Nursing	22
6	Dr. Aubdul Wahid Mohammed	Assistant Professor	Sulaimani Medical University/ College of Medicine	20
7	Dr. Deari Ahmed Ismaeil	Assistant Professor in surgery	University of Sulaimani/ College of Medicine	15
8	Dr. Abbas Tahir Rashid	Breast surgeon specialize	Ministry of health/ Breast management clinic / Sulaimani	25
9	Dr. Nariman Mohammed	Breast surgeon specialize	Faruq Medical City/ Sulaimani,	21
10	Dr. Hallwan AbdulRahman	Breast surgeon specialize	Ministry of health/ Breast management clinic / Sulaimani	20
11	Dr. Ara Aubdullah Muhammad	Oncoplastic breast surgeon	Ministry of health / Breast management clinic / Sulaimani	4

Appendix 8: Acceptance letter of paper one



Appendix 9: Acceptance letter of paper two



Manuscript Acceptance Letter

Dear Author(s); Kwestan Mohammed Rahim and Nizar Mohammad Tawfeeq Hamawandi.

We are pleased to inform you that our editorial board has accepted and approved your manuscript entitled:

> "Complications Post-Axillary and Breast Surgery in the Management of Early Breast Cancer"

after successfully passing the review process and revisions made by the authors. All the accepted manuscripts in this journal will go under advanced English editing by our native editors. The authors will also receive the galley proof of the final revision after all the quality control checks and prior to publishing the article.

* The Manuscript will published in the Issue 11, volume 2, on July of 2023. Best Regards,

Thank you for choosing to publish in our journal.

Editor-in-Chief

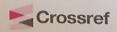
Radhwan

Prof. Dr. Radhwan Hussein Ibrahim

For information "MJN journal" TM is indexed/abstracted in;













الخلاصة

الخلفية: يعتبر الفحص المرضي للعقد الليمفاوية الإبطية في البقاء كطريقة ذهبية لتحديد المرض المنتشر للإبط في سرطان الثدي المبكر. تعتبر الإجراءات الجراحية المتقدمة لتحديد مرحلة الإبط أقل توغلا. وهنالك العديد من المرضى المنين يعانون من الآثار الجانبية مثل الالتهابات، والأورام الدموية، والأورام المصلي، وتنمل، وتيبس الكتف، وتورم الذراع، مما يؤدي إلى تأخير العلاج المساعد.

<u>الهدف:</u> تهدف الدراسة الحالية إلى وصف دور خزعة العقدة الليمفاوية الحارسة في علاج سرطان الثدي المبكر مع العقد الإبطية السلبية.

المنهجية: تم إجراء دراسة وصفية قائمة على الملاحظة على 110 امرأة يخضعن لخزعة العقدة الليمفاوية الحارسة وحدها أو بالإضافة إلى أخذ العينات للفترة من 1 مارس 2021 إلى 1 أبريل 2022. تضمنت أدوات الدراسة استبيانًا منظمًا للمقابلة، وقائمة مرجعية للمراقبة. يتألف من 7 أجزاء السمات الاجتماعية والديموغرافية، تاريخ المرض الحالي، الفحص السريري للثدي والإبط، التحقيقات)فحص الثدي (العلاج الجراحي وغير الجراحي، تقنية جراحية لخزعة العقدة الليمفاوية الحارسة)حقن صبغة زرقاء (يتم حقن الصبغة في خلايا النسيج بجانب الورم الصفاقي أو في منطقة تحت الهالة أو منطقة الهالة. مضاعفات ما بعد الجراحة.

النتائج: كان معدل تحديد العقدة الحارسة 97.56. المرضى الذين يعانون من 8 أو اكثر ورم خبيث من العقدة النتائج: كان معدل تحديد العقدة الحارسة 9.00.56. الميمفاوية الإبطية المنتشرة p=000.0. هناك الليمفاوية الإبطية المنتشرة p=0.00.0. هناك علاقة قوية بين p=0.00 والوذمة المناط كبير بين انخفاض نطاق حركة الكتف وجراحة الإبط p=0.00 هناك علاقة قوية بين p=0.00. اللمفية p=0.00.

الاستنتاج: تظل خزعة العقدة الليمفاوية الحارسة من خلال الحقن الأزرق بالميثيلين طريقة فعالة وموثوقة لتحديد ما إذا كانت الغدد الليمفاوية الإبطية مصابة بمرض نقيلي، ولا تخاذ قرارات بشأن العلاج الجهازي المساعد بعض المرضى عانى من مثل هذه المضاعفات، مما أدى إلى تأخير العلاج المساعد وتقليل جودة حياتهم.

<u>يوخته</u>

پیشهکی : نهشتهرگهری پشکنینی نهخوشیناسیی گری لیمفاوییهکانی بن بال بهردهوام دهبیت له کردنی وهک ریگهیهکی زیرین بو دیاریکردنی نهخوشی گوازراوه بو بن بال له سهرهتای شیرپهنجهی مهمکدا. ریکارهکانی نهشتهرگهری پیشکهوتوو بو خستنه رووی قوناغی توشبوونی بن بال کهمتر خانهکان بریندار ئهکات له نهستهرگهرییهکهدا. لهگهل ئهوهشدا زوریک له نهخوشهکان، تووشبوون ئهبن به کاریگهرییه لاوهکییهکانی وهک ههوکردن، هیماتوما، سیروما، پهریستیزی، رهقبوونی شان، و ئاوسانی قول، که چارهسهری یارمهتیدهری دواخست.

ئامانج : ئەم توێژینەوەيەى ئێستا ئامانجى باسكردنى رۆٽى بايۆپسى گرێ ئيمفاوييە سەنتینێلەكان بووە ئە بەرێوە بردن و چارەسەركردنى شێريەنجەى سەرەتايى مەمك كە گرێى بنچينەيى بن باٽيان نێگەتيڤە.

نامراز : توپژینهوهیهکی وهسفکهری چاودیّری نهسهر 110 ژن نهنجامدرا که تیایدا بایوّپسی پارچهیهکی بچووک نه گری ایمفاوییهکانی سهنتینیّلیان به تهنیا یان نهگهن نمونهی کهدا نی وهرگیرا نه ای نازاری 2021 تا ای نیسانی 2022 ئهنجامدرا. ئامرازهکانی تویژینهوهکه بریتی بوون نه پرسیارنامهیهکی چاوپیّکهوتنی دارپّژراو نیستی پشکنینی چاودیّری. که ۷ بهش نهخوّدهگریّت تاییهتمهندی کوّمه لایهتی-دیموّگرافی، میّرووی نهخوّشی نیّستا، پشکنینی کلینیکی مهمک و بن بان ، نیکوّنینهوهکان)سکرینکردنی مهمک (چارهسهری نهشتهرگهری و بی نهشتهرگهری، تهکنیکیی نهشتهرگهری بو بایوپسی گری نیمفاوییه سهنتینیّنهکان)دهرزیکردنی بریهی شین(، رهنگه شینهکه دهدری نه خانهکانی مهمک نه تهنیشت وهرهمهکه نه دهوروبهری وهرهمهکه یان نه دهوری گوی مهمک ، ئانوّزییهکانی دوای نهشتهرگهری.

نهنجام : پێژهی ناسینهوهی گرێی سهنتینیّل 97.56 % بووه . نهو نهخوٚشانهی که 3 یان زیاتر له سێ پوٚزهتیڤی گوازراوهی گرێ لیمفاوییهکانیان ههبوو، نهشتهرگهری دووهمیان بو کرا بو لابردنی زوٚربهی گرێ لیمفاوییهکان که نهخوٚشییهکه ئهگوازیّتهوه پهیوهندییهکی بههیّز پهیوهندییهکی بهریّز و نهشتهرگهری شان و نهشتهرگهری شان ههیه (p = 0.03) پهیهندییهکی بههیّز له نیوان لابردنی تهواوی گری لیمفاوییهکانی بن باڵ و ئاوسانی دهست دا ههیه (p<0.001).

ده رئهنجام : بایوپسی گریّی لیمفاوی سهنتینیل له ریگهی دهرزی شین میتیلین وهک ریّگهیهکی کاریگهر و متمانه پیکراو دهمیّنیّتهوه بو دیاریکردنی نهوهی که نایا گری لیمفاوییهکانی بن بال نهخوّشی گوازراوهیان تیّدایه یاخود نا. ههندیّک له نهخؤشهکان تووشی نالفرْزبوون و کاریگهری لاوهکی دوای نهشتهرگهری بوون که بووهته هؤی دواکهوتنی وهرگرتنی چارهسهری دوای نهشتهرگهری، وه کهم بوونهوهی کوالیّتی ژبانیان .



حکومهتی ههریّمی کوردستان-عیّراق ئهنجومهنی وهزیران وهزارهتی خویّندنی بالا وتویّژینهوهی زانستی سهروّکایهتی زانکوّی سلیّمانی کوّلیّژی پهرستاری

رۆڵى وەرگرتنى نموونەى شيكارە گرى ئىمفاوى سەنتىنىل ئە چارەسەركردنى شىرپەنجەى سەرەتايى مەمك كە گرى ئىمفاوييەكانى بن بائيان نىگەتىقن ئە ئەخۆشخانەكانى شارى سلىمانى

ئەم تيزە

پیشکهشه به ئهنجومهنی کولیّری پهرستاری له زانکوی سلیّمانی کراوه وهک بهشیّک له پیرویستیهکانی بهدهست هیّنانی بروانامهی فهلسهفهی دکتورا له پهرستاری پیکهیشتووان

لهلایهن کونستان محمد رحیم ماستهر له پهرستاری ههناوی-نهشتهرگهری

> **به سهرپهرشتی** پروّفیسوّری یاریدهدهر د .نزار محمد توفیق

۲۰۲۳ شباط ۲۷۲۳ روشه می ۱۶۶۶ صفر