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Dissertation

"A STUDY ON LOCAL INJECTION OF METHYLPREDNISOLONEACETATE TO PREVENT SEROMA FORMATION AFTER MASTECTOMY"

Dissertation submitted to

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI-600032

In partial fulfilment of the regulations for the award of the degree of

M.S. (General Surgery)

Branch-1

THE TAMILNADU Dr. M.G.R MEDICAL UNIVERSITY

CHENNAI

MAY 2020

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CERTIFICATE

This is to certify that, the dissertation entitled **"A STUDY ON LOCAL INJECTION OF METHYLPREDNISOLONEACETATE TO PREVENT SEROMA FORMATION AFTER MASTECTOMY"** Is the bonafide work done by **Dr.SHYAMSUNDAR.R**, during his **M.S.(General surgery)** Course2017-2020, done under my supervision in partial fulfilment of the requirement of the M.S (BRANCH-1) –General surgery of the Tamilnadu Dr. M.G.R Medical University, May 2020 Examination.

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DECLARATION

I, certainly declare that this dissertation titled **"A STUDY ON LOCAL INJECTION OF METHYLPREDNISOLONEACETATE TO PREVENT SEROMA FORMATION AFTER MASTECTOMY"** represents a genuine work of mine. The contributions of any supervisors to the research are consistent with normal supervisory practice, and are acknowledged.

I also affirm that this bonafide work or part of this work was not submitted by me or any others for any award, degree or diploma to any other University board, either in India or abroad. This is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfilment of the rules and regulations for the award of Master of Surgery Degree Branch I (General Surgery).

DATE:

PLACE:

DR.SHYAMSUNDAR .R

(POST GRADUATE)

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ACKNOWLEDGEMENT

, As I walk down the memory lane I realize with a deep sense of humility that what I have done now would not have materialized, but for certain luminaries, who have enlightened my path to wisdom.

"*Surgery is learnt by apprenticeship and not from textbooks, not even from one profusely illustrated" – Ian Aird.*

While I put these words together it is my special privilege and great pleasure to record my deep sense of gratitude and indebtness to my revered Professor and Guide **Prof. M.ALLI M.S. , D.G.O** but for whose constant guidance, help and encouragement this research work would not have made possible. The unflinching academic, moral and psychological support will remain ever fresh in my memory for years to come. Words cannot simply express my gratitude to her for imparting to me the surgical skills I have acquired.

I place on record my profound gratitude to **Prof. R.KANNAN M.S,** for his support, keen interest and the constant encouragement he has given during the course of this thesis work.

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I would like to express my heartfelt thanks to my professor, **PROF. M.ALLI. M.S** whose constant motivation and encouragement kept me strive harder and better to complete the thesis work.

I would also like to thank **DR.M.KRISHNAMOORTHY, DR.M.KALYANKUMAR, DR. M.SABARIGIRIEASAN M.S.** Assistant Professors of Surgery for all of them have given me invaluable advice, guided me on and have been most kind and patient to me.

My sincere thanks to the entire, Institute of Pathology and radiology for granting me permission and helping me to conduct this study.

All along the way I have been supported and encouraged by all my associate professors who helped me to reach where I am.

I also thank my fellow postgraduate *Dr.Naveen* for his keen interest upon the sample collection and assimilation work. And special thanks to my junior PG *Dr.Tamilkovan, Dr.aishwarya* for her timely help in documentation of patient details and statistical analysis.

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I thank the Dean, MMC & RGGGH for permitting me to conduct this study.

With deep reverence, I salute my parents and I thank the Almighty for blessing me a wonderful family to whom I have dedicated this thesis and leave unsaid what they mean to me.

What good is a potter without his clay and what good is a study without the active participation of the patients. My heartfelt thanks go to each and every patient who agreed to be a part of this study and also my apologies to them in case of any inconvenience caused.

`

LIST OF ABBREVATIONS

DCIS - Ductal carcinoma insitu

LCIS - Lobular carcinoma insitu

RR- Relative risk

OR-Odds ratio

HRT-Harmone replacement therapy

FNAC- Fine needle aspiration cytology

CT- Computed tomography

MRI- Magnetic resonance imaging

USG-Ultrasonography

LFT- Liver function tests

CEA-Carcinoembryonic antigen

MRM- Modified radical mastectomy

BCS- Breast conservation surgery

LABC- Locally advanced breast cancer

QUART- Quadrantectomy with axillary dissection followed by external beam radiotherapy

AJCC- American joint committee on cancer

ER- Estrogen receptor

PR- Progesterone receptor

Her2/neu- Human epidermal growth factor

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INDEX

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INFORMATION SHEET

TITLE: ***"LOCAL INJECTION OF METHYLPREDNISOLONE - ACETATE TO PREVENT SEROMA FORMATION AFTER MASTECTOMY"***

Name of Investigator: Dr. SHYAMSUNDAR R

Name of Participant:

Purpose of Research:. To EVALUATE THE PROPHYLACTIC EFFECT AGAINST SEROMA FORMATION OF A SINGLE DOSE OF STEROID IN THE MASTECTOMY CAVITY

Study Design: Randomized Control Trail

Study Procedures: Patient will be divided into two groups Group 1 and Group 2 based on the injection of single dose of methylprednisoloneacetate. Two groups will be monitored for seroma formation and the data collected will be analyzed.

Possible Risks: No risks to the patient

Possible benefits

To patient : A better understanding of their problem so has to devise a plan of management which suits their needs.

To doctor & to other people: If this study gives positive results, it can help determine the role of single dose of methylprednisoloneacetate in the

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treatment of patients with seroma formation after mastectomy. This will help in providing better and complete treatment to other patients in future.

Confidentiality of the information obtained from you: The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared

Can you decide to stop participating in the study: Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time

How will your decision to not participate in the study affect you: Your decision will not result in any loss of benefits to which you are otherwise entitled.

Signature of Investigator Signature of Participant

Date :

Place :

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PATIENT CONSENT FORM

Study Title:

"LOCAL INJECTION OF METHYLPREDINISOLONE ACETATE TO PREVENT SEROMA FORMATION AFTER MASTECTOMY

Study Centre: Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

In-Patient's Number :

Patient may check (☑) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.	❑
I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.	❑
I understand that sponsor of the clinical study, others working on the sponsor's behalf, the Ethics committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from	❑

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the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.	
I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with]the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.	❑
I hereby consent to participate in this study	❑
I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests and to undergo treatment	❑

Signature/thumb impression

Patient's Name and Address:

Signature of Investigator

Study Investigator's Name:

Dr. SHYAMSUNDAR R

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URKUND

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https://basicmedicalkey.com/the-breast-2/

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NAME	
AGE/SEX	
IP NUMBER	
PRESENTING COMPLAINTS	
OPERATIVE PROCEDURE	
SEROMA FORMATION	
WOUND INFECTION	
WOUND DEHISCENCE	

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CERTIFICATE – II

This is to certify that this dissertation work titled "**LOCAL INJECTION OF METHYLPREDNISOLONE ACETATE TO PREVENT SEROMA FORMATION AFTER MASTECTOMY"** of the candidate **Dr. R.SHYAMSUNDAR** with registration Number 221711018 for the award of **M.S degree** in the branch of **General Surgery**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows(8%) percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.Shyamsundar.R
Post Graduate in M.S. General Surgery
Institute of General Surgery
Madras Medical College
Chennai

Dear Dr.Shymsundar.R.

The Institutional Ethics Committee has considered your request and approved your study titled **"LOCAL INJECTION OF METHYLPREDNISOLONEACETATE TO PREVENT SEROMA FORMATION AFTER MASTECTOMY " - NO.12012018**

The following members of Ethics Committee were present in the meeting hold on **09.01.2018** conducted at Madras Medical College, Chennai 3

1. Prof.P.V.Jayashankar :Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., Dean,MMC,Ch-3 : Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3 : Member Secretary
4. Prof.N.Gopalakrishnan,MD,Director,Inst.of Nephrology,MMC,Ch : Member
5. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3 : Member
6. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC : Member
7. Prof.Shanthy Gunasingh, Director, Inst.of Social Obstetrics,KGH : Member
8. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai : Member
9. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3 : Member
10. Prof.K.Ramadevi,MD., Director, Inst. of Bio-Chemistry,MMC,Ch-3 : Member
11. Prof.Bharathi Vidya Jayanthi,Director, Inst. of Pathology,MMC,Ch-3: Member
12. Thiru S.Govindasamy, BA.,BL,High Court,Chennai : Lawyer
13. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
14. Thiru K.Ranjith, Ch- 91 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

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INTRODUCTION

Seroma is defined as a serous fluid collection that develops under the skin flaps during mastectomy or in the axillary dead space after axillary dissection which usually begins to develop on the seventh post-operative day, reaches a peak on the eighth day and slows continuously until the sixteenth day when it generally resolves. It ends up in prolonged hospitalization and outpatient follow-up, further adding to the miseries of the breast cancer patients and may also delay subsequent adjuvant therapies. There are various techniques in research and practice reported to prevent or diminish seroma formation, but no single method has been shown to be constantly and reliably effective.

It is proposed that thorough attention applied to techniques of the surgery itself; to reduce the leakage from dissected vessels and lymphatics and to obliterate the dead space may reduce the incidence of seroma formation. Use of electro cautery, ultrasonic dissection, harmonic or laser scalpel and other techniques like drains, sealants and sclerotherapy may also be used but their usefulness and cost effectiveness are debatable.Surgical technique of obliterating dead space using flap fixation or quilting has been introduced with promising results. Some drugs have also been used

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which have shown efficacy in reducing seroma fluid for example betaglucan. The drainage volume during the first two postoperative days, total seroma volume during days 1–5 and the number of seroma punctures were reduced, but not significantly. There were no differences in wound healing time or rate of infectious complications between the groups. As it is proven by literature that seroma formation is by far the most common complication after mastectomy leading to increased morbidity, psychological trauma, increased length and cost of treatment and flap fixation is a promising method for preventing seroma formation. This will not only provide enhanced recovery and satisfaction to patients undergoing mastectomy but also reduce hospital stay, cost of treatment and use of antibiotics.

Seroma formation is a common problem after mastectomy. The incidence various between 30% to 92%. It is often an ongoing problem after removal of the suction drain, and repeated skin puncture is necessary to remove the seroma. In addition to many ambulatory visits this also leads to an increased risk of infection, and the adjuvant treatment can be delayed for several weeks.

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Different procedures have been tried to avoid seroma formation. Among these are for eg : immobilisation of the arm and shoulder after mastectomy, different drain regimens, closing of the dead space of the cavity, different chemical substances as thrombin, tranexamacid and fibrin. None of these results has been successful.Seroma formation is most likely the result of the inflammatory response due to wound healing. In the seroma fluid several factors have been detected that support this assumption. These factors are: high levels of IgG, leucocytes, granulocytes, proteinases, proteinases inhibitors, different kinds of cytokines (tPA, uPA,, uPAR, PAI-1, PAI-2, IL-6 og IL-1□).On the basis of this, an inhibition of the inflammatory response might result in a decrease of seroma formation, and perhaps improve quality of life after mastectomy.Steroids inhibit the inflammatory response for example by inhibition of the cytokine function.

AIM AND OBJECTIVES

To assess the variations in the outcomes in patients presenting with Seroma formation after mastectomy with single dose of methylprednisoloneacetate given with those who were not given..

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REVIEW OF LITERATURE

Normal Development and Physiology

Before puberty, the breast is composed primarily of dense fibrous stroma and scattered ducts lined with epithelium. ***Puberty*** is defined as breast development and the growth of pubic hair, begins between the ages of 9 and 12 years .***Menarche*** (onset of menstrual cycles) begins at 12 to 13 years of age. These events are initiated by low-amplitude pulses of pituitary gonadotropins, which increase serum estradiol concentrations. In breast, estradiol -dependent maturation (thelarche) leads to increased deposition of fat, the formation of new ducts by branching and elongation, and the first appearance of lobular units. This process of growth and cell division is under the control of estrogen, progesterone, adrenal hormones, pituitary hormones, the trophic effects of insulin, thyroid hormone &local growth factor.

Prepubertal gynecomastia means symmetrical enlargement and projection of the breast bud in a girl before the average age of 12 years, unaccompanied by the other changes of puberty. This may be unilateral, should not be confused with neoplastic growth and is not an indication for biopsy.

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The postpubertal mature or resting breast contains fat, stroma, lactiferous ducts, and lobular units. During phases of the menstrual cycle or in response to exogenous hormones, the breast epithelium and lobular stroma undergo cyclic stimulation. The dominant process appears to be hypertrophy and alteration of morphology rather than hyperplasia. In the late luteal (premenstrual) phase, there is an accumulation of fluid and intralobular edema. This edema can produce pain and breast engorgement. These physiologic changes can lead to increased nodularity and can be mistaken for a malignant tumor.

Ill-defined masses in premenopausal women are generally observed through the course of the menstrual cycle before any intervention is undertaken. With pregnancy, there is diminution of the fibrous stroma and the formation of new acini or lobules known as ***adenosis of pregnancy***. After birth, there is a sudden loss of placental hormones, combined with continued high levels of prolactin, is the principal trigger for lactation. The actual expulsion of milk is under hormonal control and is caused by contraction of the myoepithelial cells that surround the breast ducts and terminal ductules. The contraction appears to occur in response to the pituitary-derived peptide oxytocin. Stimulation of the

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nipple appears to be the physiologic signal for continued pituitary secretion of prolactin and acute release of oxytocin. When breastfeeding ceases, the prolactin level decreases and there is no stimulus for release of oxytocin. The breast returns to a resting state and to the cyclic changes induced when menstruation resumes.

Menopause is defined by cessation in menstrual flow for at least 1 year. Menopausal symptoms such as vasomotor disturbances (hot flashes), vaginal dryness, urinary tract infections, and cognitive impairment (possibly secondary to interruption of sleep by hot flashes). Menopause results in involution and a general decrease in the epithelial elements of the resting breast .These changes include increased fat deposition, diminished connective tissue, and the disappearance of lobular units. The persistence of lobules, hyperplasia of the ductal epithelium, and cyst formation all can occur under the influence of exogenous ovarian hormones, usually in the form of postmenopausal hormone replacement therapy (HRT). HRT can lead to increased breast density, which may decrease the sensitivity of mammography.

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ANATOMY

Breast is a *modified sweat gland* derived from ectoderm, as branching epithelial cords which form lactiferous ducts. About 15-20 lobes develop during puberty, each of which drains into a single lactiferous duct. True secretory alveoli develop during pregnancy and lactation under the influence of oestrogen, progesterone and prolactin.

Secretory apparatus of the breast.

The breast is composed of acini which make up lobules, aggregation of which form the lobes of the gland. The lobes are arranged in a radiating fashion like the spoke of a wheel and converge on the nipple, each lobe is drained by a lactiferous duct. Different portions of the duct system are associated with different diseases.

1. Larger ducts are sites of duct papilloma and duct ectasia.
2. Distal smaller ducts are the sites of fibroadenoma during development of the breast.

Cyst formation and sclerosingadenosis during the involution period.

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FUNCTIONS OF HARMONES

1. Estragon—ductal proliferation
2. Progesterone—glandular proliferation
3. Prolactin—milk secretion

EXTENT

Vertically—it extends from the second to the sixth rib in the mid-clavicular line and lies overPectoralis major, serratus anterior and external oblique muscles.

Horizontally—from the side of sternum to the mid-axillary line.

2/3rd of the breast rests upon pectoralis major. 1/3rd rest upon serratus anterior. At its lower medial quadrant the gland rests on the external oblique aponeurosis, which separates it from the rectus abdominis. Breast lies in superficial fascia.

Deep to breast, structures related are Retromammary space containing loose areolar tissue, pectoral deep fascia, muscles (pectoralis major, serratus anterior, external oblique), chest wall. Retromammaryspace is located between deep layer of superficial fascia and pectoral (deep) fascia allowing free mobility of breast.

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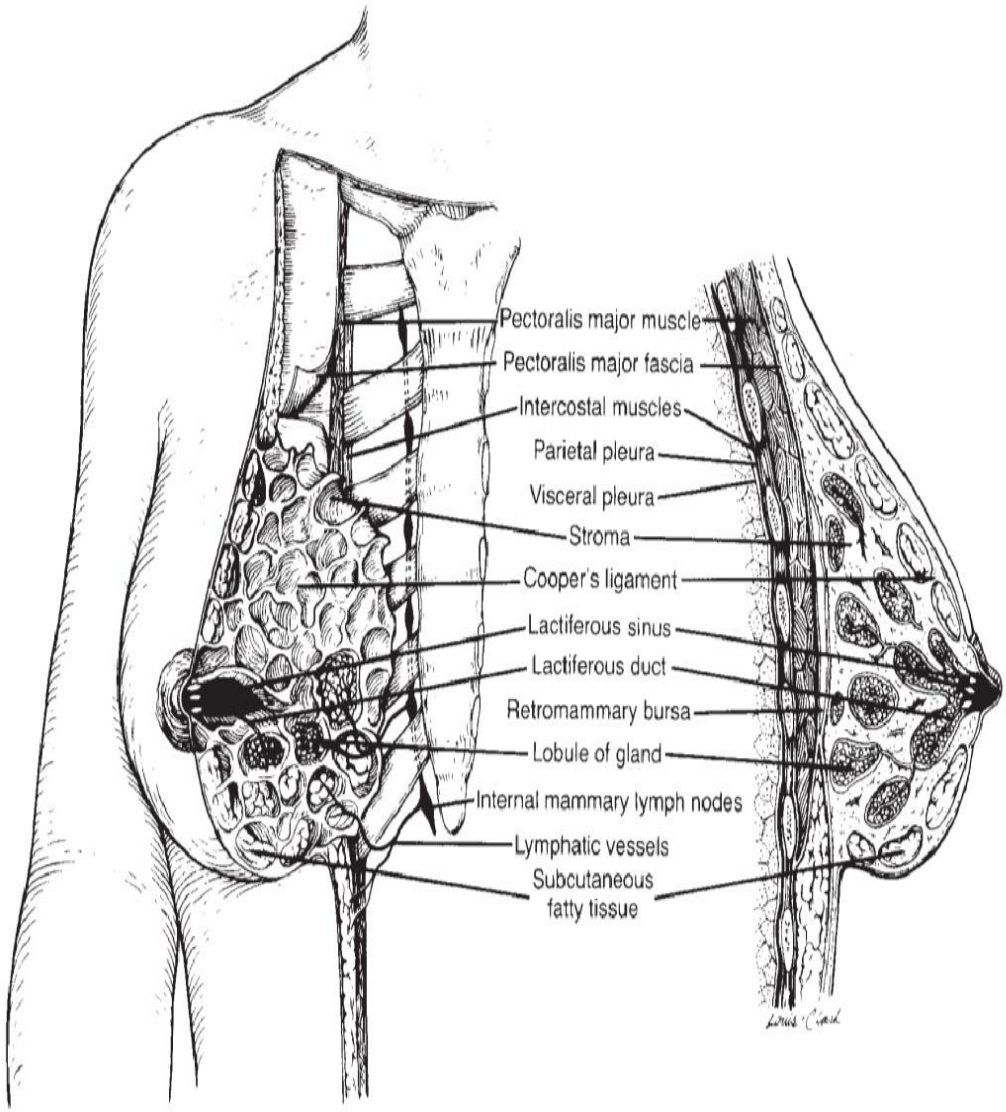

Nipple is located at the level of 4th intercostal space just below the center of the breast. It contains circular and longitudinal muscles to make nipple stiff or flat. It is pierced by 15-20 lactiferous ducts. Each duct independently opens into the nipple. It has rich sensory nerve endings. It also contains modified sweat and sebaceous glands. Nipple is supplied by 4th intercostal nerve.

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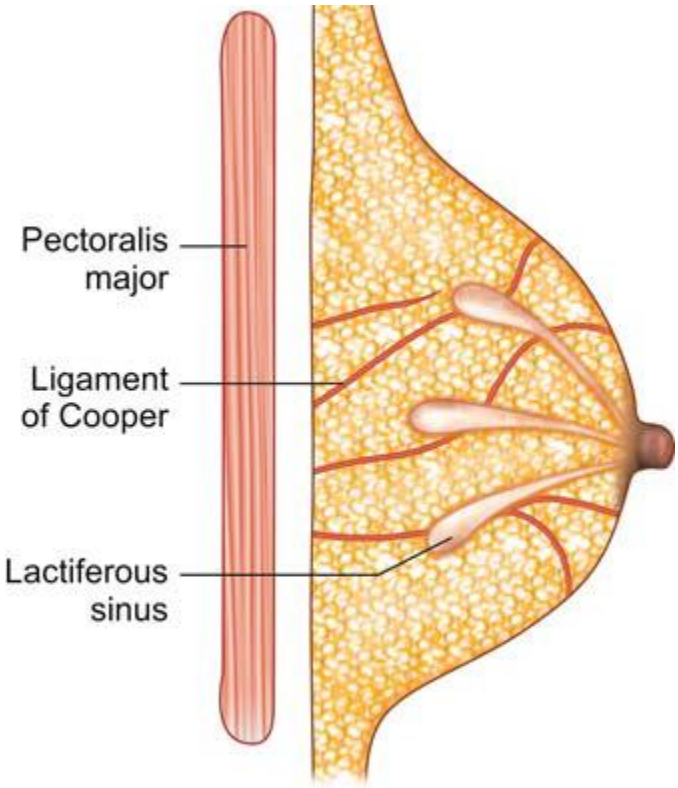
Areola is circular pigmented area around the nipple. It is rich in modified sebaceous glands which enlarge during pregnancy and lactation as Montgomery tubercles. They secrete oily lubricant to nipple and areola. Areola and nipple do not contain hair and fat beneath.



Breast parenchyma contains 15-20 lobes. Each lobe contains alveoli, lactiferous sinus and lactiferous duct (2-4 mm in diameter). Alveolus is lined by cuboidal (in rest) and columnar (in lactation) epithelium, smaller duct is by single layer of columnar epithelium, larger ducts by many layered columnar, lactiferous duct is by stratified squamous epithelium. Myoepithelial cells lie between epithelium and basement membrane from alveoli to duct.

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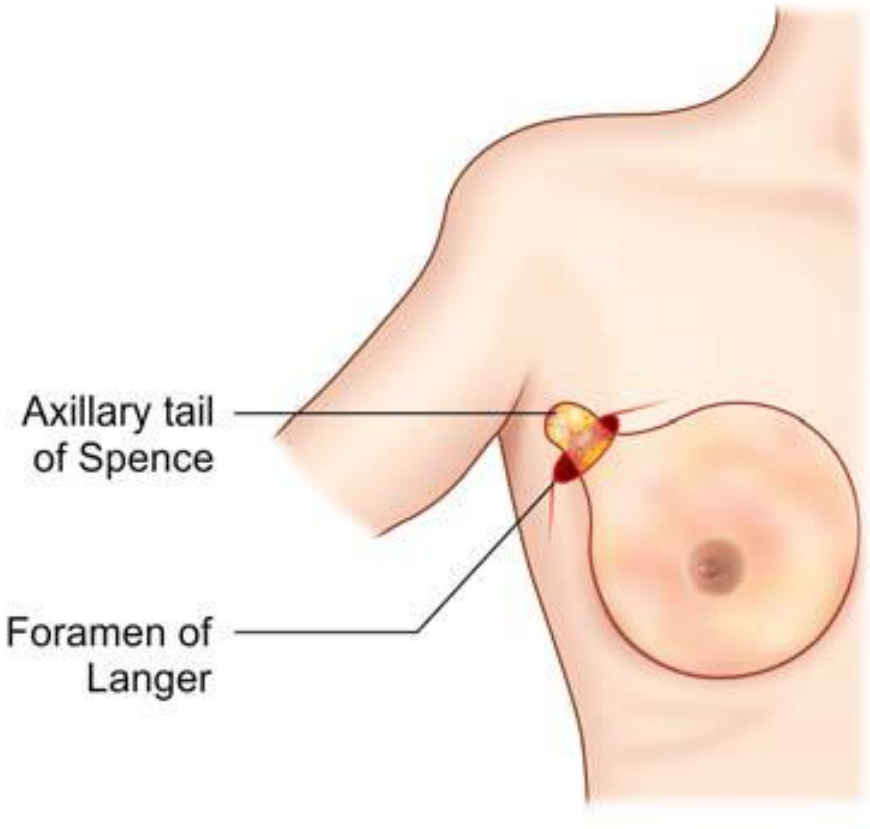
Axillary Tail of Spence This is a prolongation from the outer part of the gland which passes up to the level of the 3rd rib in the axilla through a defect in the deep fascia (Foramen of Langer) where it is in direct contact with the main lymph node of the breasts (anterior axillary nodes) This process of the breast gets into axilla through an opening in the deep fascia, known as foramen of Langer. When it enlarges it is often mistaken for a lipoma.

Axillary tail of Spence is deep to deep fascia.



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Ligament of Cooper The breast is anchored to the overlying skin and to the underlying pectoral fascia by bands of connective tissue called ligament of Cooper.

1. In cancer, the malignant cells may invade these ligaments and consequent contraction of these strands may cause dimpling of the skin or attachment of the growth to the skin, which in turn cannot be pinched off from the lump.
2. If the cancer grows along the ligament of Cooper binding the breast to the pectoral fascia, the breast gets fixed to the pectoralis major. It then cannot be moved along the long axis of the muscle.

Blood Supply to the Breast

1. The lateral thoracic artery, from the 2nd part of the axillary artery—30%.
2. The perforating cutaneous branches of internal mammary artery to the 2nd, 3rd and 4th intercostal spaces—60%.
3. The lateral branch of the 2nd, 3rd and 4th intercostal arteries.
4. Pectoral branches of acromiothoracic artery.
5. Superior thoracic artery.

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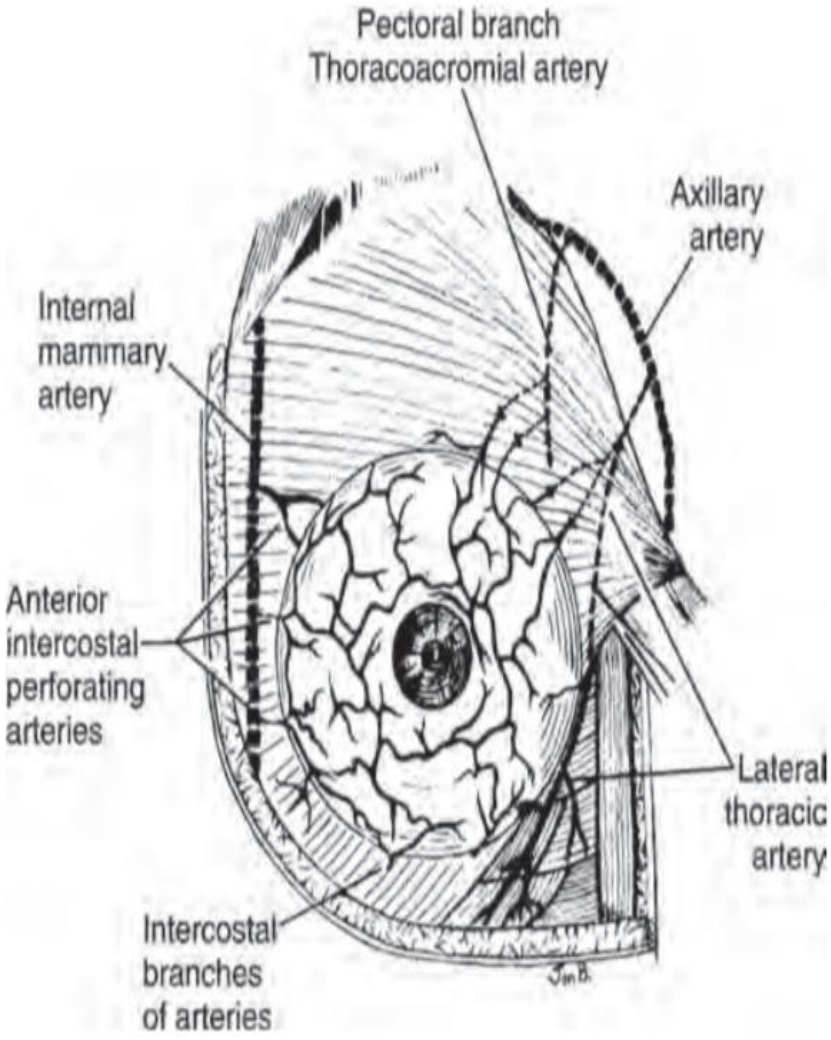

Venous Drainage:

The superficial veins from the breast characterised by their proximity to the skin drain to the axillary, internal mammary, and intercostal vessels. Through posterior intercostal veins, venous drainage communicates with paravertebral venous plexus (Batson's venous plexus). So secondaries in vertebrae, is common in carcinoma of breast.

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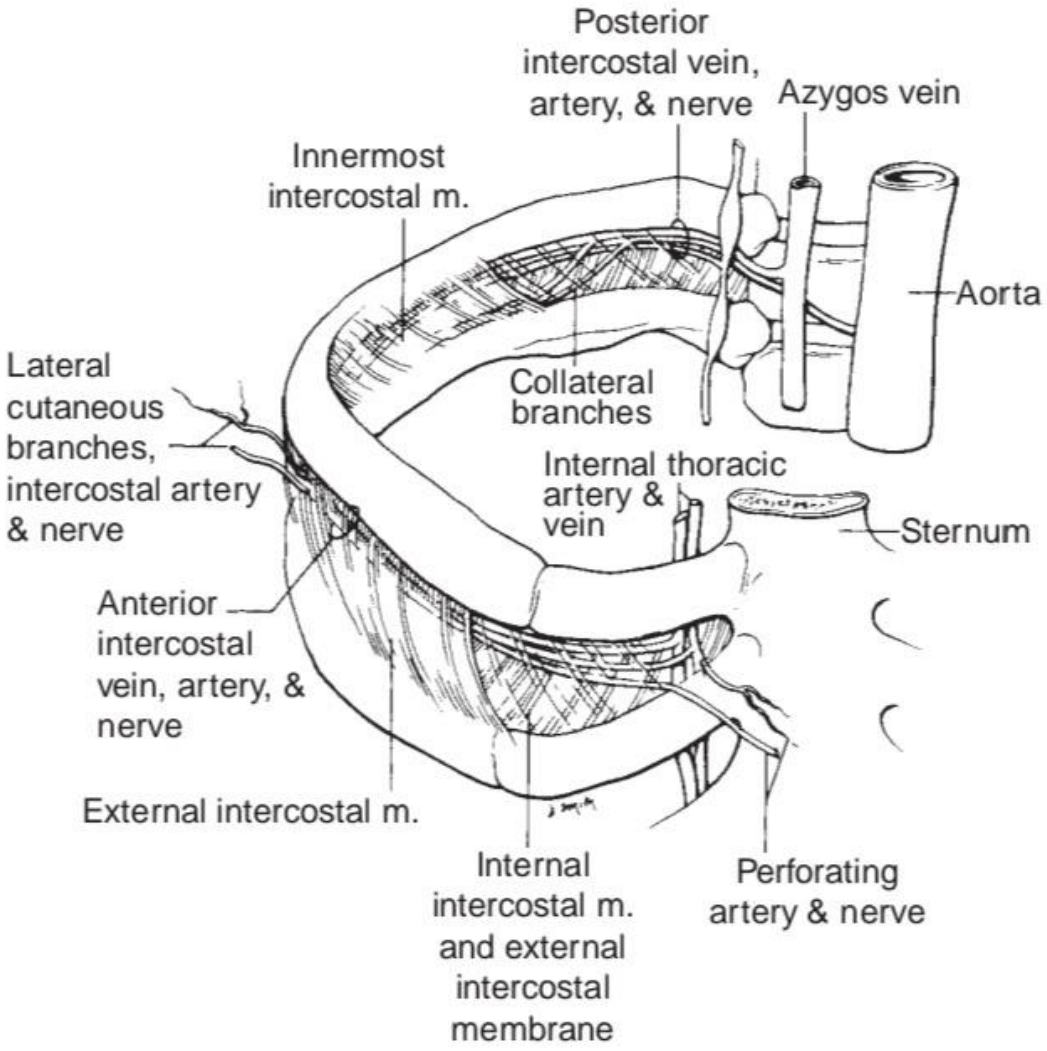

Nerves-related (During MRM)

1. Long thoracic nerve of Bell supplies serratus anterior.
2. Thoracodorsal nerve supplies latissimusdorsi.
3. Medial pectoral nerve (from medial cord of brachial plexus) which lies lateral, runs and winds from lateral margin of pectoralis minor.

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4. Lateral pectoral nerve arises from lateral cord passes through the pectorolis major either middle or medial part.
5. Intercostobrachial nerve is communicating nerve between lateral cutaneous branch of 2nd intercostal nerve and medial cutaneous nerve of arm; denervation of this nerve causes sensory loss of skin over upper medial and inner aspect of the arm, apex and lateral axilla.

Nerve supply of breast

Anterior and lateral cutaneous branches of 4th to 6th intercostal nerves.

Milk secretion is brought by prolactin hormone from anterior pituitary—not by nerves.

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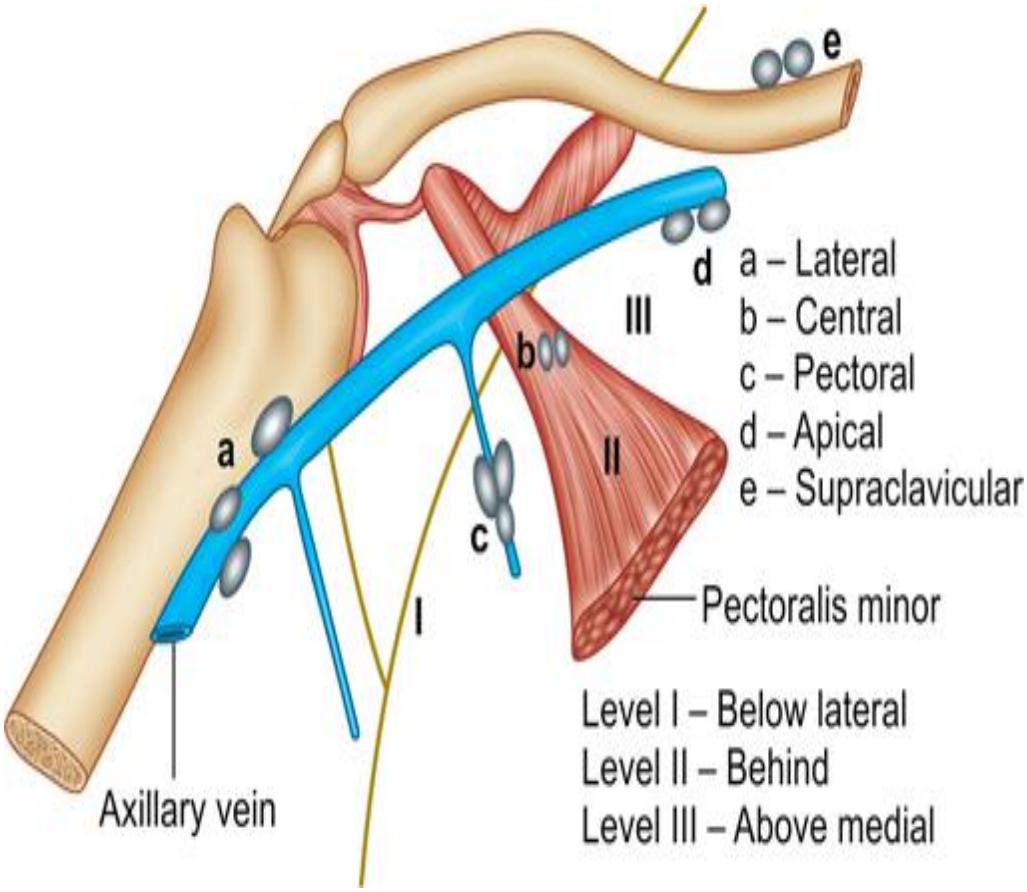
Lymphatic Drainage of the Breast



To axillary lymph nodes—75%.

1. Anterior group (pectoral, external mammary)—along lateral thoracic vessels. Main drainage node.
2. Central group—next common node. It is the node most easily properly clinically palpable in axilla.
3. Posterior group (subscapular)—rare to involve in carcinoma.
4. Lateral group—along axillary vein; rare to involve in carcinoma.

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5. Interpectoral node (Rotter's node)—signifies the retrograde spread of tumour. It lies between pectoralis major and minor.
6. Apical.- They are 4-6 nodes, also called as subclavicular or Halsted nodes. It lies most superior and deep to pectoralis minor medial to axillary vessels.

All axillary nodes drain into supraclavicular lymph nodes. 25% drains mainly from medial half of the breast into 2nd, 3rd and 4th intercostal space internal mammary lymph nodes.

Internal mammary nodes are located in retrosternal intercostal spaces 1-2 cm lateral to the sternal margin; it is vertically placed parallel to internal mammary vessels in relation to endothoracic fascia; its efferent ends in subclavicular nodes. Drainage into contralateral axilla and opposite lymph nodes also occur.

Levels of the axillary nodes (Berg's levels)

1. Level I : Below and lateral to the pectoralis minor muscle - anterior, lateral, posterior
2. Level II : Behind the pectoralis minor muscle - central
3. Level III : Above and medial to pectoralis minor muscle - apical

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CARCINOMA BREAST

When cancer occurs in the breast of women under forty, it is more rapid in its progress than when the patient is older, and also more extensive, remote sympathy likewise takes place more readily in them than in the old, so that the operation succeeds better in the latter on this account. — John Hunter, 1728-1793

Aetiology

WORLD DISTRIBUTION

Western countries -Carcinoma breast is more common

In African-American women, it is more aggressive.

It is less common in Japan, Taiwan.

It is second most common carcinoma in females. Incidence is 19-34%. Median age is 47 years. Carcinoma in one breast increases the risk of developing carcinoma on opposite breast by 3-4 times. Incidence of bilateral carcinoma is 2%.

It is more common after middle age, but can occur at any age group, after 20 years. It can be familial in 2-5% cases.

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GENETIC

Mutation of tumour suppressor genes BRCA1/BRCA2 is thought to be involved with high-risk of breast carcinoma. BRCA1 mutation is having more risk (35-45%) than BRCA2 mutation. It is located in long arm of chromosome 17, whereas BRCA2 is located in long arm of chromosome 13. BRCA1 more commonly shows ER negative status, high grade, aneuploid with raised S fraction than BRCA2 which shows ER positive status. BRCA1 is associated with increased risk in males.

Lifelong risk of breast cancer in BRCA1 and BRCA2 mutations is 50-70%. Both are associated with high-risk for ovarian cancer. Occasionally mutation of BRCA3 and p53 suppressor gene is also involved. Li-Fraumen's syndrome (LFS) is autosomal dominant condition with breast cancer inheritance (90%) along with sarcoma, leukemia, brain tumours, adreno cortical tumours. Diet low with phytoestrogens and high alcohol intake have high-risk of breast cancer. Vitamin C reduces the risk. It is more common in nulliparous woman.Attaining early menarche and late menopause have high-risk of breast malignancy.Early child-bearing and breastfeeding reduces the chances of malignancy. Early 1st child birth reduces the risk; late first child birth after 35 years increases the risk. It is more common in obese individuals.

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Breast cancer relative risk is qualified as relative risk (RR). If RR is 2.0 means, risk is twice the normal population. If RR is 0.5 means, risk is 50% less than normal population. Risk is 3-5 times more if 1st degree relative is having breast cancer. Risk is more if 1st degree relative is younger or premenopausal or having bilateral breast cancers. In males, occasionally gynaecomastia turns into carcinoma but not proved. Benign breast diseases with atypia, hyperplasia and epitheliosis has got higher risk in a patient with family history. RR in nonproliferative fibrocystic disease is 1.0; proliferative without atypia is 1.5; proliferative with atypia is 4.0 (with family history 6.5, premenopausal 6.0).

Cowden's syndrome—it is an autosomal dominant condition, with cutaneous facial lesion (100%), bilateral breast lesion (50%), GI polyps, brain, thyroid tumours. It is often associated with ataxia telangiectasia. Previous therapeutic radiation (thoracic) may predispose carcinoma breast especially when RT is given at younger age mainly for Hodgkin's lymphoma. Radial scar may predispose the carcinoma. It is a complex sclerotic condition of breast with microcyst, epithelial hyperplasia, adenosis, central sclerosis with lesions less than 1 cm in size. It mimics carcinoma clinically and mammographically. It is more common in

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individuals who are on oral contraceptive pills and hormone replacement therapy (HRT) for more than 5 years.

CONCEPTS

Presently carcinoma breast is considered as a systemic disease.

1. **Halsted concept** of spread is sequential spread. Breast—axillary lymph node—systemic spread.
2. **Fischer concept** is early to begin with itself, there is distant blood spread because of micrometastasis without nodal disease. Only tumour lesser than 1 cm size can be sequential.
3. **Spectrum concept** is new one where disease spreads loco-regionally as well as systemically which makes it to aim at both locoregional disease control as well as systemic disease control. Prior diagnosis of uterine/ovarian/colonic cancers.

Incidences in carcinoma breast

1. 30% of all female cancers
2. 20% of cancer related deaths in females
3. 2-4% bilateral
4. 2-5% hereditary

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PRESENTATION

1. Lump in the breast—most common presentation (75%)
2. 10% presents with pain 35-45% with mutation of BRCA1 gene

70% blood spread occurs to bones

Modified Gail risk assessment model

1. Age, age at menarche, age at 1st live child birth,
2. race
3. Number of 1st degree female relatives having breast cancer
4. Number of previous breast biopsies
5. Proliferative lesion with atypia

Breast carcinoma arising from lactiferous ducts is called as ductal carcinoma.

Breast carcinoma arising from lobules is called as lobular carcinoma. It is 10% common.

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Risk factors for breast carcinoma

- Breast carcinoma in 1st degree relative
- Breast carcinoma in contralateral breast
- BRCA1/BRCA2 gene mutation
- Obesity and alcohol intake
- Nulliparity
- Early menarche and late menopause

Insitu carcinoma

Preinvasive carcinoma which has not breached the epithelial basement membrane.

It may be:

- Ductal in situ carcinoma (Ductal Carcinoma In Situ, DCIS)
- Lobular in situ carcinoma (Lobular Carcinoma In Situ, LCIS).

Invasive carcinoma can occur eventually.

Classifications

I. Ductal carcinoma.

Lobular carcinoma.

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II. (a) In situ carcinoma (Noninvasive)

– DCIS (Ductal carcinoma in situ).

– LCIS (Lobular carcinoma in situ).

(b) Invasive. –

Invasive ductal carcinoma—most common type.

Adenocarcinoma with no special type (80%) is more common. 60% of this will show micro or macroscopic spread to axillary nodes. Invasive type can be special type or no special type (NST) [not otherwise specified/NOS].

Invasive lobular carcinoma. It is commonly multifocal and often bilateral.

III. Unilateral.

Bilateral—2-5% common.

IV. Unifocal.

Multifocal—tumour tissues within the same quadrant at multiple foci.

Multicentric—tumour tissues within the same breast but in different quadrant.

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Risk factors classification

Slight to moderate risk

- Florid hyperplasia
- Solid duct papilloma
- Obesity, alcohol, HRT
- Nulliparity , early menarche, late menopause

Moderate to high-risk

- Age > 60 years
- ATD / ALS/ LCIS
- History of DCIS
- Cancer on one side breast

Very high-risk

- Therapeutic radiation
- Family history of breast cancer in two 1st degree relatives
- Family history of breast and ovarian cancer
- BRCA1 and BRCA2 mutation carrier or 1st degree relative with mutation

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Foote Stewart original classification of invasive breast cancer

1. Paget's disease of nipple
2. Invasive ductal carcinoma (adenocarcinoma with productive fibrosis [scirrhous/simplex/no special type]—80%; medullary—4%; colloid—2%; papillary—2%; tubular and invasive cribriform—2%)
3. Invasive lobular carcinoma—10%
4. Rare other types—adenoid cystic, squamous cell, apocrine type

Classification of primary breast cancer

1. Noninvasive epithelial
    - LCIS
    - DCIS (intraductal)—papillary, solid, cribriform, comedo
    - Invasive epithelial
    - Invasive lobular—10%

2. Invasive ductal
        – Invasive ductal with NST (no special type)/NOS (not otherwise specifed)-70%
        – Tubular—2%
        – Colloid—2%
        – Medullary—5%

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- Medullary variant—basal like
- Invasive cribriform—2%
- Invasive papillary—1%
- Adenoid cystic—1%
- Metaplastic—1%

3. Mixed connective tissue and epithelial
    - Phyllodes,
    - angiosarcoma,
    - carcinosarcoma

Types of Carcinoma Breast

1. 1.***Scirrhous carcinoma***:

    It is 6% common. It is hard, whitish, or whitish yellow, noncapsulated, irregular, with cartilaginous consistency. It contains malignant cells with fibrous stroma.

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2. ***Medullary carcinoma*** (5%):

Also called as 'encephaloid type' because of its brain like consistency. It contains malignant cells with dispersed lymphocytes. Medullary variant with some features of pure form shows uniformly high grade aggressive tumour cells with negative ER, PR, HER2 NEU cell surface receptors (triple negative). They express molecular markers of basal/ myoepithelial cells and so now termed as basal-like breast cancers.

3. ***Inflammatory carcinoma/Lactating carcinoma/Mastitis carcinomatosis***:

Most aggressive type of carcinoma breast. It is 2% common. It is common in lactating women or pregnancy. It mimics acute mastitis because of its short duration, pain, warmth and tenderness. Clinically, it is a rapidly progressive tumour of short duration, diffuse, painful, warm often involving whole of breast tissue with occurrence of peau d' orange, often extending to the skin of chest wall . More than 1/3rd of skin over the breast is involved. Diffuse lymphoedema is due to tumour emboli within dermal lymphatics. Underlying localised palpable mass is not examined clinically. It should be differentiated from other LACB with skin involvement

where underlying palpable mass is well evident. Mammography may not show any finding except skin thickening. Inflammatory carcinoma of breast is a clinical diagnosis. Ductal or lobular type with cancer cells in dermal lymphatics is the histology. It rapidly metastasises to chest wall, bone and lungs. It is always stage IIIB carcinoma (T4d). FNAC confirms the diagnosis—it contains undifferentiated cells. Punch biopsy is ideal and better which shows undifferentiated cells. Total count is normal. Treatment- external radiotherapy and chemotherapy. Salvage surgery if possible. It has got worst prognosis. Differential diagnosis - Acute mastitis—total count is increased here.

4. ***Colloid carcinoma***:

It produces abundant mucin, both intra & extracellularly carrying better prognosis.

5. ***Paget's disease of the nipple***

It is superficial manifestation of an intraductal carcinoma. The malignancy spreads within the duct up to the skin of the nipple and down into the substance of the breast. It mimics eczema of nipple and areola. In Paget's disease, there is a hard nodule just

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underneath the areola, which later ulcerates and causes destruction of nipple. Histologically, it contains large, ovoid, clear Paget's cells with malignant features. Paget's hyperchromatic cells are located in rete pegs of epidermis containing intracellular mucopolysaccharides as clear halo in cytosol. It is 2% common. 90% is invasive ductal carcinoma. 70% shows mass underneath nipple and areola. Breast conservation surgery (BCS) is difficult here. MRM is needed.

6. ***Tubular, papillary, cribriform*** are other types of duct carcinomas.

7. ***Atrophic scirrhous carcinoma***:

Seen in elderly females. It is a slow growing tumour which has got better prognosis. FNAC is diagnostic. Mastectomy or curative brachytherapy is the treatment of choice. It is curable.

8. ***Lobular carcinoma in situ***:

It originates in terminal duct lobular unit only of female breast showing its distension and distortion. It is 12 times more common in white females. Predominantly perimenopausal. It is 3-5% common. High chance to predispose to invasive cancer. 35% of

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LCIS may develop invasive lobular carcinoma either in same or contralateral breast; 65% may develop invasive ductal cancer (same side/opposite side/both sides). LCIS is a marker/predictor of increased risk of invasive breast cancer; not an anatomical precursor unlike DCIS. It is now advocated as a risk factor for developing breast cancer. It is multifocal, bilateral (50%). It is an incidental pathological entity. Classical type carries better prognosis; pleomorphic type does not so; occasionally mixed ductal and lobular in situ may be seen. Clinically it does not form a lump. Need not be detected by mammography, as it does not turn to calcification.

BREAST IMAGING

Breast imaging techniques are used to detect small, nonpalpable breast abnormalities, evaluate clinical findings, and guide diagnostic procedures.

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MAMMOGRAM:

The primary imaging modality for screening asymptomatic women is mammography. During mammography, the breast is compressed between plates to reduce the thickness of the tissue through which the radiation must pass, separate adjacent structures, and improve resolution. On screening mammography, two views of each breast are obtained

1. Mediolateral
2. Craniocaudal.

For further evaluation of abnormalities identified on a screening mammogram or of clinical findings or symptoms, *diagnostic mammography* is indicated.

Magnification views are obtained to evaluate calcifications

Compression views are used to provide additional detail when a mass lesion is suspected. Sensitivity of mammography is limited by breast density, and 10% to 15% of clinically evident breast cancers have no associated abnormality on mammography.

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Digital mammography acquires digital images and stores them electronically, allowing manipulation and enhancement of images to facilitate interpretation. Digital mammography appears to be superior to traditional film-screen mammography for detecting cancer in younger women and women with dense breasts. Mammography in women younger than 30 years, whose breast tissue is dense with stroma and epithelium, may produce an image without much definition. As women age, the breast tissue involutes and is replaced by fatty tissue. On mammography, fat absorbs relatively little radiation and provides a contrasting background that favors detection of small lesions. Computer-assisted diagnosis increase the sensitivity and specificity of mammography and ultrasonography over review by the radiologist alone.

ULTRASONOGRAPHY

Ultrasonography is useful in determining whether a lesion detected by mammography is solid or cystic. Ultrasonography can also be useful for discriminating lesions in patients with dense breasts. It is not useful as breast cancer screening tool because it is highly dependent on the operator performance. Ultrasonography results in more false-positive values and requires repeat ultrasound and biopsies. screening ultrasonography doesnot reduce mortality caused by breast cancer.

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MAGNETIC RESONANCE IMAGING

MRI is used for the evaluation of breast abnormalities. It is useful for identifying

- The primary tumor in the breast in patients who present with axillary lymph node metastases without mammographic evidence of a primary breast
- Patients with Paget disease of the nipple without radiographic evidence of a primary tumor.

MRI also useful for assessing the extent of the primary tumor, particularly in young women with dense breast tissue, for evaluating for the presence of multifocal or multicentric cancer, for screening of the contralateral breast and for evaluating invasive lobular cancers.

MRI is used preoperatively to determine eligibility for breast conservation.

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American Cancer Society Risk Criteria for Breast Magnetic Resonance Imaging Screening

Women at high lifetime risk (≈20%-25% or greater) of breast cancer

- Known BRCA1 or BRCA2 gene mutation
- First-degree relative with BRCA1 or BRCA2 gene mutation
- Lifetime risk of breast cancer of ≈20%-25% or greater
- Radiation therapy to the chest between the ages of 10 and 30
- Li-Fraumeni syndrome or Cowden syndrome or a first-degree relative with one of these syndromes

Women at moderately increased (15%-20%) lifetime risk

- Lifetime risk of breast cancer of 15%-20% according to risk assessment tools based mainly on family history
- Personal history of breast cancer, ductal carcinoma in situ, lobular carcinoma in situ, atypical ductal hyperplasia, or atypical lobular hyperplasia
- Extremely dense breasts or unevenly dense breasts when viewed by mammograms

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Breast Imaging Reporting and Data System Final Assessment Category (BIRADS)

CATEGORY	DEFINITION
0	Incomplete assessment—need additional imaging evaluation or prior mammograms for comparison
1	Negative—nothing to comment on; usually recommend annual screening
2	Benign finding—usually recommend annual screening
3	Probably benign finding (<2% malignant)—initial short-interval follow-up suggested
4	Suspicious abnormality (2%-95% malignant)—biopsy should be considered
5	Highly suggestive of malignancy (>95% malignant)—appropriate action should be taken
6	Known biopsy—proven malignancy

Fine-Needle Aspiration Biopsy

Previously fine-needle aspiration biopsy (FNAB) was a common tool used in the diagnosis of breast masses.

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Procedure: FNAB be done with a 22-gauge needle, an appropriately sized syringe, and an alcohol preparation pad. The needle is repeatedly inserted into the mass while constant negative pressure is applied to the syringe. Suction is released, and the needle is withdrawn. The scanty fluid and cellular material within the needle are submitted in physiologically buffered saline or fixed immediately on slides in 95% ethyl alcohol. The slides are submitted for cytologic evaluation of the aspirated material.

Limitation of FNAB in evaluating solid masses is that cytologic evaluation does not differentiate noninvasive lesions from invasive lesions if malignant cells are identified. If FNAB demonstrates malignancy, a core needle biopsy is still required for definitive histologic diagnosis before surgical intervention. FNAB is much useful in the evaluation of a second suspicious lesion in the ipsilateral breast of a patient with a known malignancy. FNAB can be used to determine if the second lesion is malignant and confirm a diagnosis of multifocal breast cancer. It helps in determining the appropriate surgical plan. FNAB is commonly used is in the evaluation of lymph nodes that are suspicious on either physical examination or imaging, particularly high-resolution ultrasonography of the regional node. Suspicious lymph nodes can be evaluated by FNAB to determine whether metastatic disease is present. In

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this situation, FNAB has a reported sensitivity of approximately 90% and a specificity of up to 100%. Determining whether the tumor has spread to the lymph nodes is an important step in the initial staging of breast cancer that provides prognostic information and helps determine appropriate management strategies

Core Needle Biopsy

Core needle biopsy is the method of choice to sample breast lesions. Core needle biopsy can be performed under mammographic (stereotactic), ultrasound, or magnetic resonance imaging (MRI) guidance. Mass lesions that are visualized on ultrasonography can be sampled under ultrasound guidance, calcifications and densities that are best seen on mammography are sampled under stereotactic guidance. During stereotactic core needle biopsy, the breast is compressed, most often with the patient lying prone on the stereotactic core needle biopsy table. A robotic arm and biopsy device are positioned by computed analysis of triangulated mammographic images.

Procedure: After local anesthetic is injected, a small skin incision is made, and a core biopsy needle is inserted into the lesion to obtain the tissue sample with vacuum assistance. There are standards for the

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appropriate number of core samples to be obtained for each type of abnormality being sampled. A clip should be placed to mark the site of the lesion, particularly for small lesions that may be difficult to find after extensive sampling. The specimens should be imaged to confirm that the targeted lesion has been adequately sampled.

A similar approach is used for ultrasound-guided and MRI-guided biopsy of lesions. Specimen radiography of excised cores is performed to confirm that the targeted lesion has been sampled and to direct pathologic assessment of the tissue. A mammogram obtained after biopsy confirms that a defect has been created within the target lesion and that the marking clip is in the correct position. Image-guided localization with either a wire or iodine-125 (125I) radioactive seed and surgical excision are required if the lesion cannot be adequately sampled by core needle biopsy or if there is discordance between the imaging abnormality and pathologic findings.

The small samples obtained by core needle biopsy necessitate proper interpretation of the pathology results. Most patients undergoing core needle biopsy have benign findings and may return to routine screening with no other intervention required. If a malignancy is detected,

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histologic subtype, grade, and receptor status should be determined from the core needle biopsy sample. The patient may proceed to definitive treatment of the cancer if it is an early-stage breast cancer. Patients with locally advanced or inflammatory breast cancer should be treated with systemic chemotherapy before surgical intervention. Depending on the size of the imaging abnormality, approximately 10% to 20% of patients with a diagnosis of DCIS on core needle biopsy are found to have some invasive carcinoma at definitive surgery.

TNM Staging (AJCC Cancer Staging Manual, 2002, Sixth Edition)

Tumour:

Tx – Tumour cannot be assessed.

T0 – No evidence of primary.

Tis – Carcinoma in situ (DCIS or LCIS)

Tis Paget's – Paget's disease of nipple with no tumour (with tumour underneath is staged according to size)

T1 mic – Microinvasion < 0.1 cm.

T1— Tumour size < 2 cm in greatest diameter (T1a—0.1-0.5 cm; T1b—0.5-1.0 cm; T1c—1-2 cm).

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T2 – Size 2-5 cm.

T3 – Size > 5 cm.

T4 – Tumour fixed to chest wall or skin (T4a—fixed to chest wall, T4b—fixed to skin, T4c-T4a + T4b, T4d—inflammatory carcinoma breast).

Node:

NX – Nodes cannot be assessed.

N0 – No nodes.

N1 mic – Node with micrometasis.

N1 – Axillary nodes—ipsilateral, mobile, discrete.

N2

N2a – Axillary nodes—ipsilateral fixed to one another and other structures.

N2b – Clinically apparent and ipsilateral internal mammary nodes in the absence of clinically palpable axillary nodes.

N3 –

N3a – Spread to ipsilateral infraclavicular lymph nodes with or without axillary nodes.

N3b – Spread to ipsilateral internal mammary nodes and axillary nodes.

N3c –Spread to ipsilateral supraclavicular lymph nodes with/ without axillary or internal mammary nodes.

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Metastasis:

MX – Metastases cannot be assessed.

M0 – No metastasis.

M1 – Distant Metastases.

Staging

Stage I : T1N0M0

Stage IIa : T0N1M0; T1N1M0; T2N0M0.

Stage IIb : T2N1M0; T3N0M0

Stage IIIa : T0N2M0; T1N2M0; T2N2M0; T3N1M0; T3N2M0

Stage IIIb : T4N0M0; T4N1M0; T4N2M0

Stage IIIc : Any TN3M0

Stage IV : Any T, any N, M

Early breast cancer—Stage I and II; T1N1, T2N1; T3N0

Locally advanced breast cancer (LABC)—Stage IIIA, IIIB

Metastatic breast cancer—Stage IV

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Differential diagnosis for carcinoma breast

Fibroadenosis

Traumatic fat necrosis

Tuberculosis of breast

Filariasis breast

Mastitis

Antibioma

Galactocele

Mondor's disease

Cystosarcomaphyllodes

Triple assessment :

Clinical assessment

Radiological imaging US/MRI/ mammography (after 40 years)

Cytological or histological analysis FNAC/core biopsy

Treatment of carcinoma breast

It is usually through a combined approach

1. Surgery
2. Radiotherapy
3. Hormone therapy
4. Chemotherapy

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MANAGEMENT OF EARLY CARCINOMA BREAST

Modalities of Treatment

1. Breast conservative surgery (BCS)—ideally done as wide local excision with axillary dissection with RT to breast and chest wall.
2. Quadrantectomy as a part of QUART therapy may be used only in selected patients.
3. RT is given to the entire breast with 4500 cGy dose.
4. Patey's operation or simple mastectomy with axillary clearance.
5. Postoperative radiotherapy in high-risk patients.
6. Hormone therapy tamoxifen 10 mg BID or 20 mg OD.
7. Sentinel node biopsy when required.
8. Regular follow-up often with radioisotope bone scan and CEA tumour marker.

In early breast cancer, breast conservative surgery like wide local excision/quadrantectomy, axillary dissection (level I and II) and postoperative radiotherapy (to the breast) is used which prevents the disfigurement and psychological trauma of mastectomy to the patient. Tumour is removed with a rim of normal tissue. Wide excision and QUART therapy are different procedures. Wide local excision is ideal and better where clearance margin is 1 cm. In quadrantectomy entire

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segment with ductal system with 2-3 cm clearance margin is achieved. But it is not advocated now as there is no benefit in outcome (survival/recurrence rate) by quadrantectomy over wide local excision.

Indications for Total Mastectomy in Early Breast Cancer

When tumour is more than 4 cm.

Multicentric tumour.

Poorly differentiated tumour—high grade.

Tumour margin is not clear of tumour after breast conservative surgery.

Adjuvant therapy after surgery in early breast cancer

- Radiotherapy
- Chemotherapy—CMF, CAF regime commonly used. Taxanes are also used
- Endocrine manipulation:
  1. Ablation
  2. Tamoxifen (receptor antagonist)—20 mg/day for 5 years
  3. Aromatase inhibitors—blocks oestrogen production. Letrozole 2.5 mg OD
  4. LHRH agonists—Goserelin 3.6 mg/28 day's cycle for 2 years

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ADVANCED CARCINOMA BREAST

Locally inoperable (adherent to chest wall) tumour.

Inflammatory carcinoma of breast.

Fixed axillary lymph nodes, or supraclavicular lymph nodes, or opposite axillary nodes.

Bilateral carcinoma breast.

Metastatic carcinoma of breast, i.e. spread to bones, liver, lungs, brain.

Locally Advanced Carcinoma of Breast (LABC)

It means locally advanced tumour with muscle/chest wall involvement, extensive skin involvement or fixed axillary nodes. It will be T3, T4a, T4b, T4c or T4d or N2 or N3.

It is investigated by FNAC of tumour/core needle biopsy/ incision biopsy/mammography of opposite breast, chest CT, CT abdomen or whole body bone scan. Biopsy is needed to assess receptor status

Present strategy of treatment for LABC

Initial neoadjuvant (anterior) chemotherapy is given to downstage and achieve cytoreduction, to target possible micrometastases first, to assess chemosensitivity. FEC, CMF, CAF regimes are used.

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Response to chemotherapy is assessed by complete responders without palpable tumour; partial responders with > 50% decrease in tumour size; nonresponders with < 50% decrease in tumour size; progressive disease with > 25% increase in size

Patients with nonresponders and progressive disease are treated by RT to breast, chest wall, axilla and supraclavicular region; taxanes; hormone therapy; surgery if operable.

Responders are later treated with total mastectomy/MRM, occasionally BCS. After surgery remaining 3 or 4 cycles of chemotherapy are completed. Later hormone therapy should be given for 5 years (tamoxifen 20 mg OD). ER +ve (> 10 fmol/ mg) patients show 75% positivity

Stage IIIA patients are classified as operable and inoperable

Inflammatory Carcinoma of Breast Inflammatory carcinoma is T4d LACB (Stage IIIB)

It is initially treated by chemotherapy or radiotherapy and later if tumour reduces in size total mastectomy with axillary clearance can be done.

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But most often it is inoperable.

After surgery, chemotherapy and tamoxifen is given.

5-year survival for inflammatory carcinoma of breast is 25-30%.

Metastatic Carcinoma of Breast

- It is blood spread into different places like bone, lungs and pleura, liver, soft tissues, brain and adrenals. It is evaluated by FNAC/incision biopsy, chest CT, LFT, U/S abdomen, CT abdomen, whole body bone scanning, CT brain, tissue study for ER/PR/HER-2 Neu receptor status.
- It is stage IV disease.
- Bone is the most common site of metastasis. Spread to vertebra is through posterior intercostal vein and Batson's venous plexus (valveless). Vertebrae, ribs, upper end of humerus and femur are common bones involved.
- Lungs and pleural spread causes 'cannon ball' secondaries, effusion, consolidation, chest wall secondaries.
- Liver secondaries may develop either by haematogenous or through lymphatics across diaphragm from lower inner quadrant of breast.

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- Brain secondaries present with headache, vomiting, convulsions, localising features.
- Soft tissue secondaries has got better prognosis; visceral secondaries has got worst prognosis.
- Response to treatment decreases with number of organs involved with secondaries.
- Receptor negative secondaries are more aggressive.
- Median survival time for metastatic breast cancer is 24 months.

Treatment concept in metastatic carcinoma of breast

- To improve quality of life.
- To relieve pain of secondaries like bone, lungs.
- To relieve neurological problems like convulsions, space occupying cranial problems.
- Treatment strategy in metastatic carcinoma of breast

Chemotherapy—CMF, CAF, Taxanes in combination. Chemotherapy in metastatic breast cancer is useful (indicated/commonly used) in rapidly spreading visceral and skin secondaries, lymphangitis or when predicted disease free survival is less than 2 years; if response is negative for first line hormone therapy; in receptor negative status.

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High dose of chemotherapy using cyclophosphamide, cisplatin, carmustine, melphalan is tried in view to get high response rate of 55-70% along with bone marrow transplant. But toxic effects are often life-threatening. Its advantages are now doubtful when compared to toxic effects.

Haemopoietic growth factor is also used along with chemotherapy to enhance the cell kill with less bone marrow toxicity. It may also allow multiple high dose chemotherapy to increase the response rate.

Radiotherapy is used in bone metastasis, brain secondaries, to prevent paraplegia in spine involvement, and advanced axillary nodes. It is also used in painful bone secondaries, chest wall secondaries.

Hormone therapy has got important role. Tamoxifen, oophorectomy, adrenalectomy, androgens, progestogens, aminoglutethimide are used. It is useful in slow growing soft tissue or bone secondaries; or predicted disease-free survival is more than 2 years or age more than 35 years.

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Blockage of over expression of epidermal growth factor (EGF)/transforming growth factor alpha (TGF-alpha) which are related to ErbB1/ErbB2 receptors in relation to aggressive carcinoma factor is tried. Palliative surgeries done are total/toilet mastectomy, fixation of bones in case of pathological fractures, spinal cord decompression to prevent paraplegia, lung resection in case of localisedsecondaries, bilateral oophorectomy.

Trastuzumab (herceptin) is monoclonal antibody used in cancers with good results. It blocks the Her-2/Neu and ErbB2 receptors. Bevacizumab and lapitinab are other newer biological agents of different actions.

Metabolic complications like hypercalcaemia may be lifethreatening emergency in metastatic breast cancer. It is treated with hydration, steroids, biphosphonates (palmidronate, clodronate) 90 mg intravenously once a month. It also reduces the demineralisation of bone, fracture, pain and paraplegia.

Bone secondaries in carcinoma breast

- Most common site of blood spread (70%)
- Lumbar vertebrae, femur, pelvis

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- Pathological fracture can occur
- Spinal compression and paraplegia
- Radiotherapy, internal fixation, spinal decompression is required
- Biphosphonates 1600 mg/day

PROGNOSTIC FACTORS IN CARCINOMA BREAST Stage 5 yr survival

I 90%

II 70%

III 40%

IV 20%

- Age: Younger the age worser the prognosis.
- Sex: Carcinoma male breast has got worser prognosis compared to female breast. Because of early spread in carcinoma male breast.
- Stage I and II has got better prognosis.
- Atrophic scirrhous has got best prognosis.
- Medullary carcinoma has got better prognosis than scirrhous carcinoma because of lymphocytic infiltration.
- Invasive carcinoma has got worser prognosis.
- Inflammatory carcinoma breast has worst prognosis.

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- ER + ve tumours has got better prognosis.
- Differentiation also decides prognosis.
- Presence of elastic fibres in histology has got better prognosis.
- Tumour proliferation stages, growth factor and oncogene factors.
- Tubular, colloid, papillary types has got better prognosis.
- Tumour grade, growth factor and oncogene factors. ErbB2—Her-2/Neu positive has got poor prognosis. ErbB1 with overexpression of epidermal growth factor (EGF), TGF alpha and cathepsin D has got poor prognosis.
- DNA flow aneuploid status has got poor prognosis. Low S phase fraction (< 5%) has got good prognosis.
- Size of the tumour—tumour size less than 1 cm has got better prognosis.
- p53 tumour suppressor gene (guardian gene) shows bad prognosis.

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MODIFIED RADICAL MASTECTOMY

HISTORY OF BREAST CANCER SURGERY

In the second century ad, ***Galen***, on his classical clinical observation of a breast carcinoma, said: "We have often seen in the breast a tumor exactly resembling the animal the crab. Just as the crab has legs on both sides of his body, so in this disease the veins extending out from the unnatural growth take the shape of a crab's legs. We have cured this disease in its early stages, but after it has reached a large size, no one has cured it."

Beginning with ***Morgagni,*** surgical resections were more frequently undertaken, including some early attempts at mastectomy and axillary dissection. In the 18th century, ***le Dran*** incorrectly postulated that breast cancer was a local disease that spread by way of lymph vessels to axillary lymph nodes. When he operated on a woman with breast cancer, he routinely removed any enlarged axillary lymph nodes.

In 1867, ***C.H. Moore***, of the Middlesex Hospital, London reemphasized complete resection of the breast for cancer and stated that palpable axillary lymph nodes should also be removed.

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In 1877, ***Banks*** supported Moore's concepts and advocated the resection of axillary lymph nodes even when palpable lymphadenopathy was not evident, recognizing that occult involvement of axillary lymph nodes was frequently present.

In 1894, ***Halsted and Meyer*** reported their operations for treatment of breast cancer. By demonstrating superior locoregional control rates after radical resection, these surgeons established radical mastectomy . Both suggested complete dissection of axillary lymph node levels I to III. Resection of the long thoracic nerve and the thoracodorsal neurovascular bundle with the axillary contents was routine. This technical maneuver contributed significantly to the surgical management of the disease.

In 1943, ***Haagensen and Stout*** described the grave signs of breast cancer (a) edema of the skin of the breast; (b) skin ulceration; (c) chest wall fixation; (d) an axillary lymph node greater than 2.5 cm in diameter; and (e) fixed axillary lymph nodes. Based on the findings, they declared that women with grave signs were beyond cure by radical surgery.

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In 1948, ***Patey and Dyson*** suggested "modified radical" mastectomy for the management of advanced operable breast cancer. It involves removal of the breast and axillary lymph nodes with preservation of the pectoralis major muscle. They proved that removal of the pectoralis minor muscle allowed access to and clearance of axillary lymph node levels I to III (Patey modification)

Madden advocated a modified RM that preserved both the pectoralis major and minor muscles ,also this approach prevented complete dissection of the apical (level III) axillary lymph nodes.

By 1980s, the surgical procedure most frequently used by American surgeons for breast cancer was modified RM. The transition from the Halsted RM to the modified RM acknowledged that (a) extirpation of the pectoralis major muscle was not essential for locoregional control in stage I and stage II breast cancer and (b) neither modified RM nor Halsted RM consistently achieved locoregional control of stage III breast cancer.

Patients received a radical or a modified RM. Node-positive patients received adjuvant cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) chemotherapy or adjuvant melphalan. After a median follow-up

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of 15 years, neither type of surgery nor type of chemotherapy was shown to affect locoregional disease-free or overall survival.

Since the 1970s, considerable progress has been made in the integration of surgery, radiation therapy, and chemotherapy to control locoregional disease, to enhance survival, and to increase the possibility of breast conservation. Locoregional control is now achieved for nearly 80% of women with advanced breast cancers.

TECHNIQUE:

The patient is positioned in supine position and intubated & put near the edge of the operating side of the table. Arm placed perpendicular to body. Rolled towels are placed in thorax and the operating side shoulder to provide accecability to axilla.

Incisions :

1. Classic stewart incision
2. Modified stewart incision
3. Classic orr incision
4. Oblique orr incision

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Elliptical incision made includes nipple-areolar complex, skin overlying the breast tissue with 1-2 cm margin around the tumour.

Flap (ideal 7-8mm) raised at right angle medially upto sternum, laterally upto anterior border of lattismusdorsi, superiorly upto clavicle & inferiorly upto rectus sheath.

Breast parenchyma with pectoral fascia removed from underlying pectoralis major muscle from its medial attachment. Perforating vessels should be ligated. Lateral attachment divided until the lateral border of pectoralis major visualized. Pectoralis minor retracted. Axilla entered after dissecting axillary investing fascia. Retraction of pectoralis major exposes lateral pectoral nerve. Axillary vein identified. All loose areolar tissue removed within the following borders- superiorly axillary vein, laterally thoroco dorsal pedicle &subscapularis, inferiorly angular vein and medially long thoracic nerve of bell. Medial pectoral nerve preserved.

COMPLICATIONS

1. SEROMA- 50-70%
2. Pain- 30%
3. Numbness- 70%

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4. Injury to axillary vein
5. Shoulder dysfunction 10%
6. Flap necrosis
7. Infection
8. Lymphedema 15%
9. Winging of scapula
10. Numbness over medial upper arm
11. Pectoral muscle atrophy
12. Weakening of internal rotation & abduction of shoulder

BREAST RECONSTRUCTION

Immediate reconstruction.

In early stages of malignancies & advanced stages where the response to neoadjuvant chemotherapy has been good

Delayed reconstruction (3-9 months after surgery).

Types

1. Silicon gel implant under pectoralis major muscle.
2. Expandible saline prosthesis with prior tissue expansion.

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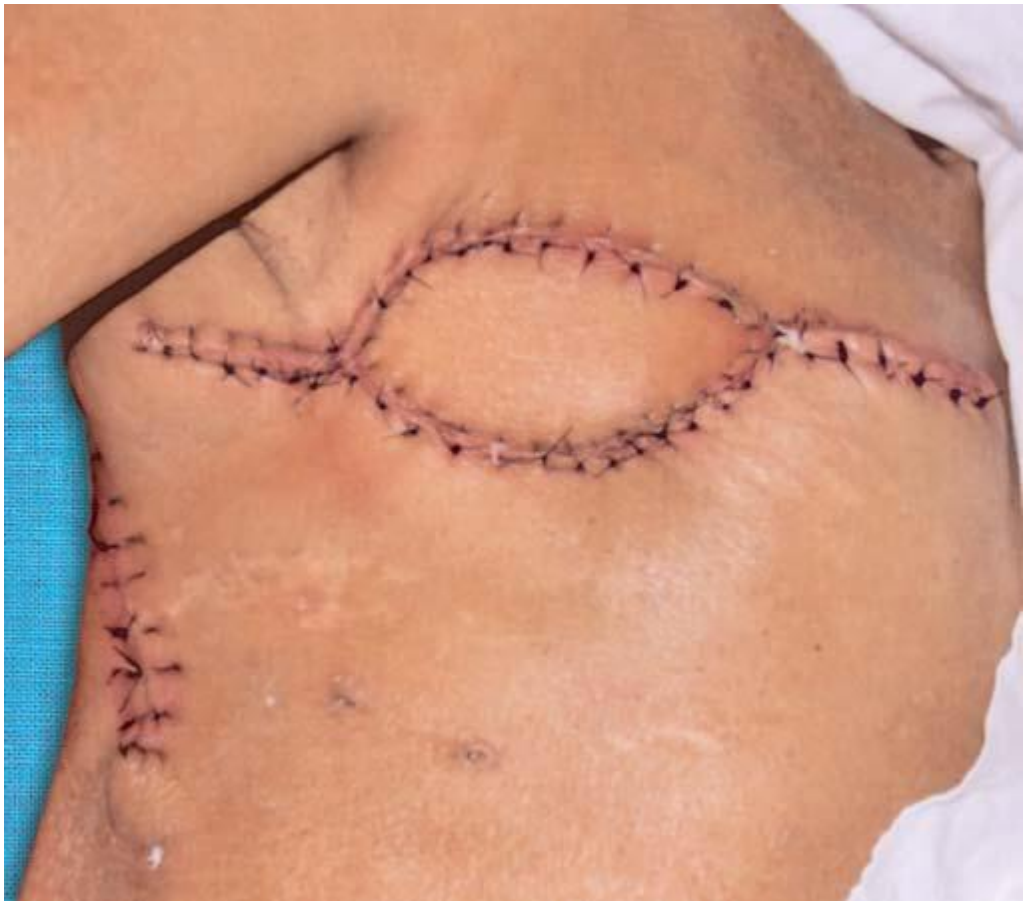
3. After radiotherapy latissimusdorsimusculocutaneous flap **(***LD flap*) or contralateral transversusabdominis muscle flap *(TRAM flap)* is used.
4. Superior gluteal flap based on superior gluteal vessels.
5. *Ruben's flap* using soft tissue pad overlying the iliac crest based on deep circumflex iliac vessels



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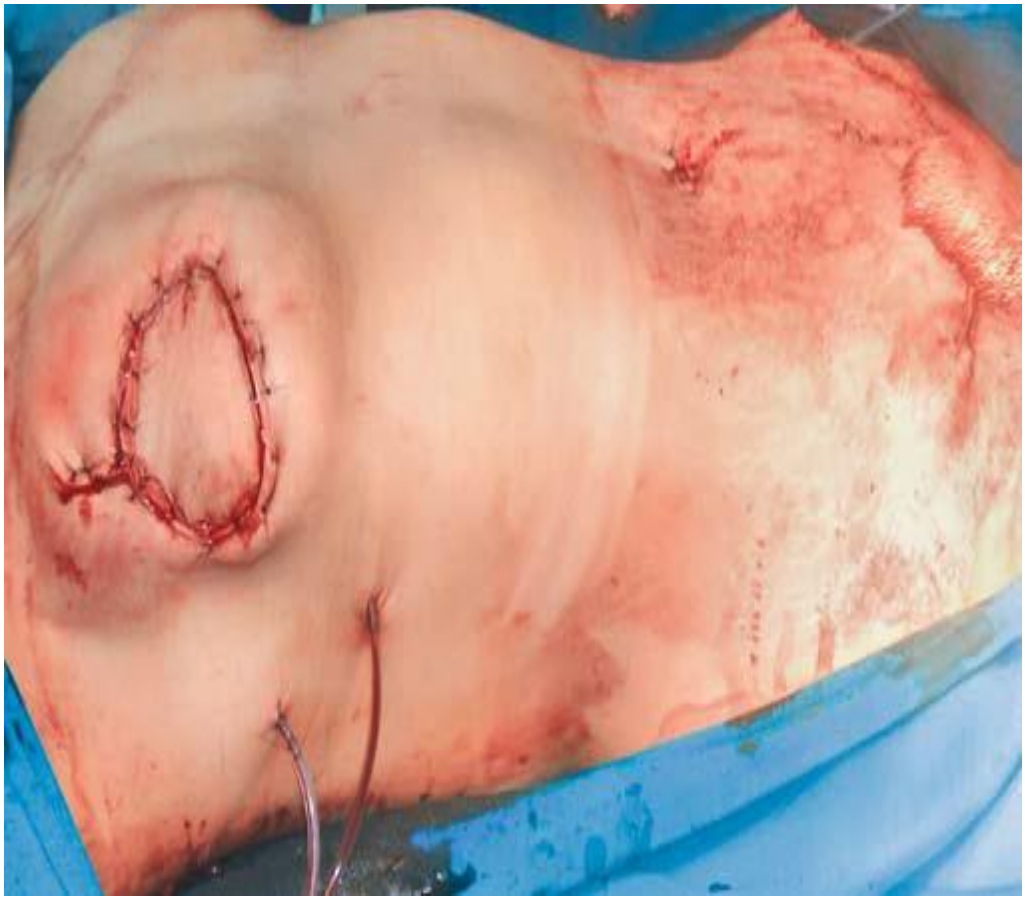

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METHODOLOGY

Title	"LOCAL INJECTION OF METHYLPREDNISOLONEACETATE TO PREVENT SEROMA FORMSTION AFTER MASTECTOMY"
Aim	To EVALUATE THE PROPHYLACTIC EFFECT AGAINST SEROMA FORMATION OF A SINGLE DOSE OF STEROID IN THE MASTECTOMY CAVITY
Objective	To assess the variation in the following outcomes in patients presenting with seroma formation after mastectomy with single dose of methylprednisoloneacetate given with those who were not given
study centre	Institute of general surgery. Madras medical college and rajiv Gandhi government general hospital, Chennai
Duration of study	January 2018 to may 2019
Study design	Randomized control trail
Sample size	40
Inclusion criteria	1.Age :18-70 2.female 3.primary breast cancer -mastectomy with sentinel node biopsy -mastectomy with/without sentinel node biopsy with axillary node dissection
Exclusion criteria	1) Patients of less than 18 years and more than 70 years. 2) Previous axillary surgery 3) Recent treatment with systemic steroid 4) Allergy to trial drug

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Ethical Clearance	Applied
Methodology	Patients who get admitted in Rajiv Gandhi hospital and who satisfy the inclusion and exclusion criteria will be observed and following data collected: 1. Details of participants including disease characteristics. 2. Details of type of intervention. 3. Details of outcomes reported. Patients who undergo mastectomy for primary breast carcinoma will be divided into two groups as Group1 and Group 2 based on randomization. Patients in Group 1 will be subjected to single dose of methylprednisoloneacetate and Group 2 will not subjected to single dose of methylprednisoloneacetate and the following will be studied. Formation of Seroma in the operative site . All the patients studied will have the following uniformly done: Installation of methylprednisoloneaceate into the mastectomy cavity at the time of drain removal .
Sponsorship(Yes/ No) If Yes details	No
Conflict of Interest	No

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SAMPLE SIZE CALCULATION:

Based on the study titled "Evaluation of wound complications in elective abdominal surgery by Sharma A.C., SinglaMamta, Shuaib Mohammad, Kumar Spandan, the sample size was calculated.

$$n=\frac{Z^2pq}{d^2}$$

(where N is required sample size, Z is reliability coefficient at 95% confidence interval, p is proportion of population with characteristics of interest is 23% [22] , d is the absolute error and ε is margin of error at minimum sample size)

Assuming a non-response rate of 10%, sample size is fixed at 40. Hence sample size is fixed at 40.

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis,

Percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significance in categorical data ChiSquare test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. In

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all the above statistical tools the probability value .05 is considered as significant level. Using odd's ratio, relative risk calculated

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RESULTS

The study included 40 patients who were selected with inclusion and exclusion criteria. All patients were followed up and the following results were obtained.

SEROMA FORMATION:

Among the 40 patients, all the 40 patients were females, diagnosed as CARCINOMA BREAST and undergone MODIFIED RADICAL MASTECTOMY. Inj methylprednisolone acetate were given to 20 patients & not given for 20 patients. In the given 20 patients , Seroma formation was present for 11(55%) patients & not present for 9(45%) patients against those who were not given had Seroma formation for 18 (90%) & no Seroma formation for 2(10%)patients. Hence inj methylprednisoloacetate significantly reduces Seroma formation . p value was 0.015

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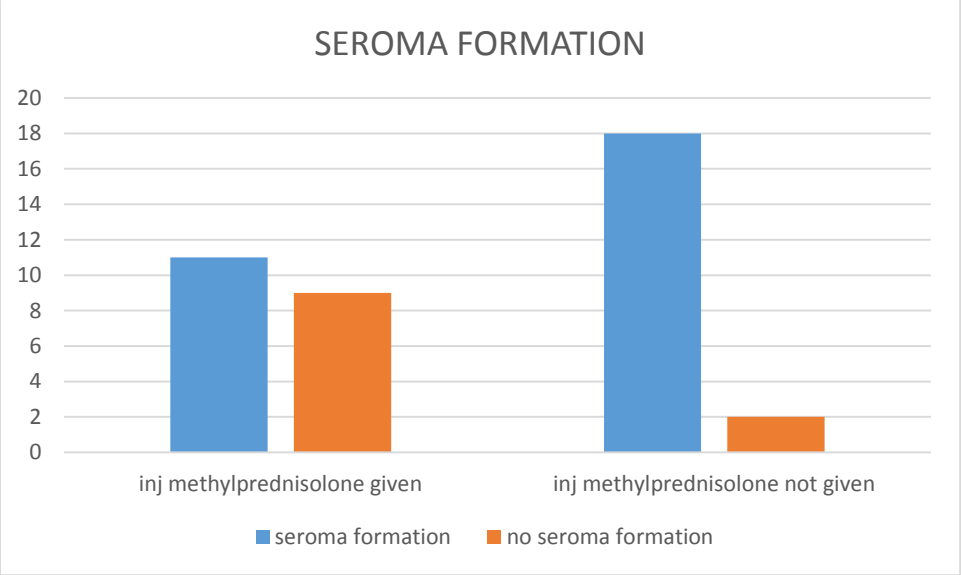
TABLE NO.1

Inj methylprednisolone acetate	Seroma formation		Total
	no	yes	
given	9	11	20
not given	2	18	20

GRAPH NO.1



Seroma formation was noted in total of 38% those who were given inj methylprednisolone acetate than 62% those who were not given inj methylprednisoloneacetate.

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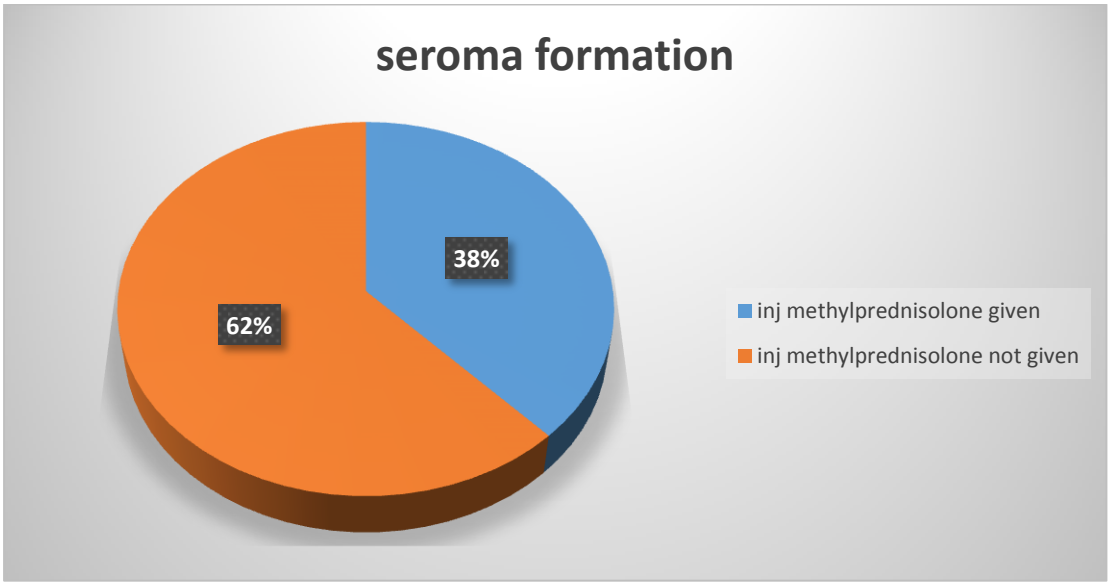
ODD'S RATIO:

$$\text{Odd's ratio} = \frac{a \times c}{b \times d}$$

Odd's ratio was found to be 7.36 and its positively correlated.

GRAPH NO 2- SEROMA FORMATION IN TOTAL STUDY



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Wound infection:

Wound infection was found in 10(50%) patients out of 20 patients who received inj methylprednisoloneacetate compared to 11 (55%) patients out of 20 patients those were not received. Hence there was not much difference among the patients who received & not received inj methylprednisoloneacetate in wound infection control. P value was found to be 0.751

TABLE NO 2

Inj methylprednisoloneacetate	Wound infection	No wound infection
Given	10	10
Not given	11	9

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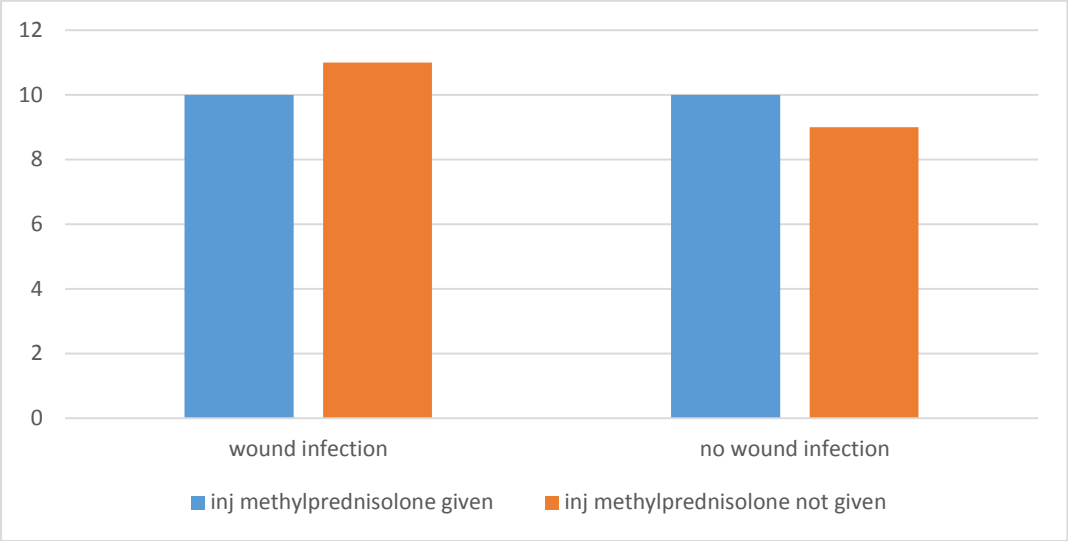
GRAPH NO-3


12
10
8
6
4
2
0
wound infection
no wound infection
inj methylprednisolone given
inj methylprednisolone not given

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WOUND DEHISCENCE:

Wound dehiscence was found in 9(45%) patients out of 20 patients who received inj methylprednisoloneacetate compared to 10 (50%) patients out of 20 patients those were not received. Hence there was not much difference among the patients who received & not received inj methylprednisoloneacetate in wound dehiscence. P value was fund to be 0.759

TABLE NO-3

	wound dehiscence	no wound dehiscence
inj hydrocortisone given	9	11
inj hydrocortisone not given	10	10

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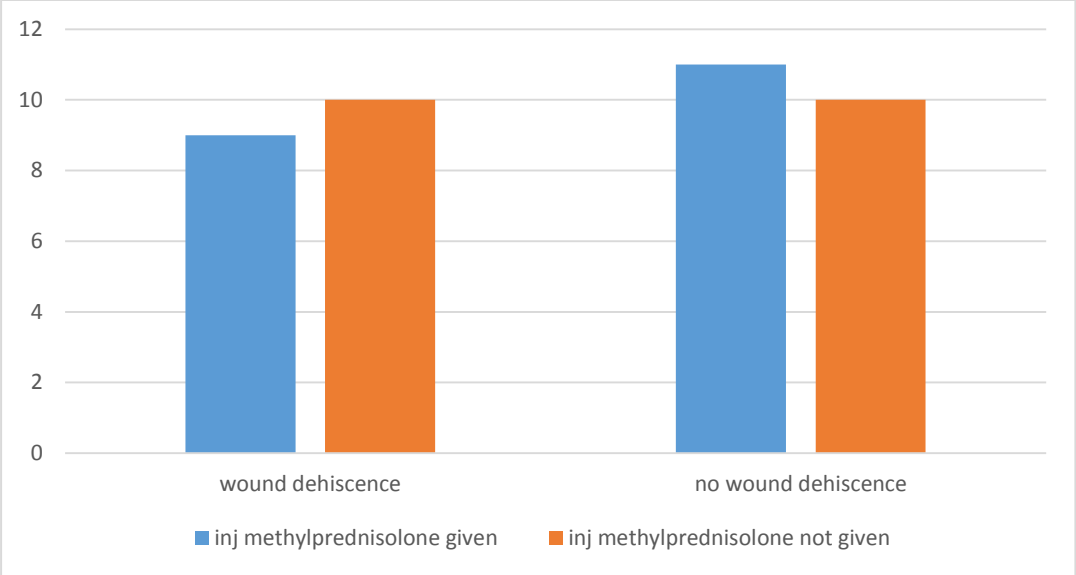
GRAPH NO -4


12
10
8
6
4
2
0
wound dehiscence
no wound dehiscence
inj methylprednisolone given
inj methylprednisolone not given

`

DISCUSSION

Seroma formation is by far the most common complication following breast surgery and the and the abundance of literature regarding various methods of its prevention is evidence enough that no single method is fully effective in its prevention Although still under research the pathogenesis of seroma formation has been associated with several precipitating factors.

Once dissection occurs, a dead space is created which is filled with serous fluid. This fluid then alters composition in the days following surgery. At first it resembles lymph with blood clots, indicating broken lymph and blood vessels due to the dissection [1, 2]. A few days later it transforms into an exudate, as the body reacts to the acute inflammatory condition following surgery. As the patient resumes moving her arm, lymphatic and blood vessels which are damaged by the dissection start oozing blood and lymph, which adds to the seroma. Therefore, the pathophysiology for seroma formation seems to be multifactorial with surgery as its trigger.

Steroids being anti-inflammatory drugs are thus an ideal candidate to be studied in preventing seroma formation which is patho-physiologically

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speaking; an inflammatory process [3]. Axelsson studied local injection of methyl prednisolone acetate versus saline in the mastectomy cavity at the time of drain removal while Taghizadeh, et al. studied patients who underwent latissimus dorsi reconstruction after mastectomy by randomizing them to either triamcinolone or saline in the cavity at the initial seroma puncture.

Qvamme G carried out a double blind randomized controlled intervention study of a single dose of 80 mg methylprednisolone versus saline on seroma formation after mastectomy. The authors observed a statistically significant reduction in the number of punctures, total seroma volume and the duration of seroma production [4, 5]. Turel, et al. applied the same technique on a rat model by injecting 30 mg/kg methyl prednisolone sodium succinate into the potential space beneath the skin flaps following Mastectomy and axillary lymph node dissection after 7th day of mastectomy, the seroma volumes were noted.

In our study, we found that injecting 120 mg of Depomedrol i/v one hour before surgery was a convenient mode of application, which helped decrease the average drain output and also decreased the days for which drainage was needed. This intervention also reduced the total incidence of

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seromas on 3rd post-operativeday as compared to the nonintervention group (i.e., 18% vs 6%) [6]. The only fact that needs consideration is the slightly higher incidence of wound infection (3% vs 9%) with steroid administration; this can be overcome with appropriate pre-operative antibiotics at intervention and post operatively. Reduction in total drainage days adds to patient comfort as well as reduces the demand for analgesia moreover the drain itself is also a source of infection.

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CONCLUSION

Since Seroma formation is the most common complication of Mastectomy and among the methods used to reduce its incidence, steroid administration seems to be the most cost effective and shows promising results. In the study , the use of methylprednisoloneacetate which is both cost effective and reduces seroma formation compared to those patients who doesn't receive inj methylprednisoloneacetate. Its routine use in every case is recommended under good antibiotic cover and wound care . local injection of methyl prednisolone has no effect in preventing wound infection and wound dehiscence.

BIBLIOGRAPHY

1. Hadi N, Soltanipour S, Talei A. Impact of modified radical mastectomy on health-related quality of life in women with early stage breast cancer. Arch Iran Med., 2012; 15(8): 504–7.
2. Wedgwood KR, Benson EA. Non-tumor morbidity and mortality after modified radical mastectomy. Ann Royal CollSurg Engl., 1992; 74(5): 314–7.
3. Sampathraju S, Rodrigues G. Seroma formation after mastectomy: pathogenesis and prevention. Indian J SurgOncol., 2010; 1(4): 328–33.
4. Gong Y, Xu J, Shao J, Cheng H, Wu X, Zhao D, et al. Prevention of seroma formation after mastectomy and axillary dissection by lymph vessel ligation and dead space closure: a randomized trial. Am J Surg., 2010; 200(3): 352–6.
5. Ribeiro GH, Kerr LM, Haikel RL, Peres SV, Matthes AG, DepieriMichelli RA, et al. Modified radical mastectomy: a pilot clinical trial comparing the use of conventional electric scalpel and harmonic scalpel. Int J Surg., 2013; 11(6): 496–500.

6. Ozaslan C, Yilmaz KB, Doğan I, Atalay C, Altinok M. Effect of mechanical closure of dead space on seroma formation in modified radical mastectomy. Turk J Med Sci., 2010; 40(5): 751–5.
7. Wolde B, van den Wildenberg FJ, Keemers-Gels ME, Polat F, Strobbe LJ.
8. Department F of Breast Surgery, Herlev Hospital, 2730 Herlev, Denmark. cax@dadlnet.dk
9. Randomized_clinical_trial_of_prevention_of_seroma_formation_after _mastectomy_by_local_methylprednisolone_injection
10. Gonzalez EA, Saltzstein EC, Riedner CS et al. Seroma formation following breast cancer surgery. Breast J 2003;9:385-8.
11. Kuroi K, Shimozuma K, Taguchi T et al. Pathophysiology of seroma in breast cancer. Breast Cancer 2005;12:288-93.
12. Watt-Boolsen S, Nielsen VB, Jensen J et al. Postmastectomyseroma. A study of the nature and origin ofseroma after mastectomy. Dan Med Bull 1989;36:487-9.
13. McCaul JA, Aslaam A, Spooner RJ et al. Aetiology of seroma formation in patients undergoing surgery for breast cancer. Breast 2000;9:144-8.

14. Schulze S, Andersen J, Overgaard H et al. Effect of prednisolone on the systemic response and wound healing after colonic surgery. Arch Surg 1997;132:129-35.
15. Taghizadeh R, Shoaib T, Hart AM et al. Triamcinolone reduces seroma re-accumulation in the extended latissimusdorsi donor site. J PlastReconstrAesthetSurg 2008;61:636-42. www.openepi.com/menu/openEpiMenu.htm
16. Okholm M, Axelsson CK. No effect of steroids on seroma formation after mastectomy. Dan Med Bull 2011;58:A4241.
17. Kuroi K, Shimozuma K, Taguchi T et al. Evidence-based risk factors for seroma formation in breast surgery. Jpn J ClinOncol 2006;36:197-206.
18. Kumar S, Lal B, Misra MC. Post-mastectomy seroma: a new look into the aetiology of an old problem. J R CollSurgEdinb 1995;40:292-4.
19. Porter KA, O'Connor S, Rimm E et al. Electrocautery as a factor in seroma formation following mastectomy. Am J Surg 1998;176:8-11.
20. Baker EA, Leaper DJ: Proteinases, their inhibitors, and cytokine profiles in acute wound fluid. Wound Repair Regen 2000;8:392-8.

21. Doolin EJ, Tsuno K, Strande LF et al. Pharmacologic inhibition of collagen in an experimental model of subglottic stenosis. Ann OtolRhinolLaryngol 1998;107:275-9.

22. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. J Am CollSurg 2002;195:694-712.

23. Mettler L, Salmassi A, Heyer M et al. Perioperative levels of interleukin-1beta and interleukin-6 in women with breast cancer. ClinExpObstetGynecol 2004;31:20-2.

24. Khan AL, Larsen F, Heys SD et al. Peri-operative acute phase response and cytokine release in women with breast cancer: modulation by polyadenylic-polyuridylic acid. Eur J SurgOncol 1999;25:574-9.

s no	name	age	sex	ip no	diagnosis	procedure	inj hydro-cortisone	seroma formation	wound infection	wound dehiscence
1	malathi	45	F	10743	CA breast	MRM	given	yes	yes	yes
2	nagarathin	60	F	4439	CA breast	MRM	not given	yes	yes	yes
3	vijaya	55	F	8564	CA breast	MRM	given	yes	yes	yes
4	amudha	46	F	11243	CA breast	MRM	not given	yes	yes	yes
5	valli	58	F	6357	CA breast	MRM	given	yes	yes	yes
6	maragatha	64	F	7645	CA breast	MRM	not given	yes	yes	yes
7	muniyamn	66	F	10221	CA breast	MRM	not given	yes	yes	yes
8	pushpa	43	F	37628	CA breast	MRM	given	no	no	no
9	lakshmi	50	F	5536	CA breast	MRM	given	yes	yes	yes
10	deivanai	61	F	1192	CA breast	MRM	given	no	no	no
11	kavitha	42	F	75643	CA breast	MRM	given	yes	yes	yes
12	kanagavall	66	F	5690	CA breast	MRM	not given	yes	yes	yes
13	indra	67	F	7765	CA breast	MRM	not given	yes	yes	yes
14	saroja	59	F	6540	CA breast	MRM	given	yes	yes	yes
15	ellamal	67	F	10003	CA breast	MRM	given	yes	yes	yes
16	revathy	47	F	9980	CA breast	MRM	not given	yes	yes	yes
17	devi	44	F	789	CA breast	MRM	not given	yes	yes	no
18	jothi	38	F	5643	CA breast	MRM	given	no	no	no
19	alamelu	54	F	23089	CA breast	MRM	given	no	no	no
20	manonmar	64	F	51111	CA breast	MRM	given	yes	yes	yes
21	selvi	45	F	4120	CA breast	MRM	given	no	no	no
22	rukku	56	F	5179	CA breast	MRM	not given	yes	yes	no
23	bhavani	30	F	3917	CA breast	MRM	not given	no	no	no
24	roja	50	F	52770	CA breast	MRM	given	yes	yes	yes
25	sankari	37	F	8920	CA breast	MRM	not given	yes	yes	yes
26	malini	55	F	6606	CA breast	MRM	not given	yes	yes	yes
27	vasantha	66	F	72301	CA breast	MRM	not given	yes	no	no
28	rajeshwari	38	F	65397	CA breast	MRM	not given	yes	no	no
29	kuppamal	66	F	2199	CA breast	MRM	given	yes	yes	yes
30	vimala	43	F	10134	CA breast	MRM	given	yes	no	no
31	nirmala	28	F	32019	CA breast	MRM	not given	no	no	no
32	logeshwari	44	F	35545	CA breast	MRM	not given	yes	no	no
33	yasodha	54	F	44432	CA breast	MRM	given	no	no	no
34	uma	58	F	665	CA breast	MRM	not given	yes	no	no
35	maheshwa	60	F	7180	CA breast	MRM	given	no	no	no
36	nagammal	66	F	78911	CA breast	MRM	given	no	no	no
37	valli	51	F	7181	CA breast	MRM	not given	yes	no	no
38	kavitha	55	F	3918	CA breast	MRM	given	no	no	no
39	jhansirani	58	F	11207	CA breast	MRM	not given	yes	no	no
40	megala	48	F	2200	CA breast	MRM	not given	yes	no	no