THE STUDY OF SURVIVAL OUTCOMES, PROGNOSTIC AND TREATMENT-RELATED FACTORS IN PATIENTS OFBREAST CANCER TREATED WITH POST-OPERATIVE RADIATION THERAPY

THESIS

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AIIMS, Jodhpur **Dr. Rishi P Nair**

All India Institute of Medical Sciences, Jodhpur

DECLARATION

I hereby declare that the thesis titled "**The study of survival outcomes, prognostic and treatment-related factors in patients of breast cancer treated with post-operative radiation therapy**" embodies the original work carried out by the undersigned at All India Institute of Medical Sciences, Jodhpur.

Dr. Rishi P Nair

Department of Radiation Oncology

All India Institute of Medical Sciences

Jodhpur (Rajasthan)

All India Institute of Medical Sciences, Jodhpur

CERTIFICATE

This is to certify that the thesis titled "**The study of survival outcomes, prognostic and treatment-related factors in patients of breast cancer treated with post-operative radiation therapy**" is a record of the bonafide research work of **Dr. Rishi P Nair** carried out under our guidance and supervision in the Department of Radiation Oncology, Department of Surgical Oncology, Department of Cardiology and Department of Pathology, All India Institute of Medical Sciences, Jodhpur, Rajasthan. Dr. Rishi P Nair has learned and performed all the clinical and analytical procedures involved in the study under guidance and supervision.

GUIDE:

DR PUNEET PAREEK

Additional Professor,

Department of Radiation Oncology

All India Institute of Medical Sciences, Jodhpur

CO-GUIDES:

DR JEEWAN RAM VISHNOI

Associate Professor

Department of Surgical Oncology

PROF. POONAM ELHENCE

Head of Department

Department of Pathology

DR SURENDRA DEORA

Additional Professor,

Department of Cardiology

All India Institute of Medical Sciences, Jodhpur

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Forwarded & Recommended by

GUIDE

Dr. Puneet Pareek

Additional Professor & Head of Department

Department of Radiation Oncology

All India Institute of Medical Sciences, Jodhpur

DEDICATED

TO

MY MOTHER

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Dr. Rishi P Nair

LIST OF ABBREVIATIONS

EBC	EARLY BREAST CANCER
LABC	LOCALLY ADVANCED BREAST CANCER
LN	LYMPH NODE
N+	NODE POSITIVE
RT	RADIATION THERAPY
QOL	QUALITY OF LIFE
ER	ESTROGEN RECEPTOR
PR	PROGESTROGEN RECEPTOR
HER-2	HUMAN EPIDERMAL GROWTH FACTOR-2
NACT	NEO ADJUVANT CHEMOTHERAPY
EORTC	EUROPEAN ORGANIZATION FOR RESEARCH AND TREATMENTOF CANCER
HRQOL	HEALTH RELATED QUALITY OF LIFE
NCCN	NATIONAL COMPREHENSIVE CANCER NETWORK
5FU	5 FLUORO-URACIL
GY	GRAY
IV	INTRAVENOUS
RCT	RANDOMISED CONTROLLED TRIAL
TEC	TAXANE, EPIRUBICIN, CYCLOPHOSPHAMIDE

TAC	TAXANE, ADRIAMYCIN, CYCLOPHOSPHAMIDE
FEC	5FU, EPIRUBICIN, CYCLOPHOSPHAMIDE
AC-T	ADRIAMYCIN CYCLOPHOSPHAMIDE F/ TAXANE
OS	OVERALL SURVIVAL
PFS	PROGRESSION FREE SURVIVAL
DFS	DISEASE FREE SURVIVAL
LVI	LYMPHOVASCULAR INVASION
PNI	PERINEURAL INVASION
DCIS	DUCTAL CARCINOMA IN SITU
LCIS	LOULAR CARCINOMA IN SITU
MTD	MAXIMUM TOLERABLE DOSE
OAR	ORGANS AT RISK
BSC	BEST SUPPORTIVE CARE
GLOBOCAN	GLOBAL CANCER OBSERVATORY
NSABP	NATIONAL SURGICAL ADJUVANT BREAST AND BOWEL PROJECT (NSABP)
CALGB	CANCER AND LEUKEMIA GROUP B
SEER	SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS PROGRAM
ACOSOG	ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY
SOFT	SUPPRESSION OF OVARIAN FUNCTION TRIAL
TEXT	TAMOIFEN AND EXEMESTANE TRIAL

EBCTCG	THE EARLY BREAST CANCER TRIALISTS' COLLABORATIVE GROUP
START	THE UK STANDARDISATION OF BREAST RADIOTHERAPY
FAST	FASTer RADIOTHERAPY FOR BREAST RADIOTHERAPY
OCOG	ONTARIO CLINICAL ONCOLOGY GROUP
TROG	TRANS-TASMAN RADIATION ONCOLOGY GROUP
RMH/GOC	ROYAL MARSDEN HOSPITAL AND GLOUCESTERSHIRE ONCOLOGY CENTRE
BACCARAT	BREAST CANCER AND CARDIOTOXICITY INDUCED BY RADIOTHERAPY
HF-WBI	HYPOFRACTIONATED- WHOLE BREAST IRRADIATION
CF-WBI	CONVENTIONAL FRACTIONATED - WHOLE BREAST IRRADIATION
ALND	AXILLARY LYMPH NODE DISSECTION
SLNB	SENTINEL LYMPH NODE IOPSY
PCR	PATHOLOGICAL COMPLETE RESPONSE
PBCR	POPULATION-BASED CANCER REGISTRY
HBCR	HOSPITAL-BASED CANCER REGISTRY
ESMO	EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY.
WHO	WORLD HEALTH ORGANISATION
IHC	IMMUNOHISTOCHEMISTRY
TNBC	TRIPLE NEGATIVE BREAST CANCER
BCS	BREAST CONSERVATIVE SURGERY

MRM	MODIFIED RADICAL MASTECTOMY
PMRT	POST MASTECTOMY RADIOTHERAPY
3DCRT	3D CONFORMAL RADIOTHERAPY
VMAT	VOLUMETRIC MODULATED ARC THERAPY
LAD	LEFT ANTERIOR DESCENDING ARTERY
LCX	LEFT CIRCUMFLEX ARTERY
LCA	LEFT CORONARY ARTERY
MHD	MEAN HEART DOSE
CTRCD	CANCER THERAPY-RELATED CARDIAC DYSFUNCTION
LVEF	LEFT VENTRICULAR EJECTION FRACTION
NT PRO BNP	N-TERMINAL (NT)-PRO HORMONE BNP
MPI	MYOCARDIAL PERFORMANCE INDEX
TWPTE	T WAVE PEAK TO END TIME
BRCA	BREAST CANCER GENE
PIC3KA	PHOSPHATIDYLINOSITOL-4,5-BISPHOSPHATE 3-KINASE CATALYTIC SUBUNIT ALPHA
PTEN	PHOSPHATASE AND TENSIN HOMOLOG DELETED ON CHROMOSOME 10
RTOG	RADIATION THERAPY ONCOLOGY GROUP
LA	LOCALLY ADVANCED
LRC	LOCOREGIONAL CONTROL
RFS	RECURRENCE FREE SURVIVAL

DRFI	DISEASE RECURRENCE FREE INTERVAL
BCSS	BREAST CANCER SPECIFIC SURVIVAL
CTRT	CONCURRENT CHEMORADIOTHERAPY
GNI	GROSS NATIONAL INCOME
OC	ORAL CONTRACEPTIVES
HRT	HORMONE REPLACEMENT THERAPY
BD/BID	TWICE DAILY
SBRT	STEREOTACTIC BODY RADIOTHERAPY
R/M	RECURRENT OR METASTATIC
OBD	OPTIMUM BIOLOGICAL DOSE
QLQ	QUALITY OF LIFE QUESTIONNAIRE
ECOG PS	EASTERN COOPERATIVE ONCOLOGY GROUP PERFORMANCE STATUS
LFT	LIVER FUNCTION TEST
KFT	KIDNEY FUNCTION TEST
CBC	COMPLETE BLOOD COUNT
CPMS	COMPUTERISED PATIENT MANAGEMENT SYSTEM
T2DM	TYPE 2 DIAETES MELLITUS
BC	BREAST CANCER
BMI	BODY MASS INDEX
OPD	OUTPATIENT DEPARTMENT

LRR	LOCAL RECURRENCE RATES
MTX	METHOTREXATE
CR	COMPLETE RESPONSE
PD	PROGRESSIVE DISEASE
PR	PARTIAL RESPONSE
CTCAE	COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS

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INTRODUCTION

BACKGROUND

BURDEN OF DISEASE:

With the advances in medical sciences heralding in an era where mortality due to diseases such as stroke and coronary heart disease are on a decline; cancer is now taking the spotlight as one of the leading causes of death worldwide with an estimated count of 1.3 million new cancer cases and 10 million cancer deaths worldwide in 2020. With an incidence of 2.3 million cases, female Breast cancer has now overtaken Lung cancer as the most commonly diagnosed cancer worldwide.(1) Breast cancer is also the most common cancer among Indian females with an age adjusted rate of 25.8 per 100,000 women and mortality of 12.7 per 100,000 women (2)

When compared to the Western population, Indian women's breast cancer epidemiology is very different. In India, a bigger percentage of breast cancer patients tend to be premenopausal, and the peak age is between 40 and 50 years. In the Western world, the median age of women at the time of breast cancer diagnosis is roughly 61 years, with the peak age being 60 to 70 years.(3)

OVERVIEW OF STAGING AND SUBTYPES:

Invasive ductal carcinoma and invasive lobular carcinoma account for 80% to 85% and 10% to 15% of all occurrences, respectively, of invasive breast cancer. The remaining 1% of invasive breast cancers are other histologic cancer subtypes.

The expression of biomarkers such the human epidermal growth factor receptor 2 (HER-2), progesterone receptor (PR), and oestrogen receptor (ER) determines how IHC is characterized. Approximately 75% of patients with breast cancer are thought to have hormone receptor (HR)-positive pathology, defined as having ER and PR expression of greater than 1%. Additionally, according to IHC measurements, HER2 is amplified or overexpressed in 15% to 30% of breast cancer cases. Triple-negative breast cancer (TNBC) refers to tumours that do not express ER, PR, or overexpress HER2. These tumours are more aggressive and have greater metastasis and recurrence rates than other breast cancer subtypes. The prevalence of TNBC is estimated to be 31% in India, which is substantially greater than the prevalence of 12% to 17% in the West. Lehmann et al. further identified the different groups named in TNBC subtypes Basal like-1, Basal like-2, Immunomodulatory,

Mesenchymal, Mesenchymal Stem Cell like, and Luminal Androgen depending upon expression of distinct genes(4)

The American Joint Committee on Cancer's Cancer Staging Manual, 8th edition, expanded breast cancer staging in 2017 by integrating prognostic biomarkers (such as histologic tumour grade, ER, PR, HER2, and multigene test-based risk prediction) with the traditional anatomic TNM staging. This was done in consideration of the significance of molecular characterization. There are currently many different combinations of anatomical, clinical, and prognostic breast cancer stages as a result of this.(3)

MOLECULAR PATHOGENESIS AND RISK FACTORS FOR BREAST CANCER

There are three main genetic routes for cancer development(5):

1) **Dominant route** (50-60%): Individuals with germline BRCA2 mutations inherit them. These cancers frequently have chromosome 16q loss, gain in chromosome 1q and mutations to PIK3CA. These cancers lack HER2 and are ER positive. As their mRNA expression pattern resembles that of healthy breast luminal cells, ER positive tumors are often known as "luminal" cancers.

2) **Pathway connected to HER2 gene amplifications on chromosome 17q:** These make up 20% of malignancies. They are ER-positive or ER-negative tumors that are HER2-positive. TP53 germline mutations are most frequently associated with this pathway breast cancer in patients (Li-Fraumeni syndrome)

3) **Pathway independent of ER-mediated changes in gene expression & HER2 gene amplifications:** This subtype includes 15% of all cases of breast cancer. They are HER2 and ER-negative. Germline BRCA1 mutations are frequently linked to tumors. Associated with mutations in TP53.The "basal like" pattern of mRNA expression found in tumors resembles that of healthy myoepithelial cells.

Risk factors for breast carcinoma include Age ,Age at menarche , Age at first live birth , First degree relatives with breast cancer , Atypical hyperplasia , Race/Ethnicity , Estrogen exposure , Breast density , Radiation exposure , Prior Benign breast disease , Diet - Alcohol , Obesity , Breast feeding , Carcinoma of contralateral breast(5)

Maria at al demonstrated that 9 risk factors had potential causal effects on breast cancer-specific survival: alcohol consumption, BMI, height, mammographic density, menarche, menopause, physical activity, smoking, and T2DM.(6)

CLINICAL PRESENTATION:

Since there are few mammographic facilities in this area and no national breast-screening program, breast lumps continue to be the most common mode of presentation; In addition to this, the prevalence of traditional medicine practitioners in many locations, genetic, social, and cultural factors, as well as the proximity to medical centers with cancer facilities, have a significant impact on incidence and survival.(7)Younger age group has been associated with larger tumor size, higher number of metastatic lymph node, poor grade, low rate of hormone receptor status and poorer overall survival. (8)

MANAGEMENT OF BREAST CANCER

BC management is multidisciplinary and has advanced significantly. Mastectomy followed by adjuvant chemotherapy was once a common course of treatment for locally advanced BC, triple-negative breast cancer, and tumors expressing HER2neu (human epidermal growth factor receptor. Currently, it combines both a systemic therapy method that targets the entire body and a loco-regional approach that uses surgery and radiation therapy to focus on just the tumor. Endocrine therapy, chemotherapy, anti-HER2 therapy, bone stabilizing drugs, polymerase inhibitors for BRCA (breast cancer gene) mutation carriers, and, more recently, immunotherapy are all examples of systemic therapy. But the majority of patients continue to have primary ablative surgeries. A promising method for diagnosing diseases with hormone receptors is gene expression profiling.

We have come a long way from employing chemotherapy medications like cyclophosphamide, methotrexate, etc. in the 1970s to using their modified procedures such anthracycline-based combination chemotherapy in the 1980s and 1990s. The most recent additions, taxanes, have a bright future. In order to lessen normal tissue toxicity and overall treatment time, BC radiation therapy has progressed from 2D to 3D conformal radiotherapy and expedited partial breast irradiation. Intensity-modulated radiation therapy and deep inspiration breath-hold are two of the more recent advances, although they are still out of reach for many people. With brachytherapy, the situation is the same.

Triple-negative breast cancer has terrible prognoses, and the only real therapeutic option is systemic chemotherapy. The current landscape of BC treatment may shift as a result of immunotherapy, poly(adenosine diphosphate-ribose) polymerase inhibitors, and antibody-drug conjugates. Therefore, making a sensible choice is crucial.

A practical alternative to complete mastectomy and breast conservation therapy is provided by the rapidly developing specialty of oncoplastic breast surgery. Oncoplastic breast surgery is still in its infancy but is anticipated to become widely used in the near future due to its economic viability, cost-effectiveness, and suitability for a low-resource country like India.(9)

PROGNOSIS OF BREAST CANCER

The prognosis of breast cancer patients in India as seen by P. Viral et al showed an 10 year overall survival(OS) of 66% and Breast cancer specific survival(BCSS) of 70%(10) which is comparable to the global average (11). Increase in breast cancer survival also becomes apparent as we trace follow up data over the years (12)which can be mainly attributed to the myriad improvements and discoveries made in managing breast cancer from Halstead's Radical mastectomy to Patey's modification of Halstead approach, Bernard Fisher's contributions in Breast conservative surgery to impact of Oophorectomy as shown by Thomas Beatson, in the surgical aspect; as well as development of more effective and lesser toxic Radiotherapy and chemotherapy regimens through the years.

The risk of disease recurrence has shown to have decreased with radiation from 60% to 70% and 50% to 60%, for invasive and non-invasive breast cancer respectively, by a variety of studies(13–16). Newer techniques are being researched to further decrease dose to normal tissue and Organs at risk such as heart and lung. Some studies have even shown dose to coronary arteries as a better surrogate marker to cardiac toxicity compared to mean heart dose.

This study aims at evaluating patients of non-metastatic breast cancer who have received adjuvant radiation at our center and correlating risk factors, prognostic factors and survival outcomes in the same.

AIMS AND OBJECTIVES

Aim of study-

To study the survival outcomes, prognostic and treatment related factors in patients of breast cancer treated with post-operative radiation therapy in AIIMS, Jodhpur.

Objectives-

Primary Objective-

1. To assess the treatment outcomes as Overall Survival, Disease-free survival, Progression-free survival.
2. To study various dose related parameters to the target, Organs at Risk (OARs) like Heart, Coronary vessels ; biopsy and IHC status and available clinical information about cardiac health including investigations like Echocardiography if done.

Secondary Objective-

1) Assessing the demographic profile of the patients suffering from the disease.

REVIEW OF LITERATURE

Epidemiology:

The advances in the management of breast cancer have now brought hope to the patients suffering from this commonest malignancy of females worldwide. The prognosis also depends on many factors including the quality of health care received. A recent study by Sankaranarayanan et al showed that patients of localized breast cancer and metastatic breast cancer had a 5 year OS of 89.6% and 26.7% respectively in countries such as Hong Kong, Singapore, and Turkey, where health services are well developed with advanced diagnostic and treatment centers and high per head GNI values; compared to a 5 year OS of 76.3% and 14.9% respectively in countries such as India, Costa Rica, Philippines, etc. with moderately developed facilities.(17)

The International agency for research on cancer has shown a projected estimate of 0.27 million and 3 million new breast cancer cases in India and worldwide respectively between 2020 and 2040 with an estimated mortality of 0.15 million and 1 million in India and worldwide respectively, during the same duration with almost half the world breast cancer incidence and mortality concentrated in Asia.(18,19)

A study by Ajay Gogia et al from AIIMS, Delhi revealed the TNM (AJCC-7th edition) stage distribution of Breast cancer patients as: Stage I was represented by 4.01%, stage II by 32.70% , stage III by 42.02%, and stage IV by 21.26% patients.(20)

Sundriyal et al in his study revealed that male breast cancer incidence in India was around 1.03% which was similar to western data which show a prevalence of 0.9%. But he also showed that male breast cancer in India occurred at a younger age group(60 years) compared to western population.(21,22) Saxena et al revealed in his study of breast cancer patients in North India that the religious distribution of breast cancer patients included 87%, 7.7% and 5.3% belonging to Hindus, Muslims and Christian communities respectively.(23)

Kakkar et al in his study showed that only 2 patients, or 0.48% of the women under observation, had bilateral breast lesions, whilst 45.95% of the women had left-sided breast tumor’s, 225 patients, or 53.57% of the women, had right-sided breast tumor’s indicating that right-sided breast cancer is more common in the North Indian population.(24)

Infiltrating ductal carcinoma (96%) was the most common histologic subtype seen in Indian studies(20)

Risk Factors:

As per Makhoul et al(25), risk factors for breast cancer can be divided into 3 categories:

1) Due to increased and prolonged oestrogenic stimulation.
2) Due to exposure to exogenous carcinogens such as tobacco, alcohol and others.
3) Genetic mutations causing decreased ability to repair mutations (BRCA ½, PTEN, p53, etc)

Age less than 35 is a stand-alone risk factor for more aggressive features such as ER/PR negativity, high grade, node-positivity, Bilateral malignancy, and increased risk of recurrence. With every decrease in age by 1 year in women aged less than 35 years, the risk of death increases by 5%. Meanwhile, this mortality risk was not seen in patients aged 35-50.(26,27)

Women who have 2 or more relatives having breast cancer show a 2.5-fold increase in the risk of breast cancer. A family history of ovarian cancer can also be a predisposition for breast cancer, especially in those with BRCA 1/2 mutations.(28,29)

The occurrence of certain events, including pregnancy, breastfeeding, age of menarche, menopause, as well as their duration and any accompanying hormonal imbalance, are therefore critical in determining the likelihood of inducing carcinogenic processes in the breast microenvironment which is especially susceptible to changes in estrogen status. Pregnancy has been long considered a protective factor against breast cancer. In fact, Anders Husby et al in his study involving a cohort of 2.3 million Danish women demonstrated that this protective effect was restricted mainly to those pregnancies lasting longer than 34 weeks and was not translated to those at 33 weeks or below.(30)

Analysis of the Women's CARE Study, a population-based case-control study of breast cancer patients revealed that while lactation is linked to a lower risk of both receptor-positive and negative tumor’s; parity, and age at first birth are solely linked to a lower risk of receptor-positive tumor’s. This implies that lactation and parity both portray their protective function through different mechanisms.(31)

Mahavir et al in his study of breast cancer in Northern India discovered that when BMI at the time of diagnosis increased, so did the likelihood of having breast cancer. 46.1% of the study participants had a BMI that was within the normal range (18.5-23) in the current study. In comparison to patients with normal BMI, those with BMIs < 18.5 had a lower risk of acquiring breast cancer. Although other studies showed that the risk of breast cancer with obesity was more pronounced in the post-menopausal patients, his study showed the predilection in both pre and post-menopausal patients.(32)

McCarthy et al studied the relationship of established risk factors with breast cancer subtypes. (33)All four tumor subtypes were linked to higher risks of breast density, with ER/PR+HER2 and TNBC showing a larger correlation among premenopausal women. However, there were different sets of risk factors for TNBC (age, race, BMI, and density), ER/PR+HER2+ (prior biopsy, atypical hyperplasia, BMI, and density), ER/PR-HER2+ (family history and density), and ER/PR+HER2- (age, race, prior biopsy, atypical hyperplasia, age at first birth, age at menarche, family history, BMI, and density). Additionally, they discovered that TNBCs were more likely than other subtypes to be diagnosed as interval malignancies and had a lower screen detection rate.

Anothaisintawee et al in his meta-analysis showed that Breast cancer risk is markedly increased by Oral Contraceptive use, Hormone Replacement Treatment, and Diabetes Mellitus. When compared to women who weren't exposed to these factors, the risk associated with exposure to them was 10% to 23% higher. On the other hand, breastfeeding may reduce the incidence of breast cancer by about 10%. The results of subgroup analyses based on Caucasian and Asian studies showed that the effects of DM and breastfeeding on breast cancer risk were comparable to general pooling in both Caucasians and Asians, however the impacts of OC in the 2 subgroups produced nonsignificant effects. Additionally, HRT's effects were only seen in Caucasians and not in Asians.(34)

Prognostic factors:

Age: Dinshaw et al in his study from Tata Memorial Hospital demonstrated that Although age >40 was associated with a trend towards improved survival, it was not statistically significant. Age under 40 years old was only linked to an increase in local recurrence. (35)

Clinicopathologic findings supported earlier studies showing that younger women had breast tumor's that were larger (P =.012), more severe (P =.0001), more lymph node-positive (P

=.008), less ER-positive (P =.027), more frequently overexpressed Her2/neu (P =.075), and tended to have worse disease-free survival.(36)

Other international studies have also shown that In addition, across all histological subtypes and stages, breast cancer survival rates are much lower for women under 40 than for older women. The debate, however, centers on whether age in and of itself is a risk factor for a poorer prognosis. This theory has been debunked by a number of studies, which instead suggest that the influence of early age on outcome is only a reflection of the overrepresentation of other known prognostic pathological variables.(37,38)

Religion

Although there were significant differences in the stages of the disease at diagnosis between Hindu, Muslim, Christian, and Parsi communities, Badwe et al study's of the clinical and pathological characteristics, patterns of relapse, and prognosis of breast cancer in these groups of people found no differences in the overall 5-year survival. Even after matching for illness stage and menopausal state, this held true.(39)

Menstrual status and BMI

Klienfeld et al in his study suggest that breast cancer in menstruation women has a worse prognosis and is more likely to be malignant, especially in younger age groups.(40)

In their meta-analysis, Zahra et al. showed that the incidence of breast cancer during the premenopausal period is not significantly influenced by body mass index. On the other hand, in the postmenopausal population, being overweight or obese may have a minor but considerable impact on breast cancer.(41)

In order to incorporate the association between BMI as an indicator of obesity and prognosis in breast cancer, a meta-analysis was conducted by Ryu et al. The results of this study revealed that high BMI had a negative impact on the prognosis in breast cancer with statistical significance.(42)

Laterality of Breast cancer

Amer et al demonstrated in his trial that there were no significant relationship between Laterality and survival but a SEER analysis showed that site of primary had a impact on

survival favouring right over left and upper and lower inner quadrants showing better prognosis.(43,44)

Pre-surgical staging of breast cancer

Sathwara et al showed in his review of breast cancer survival studies in India that presurgical staging was an independent risk factor for survival.(45)This is also demonstrated in a study by Sant et al in the EUROCARE group study(46) in which Overall, the five-year relative survival rate was 79%; however, it ranged from 98% for early, node-negative (T1N0M0) tumours to 87% for big, node-negative (T2-3N0M0) tumours to 76% for node-positive (T1-3N+M0) tumours to 55% for locally progressed (T4NxM0) tumours to 18% for metastatic (M1) tumours.

Role of Neoadjuvant chemotherapy

A meta analysis by Chen et al showed that NACT had no role in survival outcomes but presence of pathological complete response corresponded with better survival when compared to Adjuvant chemotherapy resulting in increase in the rate of BCS.(47) This was similarily seen in an Indian systematic review and meta analysis by Mona Pathak et al which showed NACT has no major impact on breast cancer survival. However, it is associated with increased BCS rates. NACT downgrades tumour size facilitating more BCSs without increasing LRR. The evidences were graded for all outcomes as high except DFS and BCS as moderate.(48) However another meta analysis on TNBC patients showed that in terms of enhancing OS and DFS, NACT with a pathological complete response outperforms AC-T. However, when patients have residual illness, the results are the opposite.(49)

Nodal Dissection

Nair et al in her study demonstrated that nodal positivity significantly correlated with the Disease free survival in both Early breast cancer and LABC.(50) Risk of death was still significantly lower for cases with 10 or more lymph nodes removed compared to no nodes removed. Risk of death increased significantly with increased number of positive nodes and increased ratio of positive to total nodes removed.(51)

Histopathological findings

James R Bundred et al in his studies, showed that Following breast conserving surgery for early-stage, invasive breast cancer, involved or close pathological margins are linked to greater local and distant recurrence. Obtaining a minimum clean margin of at least 1 mm should be the goal for surgeons. Tumor on ink margins and close margins were linked to higher rates of local and distant recurrence when compared to negative margins. Compared to wider (tumour >2 mm) margins, positive or narrow margins (tumour on ink or <2 mm) were linked to higher mortality rates.(52)

Zhang et al also showed in his meta-analysis indicating favourable prognosis for the mucinous, tubular, and papillary subtypes of breast cancer. HR+/LN- patients with Mucinous Carcinoma, Tubular Carcinoma, Papillary Carcinoma, Adenoid Cystic and Cririform Carcinoma likely derive no benefit from adjuvant chemotherapy.(53)

Emre et al in his trial showed that LVI(lympho-vascular invasion) and perineural invasion (PNI) are poor predictors of long-term survival in individuals with late recurrence. On the early and late recurrences, molecular subtypes and LVI were successful. However, only the early recurrence was linked to lymph node positivity and grade. LVI and PNI were the prognostic variables for DFS after 5 years.(54)Other studies have also shown the negative prognostic effect of PNI,LVSI on Locoregional recurrence rates.(55)

Nehmat et al demonstrated in her meta analysis that the triple negative and HER2+/HR- subtypes had the highest likelihood of reaching pCR, and there was evidence that adding HER2-directed therapy with NAC had a significant impact on achieving pCR in the latter subtype. Choudhary et al demonstrated that all other tumour groups had noticeably better probabilities of reaching pCR following neoadjuvant chemotherapy compared to hormone receptor-positive tumours with HER2-negative status. Better DFS and OS results were linked to hormone receptor status and achieving a pCR after neoadjuvant chemotherapy, especially in patients with HER2-positive and TNBC malignancies.(56,57)

Bloom et al in his landmark trial demonstrated the significant differences in overall survival between grades as 75%,47%, 32 % for Grade 1,2 and 3 respectively.(58)

Saber et al in his study of 29833 patients showed that the most often diagnosed subtype (59.0%) was luminal A, which also had the highest survival rates. Triple-negative had the lowest survival rates. Age and stage at diagnosis had a dose-response effect on the risk of

death for all subtypes, with the HER2-enriched subtype showing the strongest association. Severe comorbidity (Charlson Comorbidity Index score 3) also raised the risk for all molecular subtypes.(59) However, pathological node involvement and triple negativity (HR 1.9, 95% CI 1.36-2.90, p = 0.001) were linked with poor OS. Clinical stage (stage III), triple negativity, and HER2 neu positivity were associated with worse RFS.(20) Compared to populations in the West, India has a significantly greater prevalence of TNBC. Up to one in three breast cancer patients may have triple-negative illness. In India, patients with breast cancer may experience poor outcomes as a result of this finding.(60)

Aness et al demonstrated that although not statistically significant, the prevalence of DCIS was linked to a tendency toward increased 5-year disease-free survival and overall survival. Additionally, DCIS was linked to younger patient ages, smaller tumour sizes, fewer palpable tumours, more high-grade tumours, and invasive ductal histology. However, DCIS was not a independant indicator of increased disease-free or overall survival.(61)

Determinants of survival in metastatic disease

Chen et al in a SEER population-based analysis showed that elderly individuals in stage IV patients were less likely to just have distant lymphatic dissemination and more likely to have lung metastasis. bone continued to be the most frequent site of breast cancer metastasis (65.1%), followed by the lung (31.4%), liver (26.0%), and brain (8.8%) metastasis. Compared to older patients (28.3%), a higher percentage of younger (34.9%) and middle-aged (36.2%) patients had numerous metastatic locations. Elderly patients had the worst prognosis in terms of both overall survival and survival from breast cancer specifically, whereas younger patients had the greatest prognosis. Furthermore, compared to other metastatic patients, patients with bone metastases only had better survival. The groups with only brain metastases and numerous sites of metastasis had the worst prognoses.(62)

The total median survival period following metastasis was one month for liver metastasis, three months for brain metastases, and 12 months for bone and lung lesions. Patients with numerous metastatic locations had a median survival of 7.5 months. There was no connection between survival after metastasis and time before relapse.(63)

Management of Breast Cancer:

Neoadjuvant chemotherapy in breast cancer

Nearly 41.7% of all breast cancer patients in India receive neoadjuvant chemotherapy(20). Chemotherapy administered before or after surgery had no different effects on disease-free (DFS) and overall survival, according to large clinical trials like EORTC 10902 and NSABP B-18. Other advantages (such as converting mastectomy patients to breast-conserving surgery [BCS]) and some potential drawbacks have been researched and are widely acknowledged. The most popular neoadjuvant chemotherapy (NAC) regimen for all early breast cancer subtypes, anthracycline plus taxanes-based chemotherapy, is linked to high rates of clinical response (up to 90% in NSABP B-27). Trastuzumab with or without Pertuzumab should be given concurrently with a taxanes to patients with breast cancer that has tested positive for the human epidermal growth factor receptor 2 (HER2) gene. In the GeparSixto and CALGB 40603 investigations, the inclusion of carboplatin resulted in a higher pathological complete response (pCR) rate for patients with triple negative breast cancer (TNBC), despite increased toxicity and without a significant increase in BCS rate.(64)

Surgery in breast cancer-Significant changes have been made to breast surgery over time. First, up until the 1960s, Halsted's radical mastectomy was widely accepted as the norm of care. Patey developed the modified radical mastectomy (MRM), which removes the breast, pectoralis major fascia, and level I and II axillary lymph nodes, in order to lower morbidity. In contrast to less invasive procedures, patients treated with Halsted radical mastectomy did not significantly outlive their counterparts, according to the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-04 trial. Additionally, it was discovered that standard axillary lymph node dissection (ALND) is excessively aggressive in node-negative disease. As a result, this trial signalled the shift toward a more conservative surgical approach to treating breast cancer. When combined with radiation therapy, BCS was first proven to be a viable therapeutic option for early invasive breast cancer in the NSABP B-06 trial . When compared to patients who underwent modified radical mastectomy, participants receiving BCS with or without radiation showed no appreciable change in overall survival (OS) or disease-free survival (DFS). In patients who received lumpectomy without radiation, the rate of local regional recurrence (LRR) was considerably greater. BCS was further established by the Milan Cancer Institute (Milan I Study) as the accepted standard of therapy for early breast cancer (less than 2 cm in diameter). The adoption of treatments like nipple/skin sparing

mastectomy in patients who have tumours with fewer favourable characteristics than those in the studies in which these approaches were initially evaluated is also plausible given the popularity of newer, less invasive mastectomy techniques.

In the past ten years, axilla management has transformed. The quality of life is significantly impacted by ALND's severe morbidity, which includes lymphedema, restricted shoulder movement, and arm sensory problems. The NSABP B32 experiment proved that ALND has no survival benefit in people with a negative SLNB. Nodal involvement is categorised as solitary tumour cells, macro-metastatic (>2mm), or micro-metastatic (2mm) (ITC). In patients with ITC or micro-metastatic disease on SLNB, many surgeons no longer perform ALND as a result of the findings of the IBCSG 23-01 and AATRM 048 studies.

For many surgeons, the ACOSOG Z0011 was a game-changer. Following breast conserving surgery (BCS), SLNB, and adjuvant whole-breast irradiation, patients with T1 to T2 cancers and fewer than 2 positive SLNs were randomly assigned to receive ALND versus no ALND. In comparison to individuals who received ALND, the SLNB group had better 5-year OS and DFS. The ALND group also had a higher 10-year LRR, however it was not statistically significant.(65)

Bloom proposed the current best known grading scheme in 1950. His initial classification was based on three key characteristics: the degree of tubule development, nuclear characteristics, and mitotic activity. Low grade and high grade tumours were his two categories for categorising breast carcinomas. This classification was improved By Bloom and Richardson's modification in 1957. He included a score of 1 to 3 to each criterion according to mild, moderate, or marked degrees without altering the elements of classification. Scores ranged from 3 to 9 overall. Elston changed this classification further by limiting its use to invasive ductal carcinoma and omitting particular varieties such mucinous, medullary carcinoma. By measuring the mitotic activity, Elston and Ellis changed the Bloom and Richardson grading system. This is also known as the Bloom and Richardson system as modified by Nottingham.(66)

Post surgical response assessment-There are several techniques for assessing the effectiveness of chemotherapy on tumours, including:Residual Cancer Burden, Miller-Payne, Pinder, Sinn, and Sataloff .Miller Payne grading: Following chemotherapy, the residual tumour was removed (mastectomy or wide local excision with axillary surgery). Using a five-

point histological grading system with a reduction in tumour cellularity as the key characteristic, the excised tissue was evaluated and the response to chemotherapy scored in comparison to a pre-treatment core biopsy. In patients with big and locally advanced breast tumours receiving such therapy, this grading system, which evaluates the histological response to initial chemotherapy, can predict overall survival and the disease-free interval.(67)

Need for Adjuvant chemotherapy in Hormone positive, Her 2 negative tumours-Recurrence risks vary according to breast cancer subtypes and stages. Hormone-positive Early-stage HER2-negative breast cancer is associated with a 10%–15% chance of distant recurrence over 10 years and only a 2%–3% absolute benefit from chemotherapy, which is roughly equivalent to the risk of toxicities that are fatal, life-threatening, or permanently altering. Predicting the likelihood that the disease will recur is the best strategy to avoid overtreating patients with breast cancer. If this is successfully accomplished, only those patients who have a higher chance of experiencing such recurrences will receive adjuvant chemotherapy, preventing the overtreatment of those who may not require it. IHC4, luminal A/B subtyping, and PREDICT are currently some of the risk assessment methods that are often employed in India.(3)

Hormonal therapy-The basis for hormone treatment, which effectively deprives tumour cells of hormones, is that breast cancer tumour cells still have the ability to thrive when exposed to female sex hormones; removing these hormones inhibits the proliferation of cancer cells. The benefits of hormonal therapy are at least a 47% risk reduction for recurrence and a 26% reduction in mortality. This benefit alone outweighs the combined gains from all other adjuvant therapies.(68) Premenopausal women since decades have been shown to benefit from Tamoxifen while Aromatase inhibitors are rapidly usurping its position in post menopausal women. The 12-year DFS with 4.6% absolute improvement and DRFI with 1.8% absolute improvement, but not OS 90.1% versus 89.1%, continued to be significantly improved for patients assigned to exemestane plus ovarian function suppression over tamoxifen plus ovarian function suppression, according to a recent update on the SOFT/TEXT trials.

Benefit in OS was clinically significant in patients with high-risk illness, such as women under the age of 35 (4.0%), patients with tumours larger than 2 cm (4.5%), or patients with

grade 3 (5.5%) tumours. Patients who had a low risk of recurrence did not appear to benefit from OS. (69)

Fangmeng Fu et al also showed in his analysis of 144103 US patients that Delays in the initiation of AHT more than 150 days were associated with decreased survival compared to patients who initiated therapy before 150 days in hormone receptor-positive/human epidermal growth factor receptor-2-negative disease.(70)

Sequencing of adjuvant RT and chemotherapy-The timing and sequencing of adjuvant radiation and chemotherapy has ever been a question of concern. Huang et al 's analysis of 10 retrospective trials revealed that the 5-year LRR increased from 5.8% in individuals treated within 8 weeks to 9.1% in patients treated between 9 and 16 weeks after surgery.(71)

But later, CALGB in an RCT comparing adriamycin and cytoxan to adriamycin and cytoxan, then taxane found that Radiation was postponed for patients in the adriamycin plus taxane group by an additional 84 days (4 cycles). Locoregional relapses were lower in the AC-T arm compared to the AC arm (9.7% vs. 3.7%; P =.04) despite the extra delay, even though In this RCT, the majority of the patients had negative margins. This and other studies by MD Anderson all points to that fact that , assuming all modalities are administered without undue delays, the administration of chemotherapy prior to radiation therapy does not result in abnormal rates of local relapse for the majority of patients receiving breast-conserving surgery with negative margins. It is still unclear if individuals with positive/close margins or other local recurrence risk factors will benefit from receiving radiation treatment earlier.(72,73)

Radiotherapy advances:

Conventionally breast cancer has been treated with the standard dose fractionation regimens with 50Gy in fractions of 2 Gy. Early in the 1990s, it was discovered that breast cancers and late-reacting normal tissues were both equally sensitive to fraction size, indicating that prolonged treatment time does not preferentially spare normal tissues. These findings paved the way for hypofractionated whole breast irradiation (HF- WBI), which is administered to the entire breast (with fraction sizes greater than 2 Gy), a total dose that is radio-biologically equal to a CF-WBI regimen, with or without an extra tumour bed boost. Some of the major RCTs paving the way towards Hypofractionated RT are being discussed here.

Benefit of Radiotherapy:

The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) trial revealed that overall, radiation decreased the risk of breast cancer death from 25.2% to 21.4% and the 10-year chance of any (i.e., locoregional or distant) first recurrence from 35.0% to 19% (absolute reduction 15.7%). There was a drop in the local recurrence rate of 21.2% in pN+ illness, which highlights this more clearly.(74)

Benefit of Boost:

In their experiment, Bartelink et al. found that adding a boost of 16Gy in 8# to EBRT after BCS caused 5 year local recurrence rates to be 7.3 percent and 4.3 percent, respectively, favouring the inclusion of boost. This difference was bigger in women under the age of 40. (19.5 percent with standard treatment and 10.2 per-cent with additional radiation)(75)

Hypofractionated RT vs Conventional RT in Early Breast cancer post BCS

In 1986, Royal Marsden Hospital and Gloucestershire Oncology Centre (RMH/GOC) in the United Kingdom began the first significant randomised experiment. Two HF-WBI arms (42.9 Gy in 13 fractions or 39 Gy in 13 fractions, each provided every other day) and one CF-WBI arm (50 Gy in 25 fractions) were each randomly assigned to one of 1,410 patients. Regarding local recurrences, none of the HF-WBI arms significantly varied from the CF-WBI control arm. Clinical assessments of breast cosmesis, shrinkage, distortion, oedema, induration, telangiectasias, and shoulder stiffness at 10 years revealed substantial differences, with the 39 Gy arm typically doing better and the 42.9 Gy arm performing worse.(76)

A randomized HF-WBI versus CF-WBI experiment was started in Canada by the Ontario Clinical Oncology Group (OCOG). CF-WBI (50 Gy in 25 fractions administered over five weeks) or HF-WBI (42.56 Gy in 16 fractions delivered over 3.2 weeks) were the two treatment options offered to patients at random. Local relapse, overall survival, skin toxicity, and cosmetic results at 10 years were comparable and statistically insignificant.(77)

The follow-up UK Standardization of Breast Radiotherapy Trial A (START A) was started in 1999 with a similar design to the RMC/GOC trial, with the exception that the 42.9 Gy arm was reduced to 41.6 Gy arms due to the marginally higher rate of late normal tissue effects in the 42.9 Gy arm in the RMC/GOC trial. Local relapse, distant relapse, and overall survival at

10 years were not significantly different across the arms, while the 39Gy arm had better cosmetic results.(78)

As a more practical trial with a shorter treatment period for the HF-WBI arm, the START B trial was launched concurrently with START A. Patients were randomly assigned to either HF-WBI or CF-WBI (50 Gy in 25 fractions over five weeks) (40 Gy in 15 fractions delivered over three weeks). In accordance with departmental policy, a non-randomized elective boost of 10 Gy was administered in 5 portions. Breast shrinkage, telangiectasias, and oedema were considerably reduced in the 40 Gy arm compared to the 50 Gy arm, however there were no significant differences in breast induration, shoulder stiffness, or arm oedema. 10 year local relapse rates were not statistically different between the arms.(79)

Similarily FAST trial which compared CF-WBI (50 Gy in 25 fractions) or one of two HF-WBI arms (30 Gy or 28.5 Gy in five once-weekly fractions of 6 Gy or 5.7 Gy, respectively is currently under purview with its survival outcomes awaited. At a median follow-up of three years, 28.5 Gy in five fractions had unfavourable effects in the breast that were significantly less severe than those from 30 Gy in five fractions and comparable to those from 50 Gy in twenty-five fractions.(80) The Trans-Tasman Radiation Oncology Group (TROG) started TROG 07.01, the first randomised trial comparing CF-WBI (50 Gy in 25 fractions) with HF-WBI (42.5 Gy in 16 fractions) with or without a tumour bed boost to evaluate hypofractionation for patients with ductal carcinoma in-situ (DCIS) whose results are awaited.(81)

There was no discernible difference between HF-WBI and CF-WBI in terms of local recurrence-free survival, relapse-free survival, breast cancer-specific survival, or overall survival, according to a Cochrane analysis published in 2016. Patient-reported metrics showed that recipients of HF-WBI experienced much less acute discomfort, pain, burning/stinging, oedema, and exhaustion than those who received CF-WBI. With the exception of the 42.9 Gy arm in the RMH/GOC study, which was withdrawn for the follow-up START A trial, late breast, skin, and subcutaneous tissue toxicity either favoured HF-WBI or was comparable between HF-WBI and CF-WBI in all four large randomised trials. The START A and B trials' long-term analyses revealed very low rates of radiation pneumonitis, symptomatic rib fractures, and ischemic heart disease, with no differences between the HF-WBI and CF-WBI arms. The breast cosmesis outcomes also favoured HF WBI or were

similar. They also showed that results demonstrate that a boost is safe to use with HF-WBI and should be considered as part of treatment with the same criteria as those for CF-WBI.(82)

Hypo-fractionated RT in LABC

A recent randomised trial conducted by researchers from the Chinese Academy of Medical Sciences compared hypofractionated PMRT (43.5 Gy in 15 fractions) with conventionally-fractionated PMRT (50 Gy in 25 fractions) with RNI and no scar enhancement. Five-year locoregional recurrence, disease-free survival, or overall survival did not differ significantly from one another. While incidence of grade three acute skin toxicity was reduced in the hypofractionated group, incidence of radiation pneumonitis, lymphedema, shoulder dysfunction, and ischemic heart disease were equal between groups.(83)

Hypofractionated PMRT (42.56 Gy in 16 fractions) and conventionally-fractionated PMRT (50 Gy in 25 fractions) are being contrasted in a recently launched randomised phase III experiment (Alliance A221505). The outcomes are awaited. With the exception of the few individuals participating in START studies, follow-up is still insufficient for the bulk of these patients. Longer follow-up from these and other ongoing clinical trials will be necessary before hypofractionation with RNI is widely adopted in the locally advanced or post-mastectomy scenario.

Radiotherapy technique-Saroj Kumar et al in his Dosimetric Study Comparing 3D-CRT vs. IMRT vs. VMAT in Left-Sided Breast Cancer Patients found that there was increased low volume irradiation of the heart, lungs, and body with VMAT performing only marginally better than IMRT in coverage and decreasing lung irradiation with comparable heart irradiation, while both inverse planning modalities led to increased coverage, better Conformity Index, and better Homogenity Index and decreased high dose volumes in OARs compared to 3DCRT.(84)

Effect of lumpectomy boost-

A EORTC trial by Bartelink et al showed that Local recurrence rates over five years were 7.3 percent and 4.3 percent, respectively for patients who received RT without and with boost in Early breast cancer post BCS. The greatest benefit was seen in patients under the age of 40; at five years, their rate of local recurrence was 19.5% with conventional treatment and 10.2%

with extra boost radiation. No differences in metastasis or overall survival rates were observed at five years in the age range of 41 to 50.(75)

Another study by the Danish Breast Cancer Group revealed a 10 year cumulative incidence of breast cancer recurrence rates as 16.6%. Estrogen receptor-positive tumours, lymph node-positive disease, and tumours larger than 20 mm were linked to higher cumulative occurrences and hazards for late BCR.(85)

Dose to cardiac sustructures as a measure of Cardiotoxicity

Wennstig et al in her trial showed that Radiation doses to the LAD in women receiving conventional 3DCRT for BC between 1992 and 2012 remained high and were linked to a higher need for coronary intervention in the middle of the LAD. The findings suggest that while planning an RT treatment, the LAD radiation dose should be taken into account and kept as low as possible. Lessening the exposure to the LAD is anticipated to reduce the chance of radiation-induced stenosis in the future.(86)

Furthermore, Sophie Jacob et al in the BACCARAT study demonstrated that Mean Heart Dose is insufficient to accurately forecast each patient's exposure to the Left Ventricle and coronary arteries, particularly the Left Anterior Descending artery. It would be required to take into account the distribution of doses within these cardiac substructures rather than only the MHD for accurate radiotherapy-induced cardiotoxicity studies.(87)

Piroth et al in his DEGRO study demonstrated than the dose constraints to the Mean Heart dose and Mean LAD dose were 2.5Gy and 10Gy respectively(88)

Predictors of subclinical cardiac disease

Left ventricular ejection fraction and Myocardial performance index-

CTRCD was described by 2020 ESMO consensus recommendations as an absolute LVEF decline of >20 percentage points, an absolute LVEF decline of 10 percentage points to a value of 50%, or an absolute LVEF decline to a value of 50%. 2020 ESMO consensus recommendations defined Subclinical cardiac dysfunction as an absolute decrease from baseline in the GLS of ≥5% or a relative decrease from baseline in the GLS of ≥12% or Troponins elevation from baseline.(89,90)

Depending on the series, the incidence of trastuzumab-induced cardiotoxicity is thought to range from 1.7% when taken alone to over 20% when combined with additional chemotherapeutic medications like anthracyclines or cyclophosphamide. There are now two categories of cardiotoxicity brought on by the use of chemotherapy. The direct oxidative stress-induced death of cardiomyocytes as a result of Top2B inhibition is thought to be the cause of Type I, which is distinctive of anthracyclines. At a myocardial biopsy, it is an irreversible, dose-dependent, and clearly visible process. Type II, on the other hand, is known as trastuzumab-induced cardiotoxicity and is characterised by a temporary decline in myocardial function without causing cell death. It doesn't depend on dose and is typically reversible. (91)

These mechanisms' effects are assumed to be comparable to those of other heart diseases, in which the onset of systolic dysfunction is preceded by diastolic dysfunction. Additionally, it has been demonstrated that anthracycline use lengthens the period of isovolumetric contraction, which contributes to diastolic dysfunction. This may help to explain why, in certain studies, an increase in Tei index(Myocardial performance Index) (0.41+/- 0.08) was not accompanied by a similar decline in LVEF, but instead was linked to a three-fold increase in the risk of cardiomyopathy, whereas no such association was seen for LVEF. Tei index may be useful in identifying cardiotoxicity, however the evidence is not strong enough to support its widespread usage.(92)

NT-ProBNP and T wave Peak to end time

Isabel et al in her study showed that 239.5 pg/ml was determined to be the ideal NT-proBNP cut-off level, with maximum attainable values of 79% sensitivity and 87% specificity to detect cardiotoxicity in patients of Breast cancer treated with Transtuzumab +/- Anthracycline based chemotherapy and that NT-proBNP and Diabetes may be associated with trastuzumab-induced cardiotoxicity.Another study by Urun et al tested significant for relation bbetween Heart failure and NT ProBNP >300pg/ml(91,93)

Iqbal et al' s analysis showed a positive correlation between hs-troponin I and TpTe interval in predicting cardiac events after anthracycline based chemotherapy.(94)

Survival Outcomes

Overall survival, Disease free survival and Progression free survival varies with the population and study treatment design. Valentina et al in her study showed that On follow up, 8.9% patients had passed away, while 91.1% were still alive. The overall median DFS was 137 months, while the overall median OS was 166 months.(95). Whereas an Indian trial from AIIMS Delhi showed that the median time to relapse in the non-metastatic group was 36 months, the 3-year relapse free survival rate was 73.5%, and the overall survival rate was 82.1%. While pathological node involvement and triple negativity were linked to poor OS, clinical stage (stage III), triple negativity, and HER2 neu positive were linked to worse RFS. The median time to progression for the metastatic group was 18 months, and the 3-year progression-free survival (PFS) rate was 35% while the overall survival rate (OS) was 20%.(20)

MATERIALS AND METHODS

MATERIALS AND METHODS

Study Setting: Study was conducted in the Department of Radiation Oncology, AIIMS Jodhpur

Study design: Single arm retrospective study

Study participants: All patients of biopsy proven breast cancers had received post-operative radiation therapy in the Department of Radiation Oncology, AIIMS Jodhpur from the year 2018 to 2020.

Study Period: 2 years

Eligibility Criteria

Inclusion criteria:

1. All biopsy proven patients of breast cancer, treated with post operative radiation therapy in AIIMS, Jodhpur

Exclusion Criteria:

1. Patients treated with palliative intent.
2. Patients with incomplete/wrong contact details.

Sample size-

All patients of biopsy proven breast cancer who received post operative radiation therapy in the Department of Radiation Oncology AIIMS Jodhpur from the year 2018 to 2020. The records have been accessed from the registration records of CPMS and records in the Department of Radiation Oncology, Surgical Oncology, Pathology and Cardiology.

Study Procedure-

Radiation treatment Procedure: CT Simulation and treatment was done in the supine position with breast board and contouring done on the basis of non-contrast CT. Patients have been treated with Elekta VERSA HD machine with 6MV photon beam. Initially patients were treated with 50Gy/ 25# and later shifted to 42.56Gy/16# with either 3DCRT or VMAT.

Creation of Database:

A database was created using softwares as spreadsheets. The study database was used for entry of data obtained from various sources such as the Computerised Patient Management System (CPMS) of the Institute and records of the Department of Radiation Oncology and Pathology.

Entry of Data:

Data was captured as per the study form attached with the Database. Data was collected using:

1. Manual search and entry from CPMS and Records from Radiation Oncology and Pathology
2. Dose distribution data and DVH was obtained from the Monaco Treatment Planning System of Elekta LTD. Additional OARs were contoured like coronary arteries, Left Anterior Descending artery , Left circumflex artery etc.

All the records of patients of breast cancer who have been treated with a radical intent using post-operative adjuvant radiotherapy in AIIMS, Jodhpur was compiled. After fitting the available records to inclusion and exclusion criteria, screening of all records was made for complete availability of treatment details and contact details.

Various variables was collected related to the patient profile (age, sex, religion, geographic residence, symptoms at presentation, duration of symptoms, addiction history, comorbidities, Anthropometric parameters such as Height, weight , BMI, BSA etc,.), disease status (T stage, N stage, AJCC 8th edition prognostic stage group, histology, gross tumor, and nodal volume, level of nodal involvement, presence of LVSI, PNI, extra-nodal extension, DCIS/LCIS or nodes etc,.), and treatment factors (receipt of surgery, adequacy of surgery, nodal dissection, technique of radiotherapy, doses received, receipt of chemotherapy and agent used, cumulative dose of chemotherapy, significant gaps in radiation treatment etc,.).

The response to treatment was based on either Clinical Examination (CR, PR, SD, PD) based on WHO criteria or if the imaging of the patients after at least 3 months of completion of definitive treatment is available, same will be considered while assessing the response to treatment. The response assessment was done according to the RECIST criteria. The present status of the patient will be enquired from the contact details available through whichever means feasible. Telemedicine was used wherever necessary to examine the patient if the

patient is unable to visit the hospital. If the disease relapses or progresses after treatment, the date of biopsy if available or imaging if a biopsy is not available was regarded as the date of progression. In patients who relapse/progress, the type of relapse, time to relapse/progression and the treatment offered will also be recorded. If the patient was not contactable, the last documented visit in eHIS was taken as the last follow-up and was censored in the further time points.

Based on this data, various outcome variables was studied like overall survival(OS), disease-free survival(DFS), progression-free survival(PFS)/Recurrence free survival(RFS).

1. **Overall survival**- Defined as the time from diagnosis to death from any cause.

2.Disease free survival- The period after successful treatment during which there are no signs and symptoms of the disease that was treated.

3.Progression free survival/Recurrence free survival(RFS)-The period during and after the treatment of the disease for which the patient lives with the disease but doesn't progress.

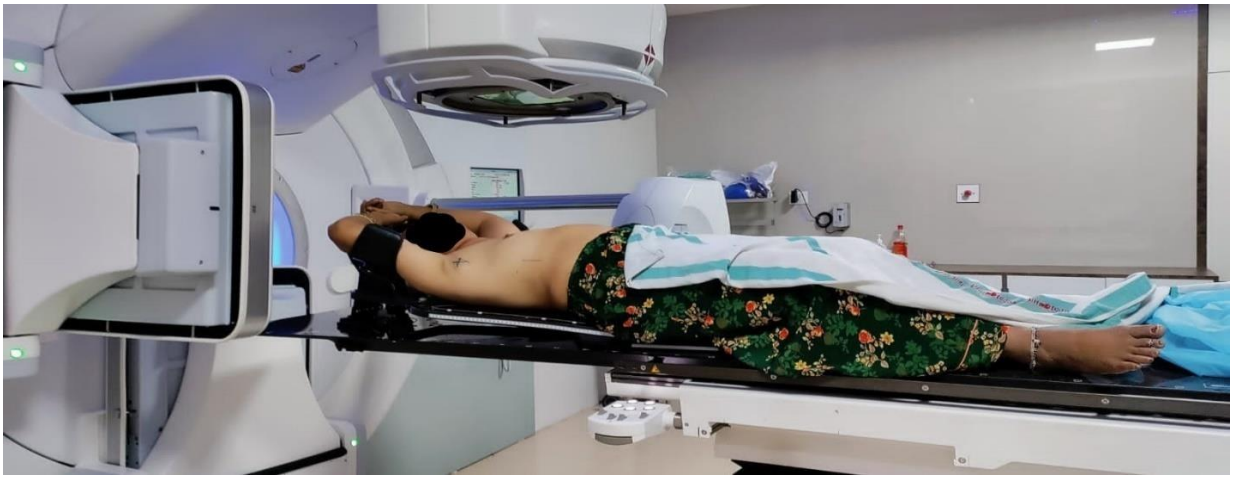
Response Evaluation-

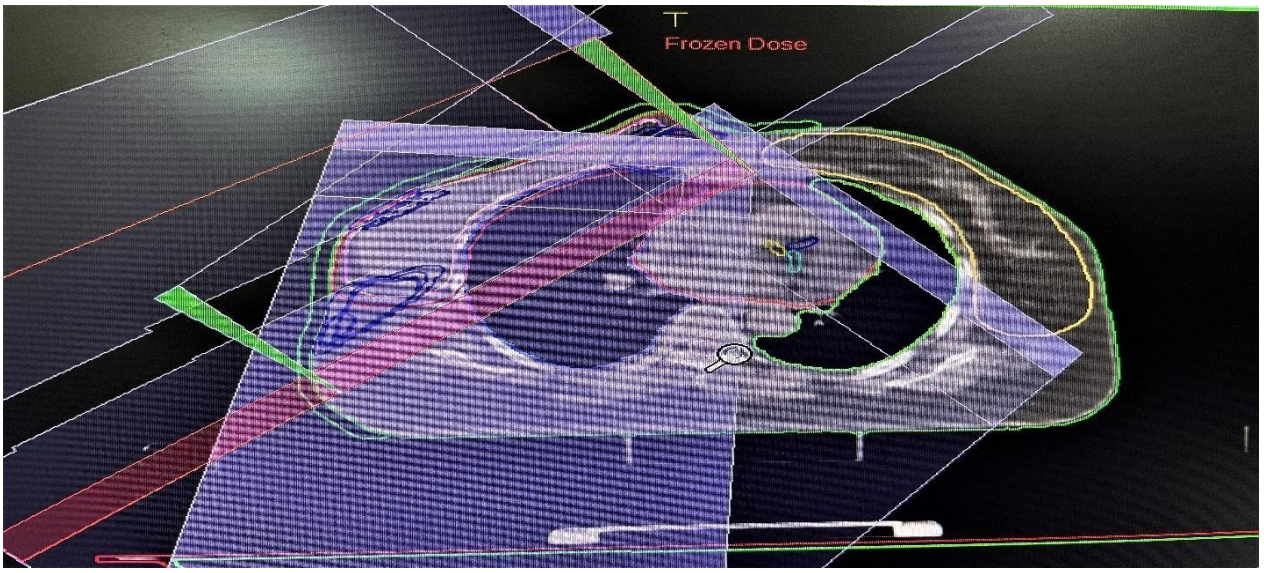
Response evaluation was done on the basis of Recurrence/Progression vs Disease Control. Wherever response assessment scans are available, iRECIST Criteria 1.1. was used.

Statistical Analysis-

All the qualitative data was expressed as frequencies and quantitative data was expressed as maximum, minimum, mean, median with range. Survival outcomes of OS, DFS, PFS/RFS was depicted using Kaplan Meier Curve and statistically significant correlation was tested with Log Rank test. Cox regression analysis was used for fitting parametric continuous data variables and illustrated with Hazard Ratio. Pearson's correlation test and Spearmann's correlation test was used for testing for correlation between parametric and non-parametric variables respectively. Shapiro Wilk's test was used for assessing for normality. A p-value of less than equal to 0.05 was taken as statistically significant. Analysis was done using Microsoft Excel and IBM SPSS.

Figures:

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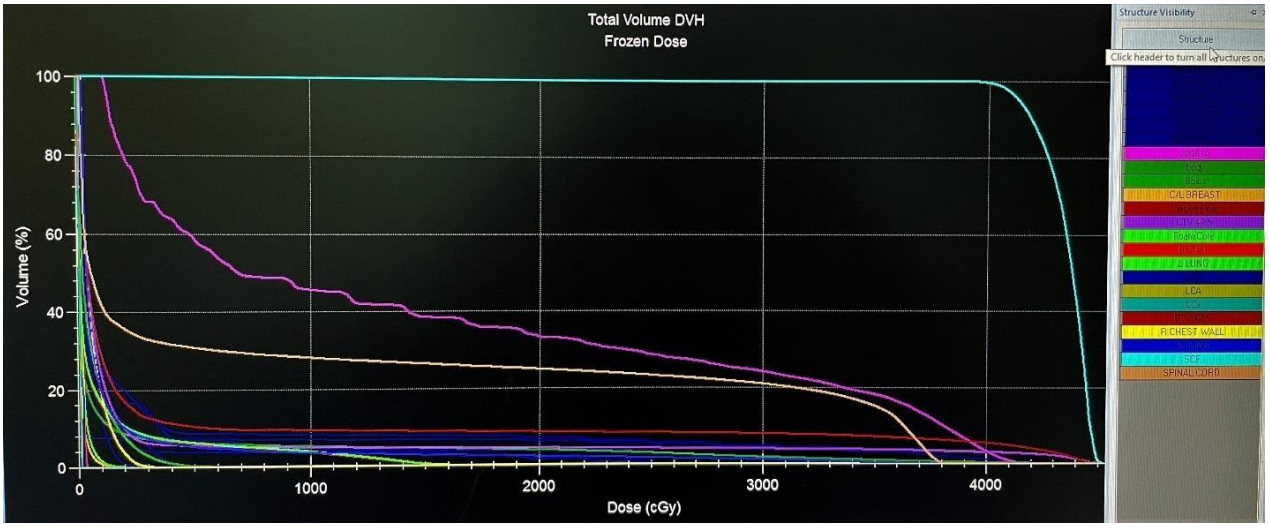
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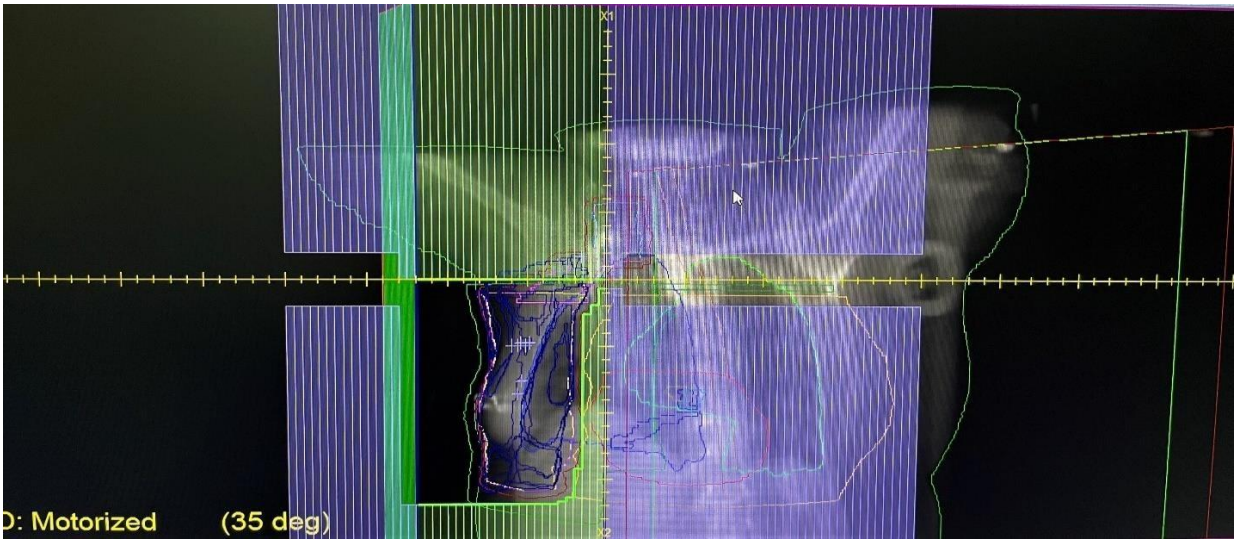
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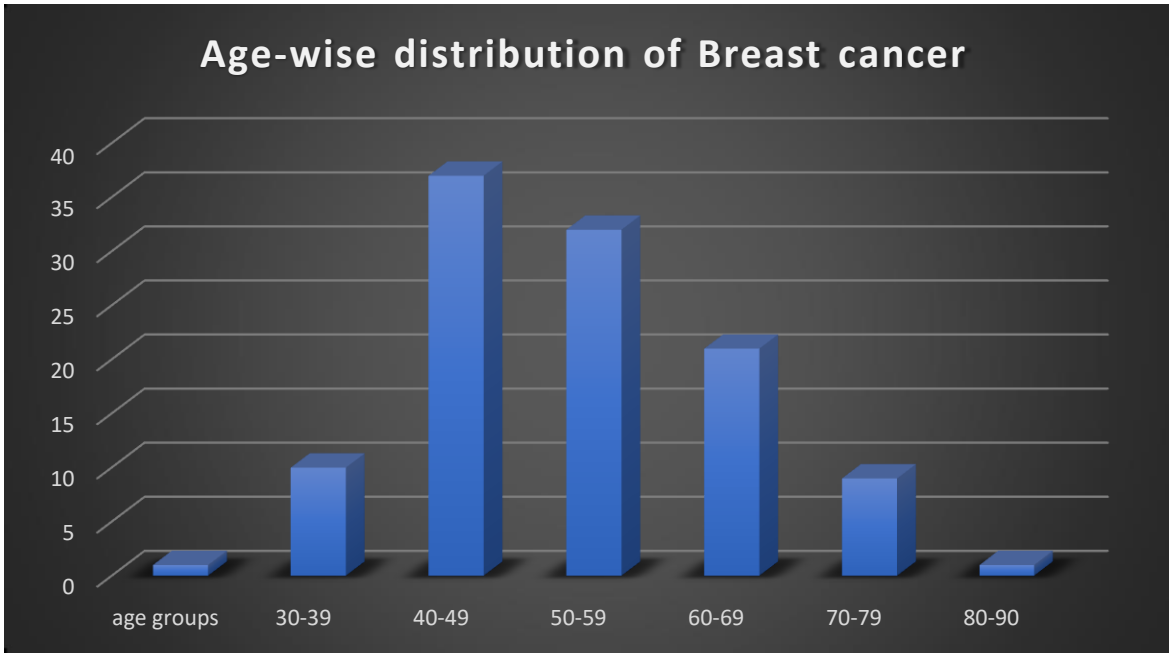
RESULTS

RESULTS

The data of 111 patients were retrieved retrospectively.

1. **AGE:**



Age groups	Frequency
20-29	1
30-39	10
40-49	37
50-59	32
60-69	21
70-79	9
80-90	1

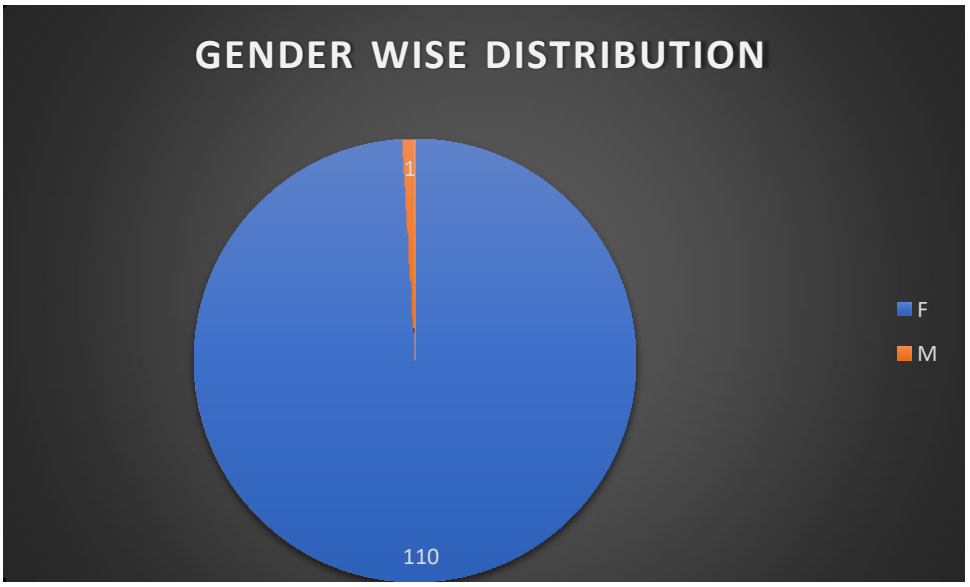
The mean ,median and mode of ages were found to be 52.72973, 52 and 42 respectively with a maximum age of 83 and minimum age of 29.

AGE

N		111
Mean		52.73
Median		52.00
Mode		42
Std. Deviation		11.534
Variance		133.035
Percentiles	25	43.00
	50	52.00
	75	63.00

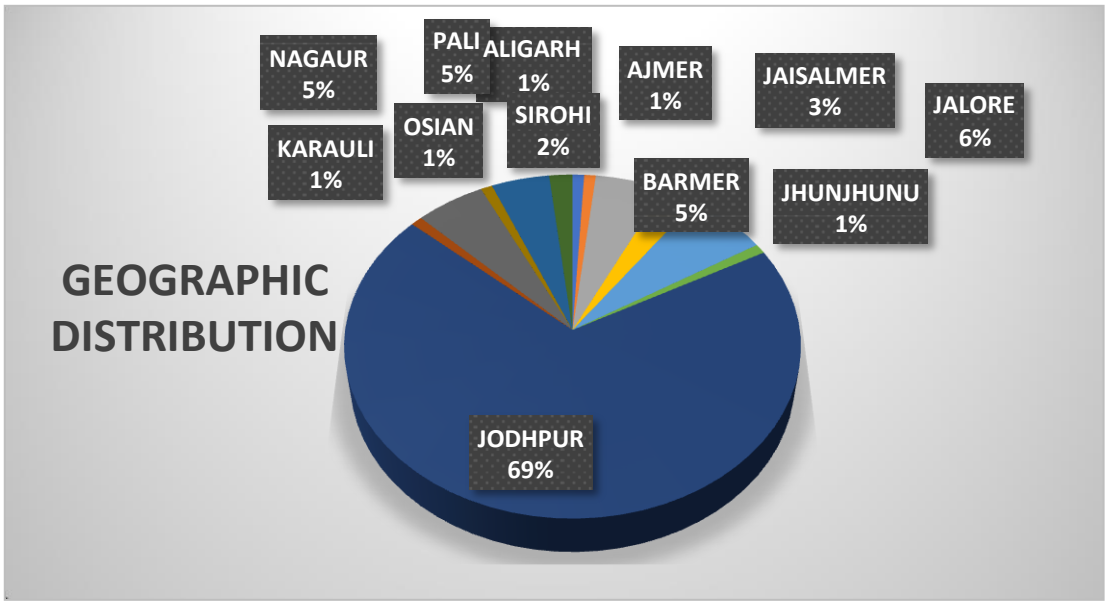
2. GENDER:

GENDER	FREQUENCY
Female	109
Male	1
Grand Total	110



Out of the 111 patients whose data were collected; 1(0.9%) was male and 110(99.1%) were female.

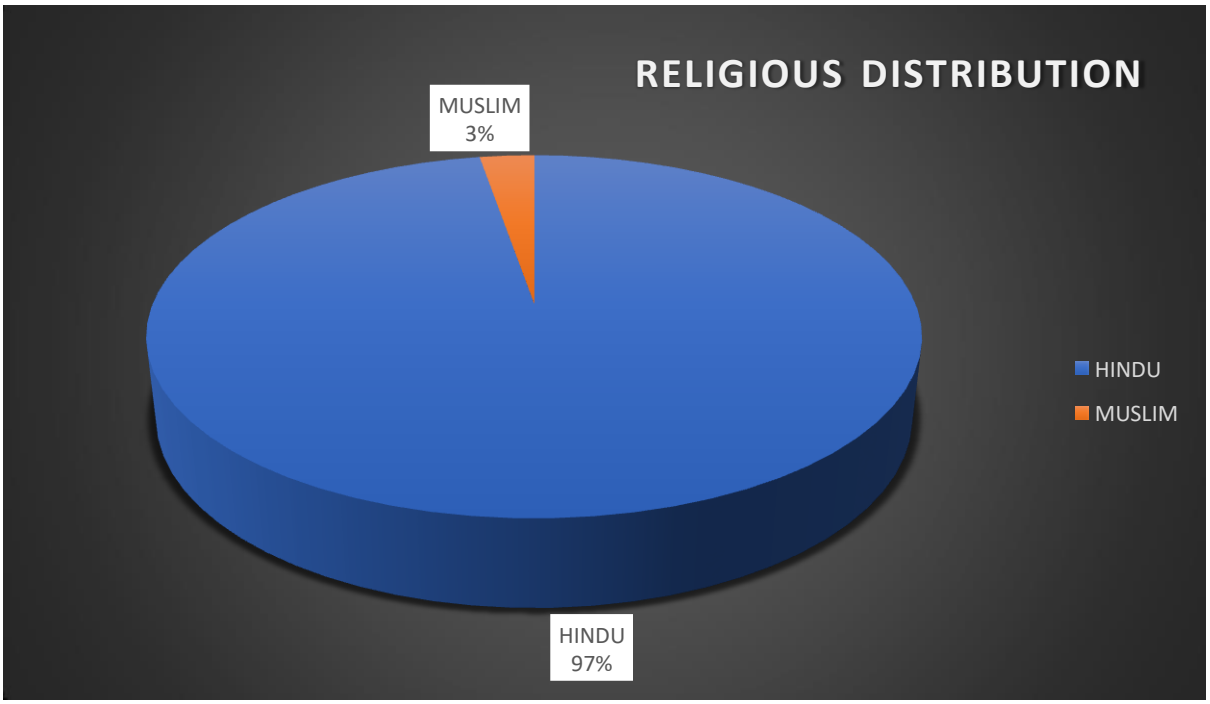
3. GEOGRAPHIC DISTRIBUTION



Majority of patients were from Jodhpur(69%) followed by Jalore(6%), Nagaur(5%), Pali(5%) ,Barmer(5%), Jaisalmer(3%), Sirohi (2%), Osian, Aligarh, Ajmer, Jhunjhunu, Karauli(1% each).

GEOGRAPHICAL REGIONS	FREQUENCY
Ajmer	1
Aligarh	1
Barmer	6
Jaisalmer	3
Jalore	7
Jhunjhunu	1
Jodhpur	77
Karauli	1
Nagaur	6
Osian	1
Pali	5
Sirohi	2

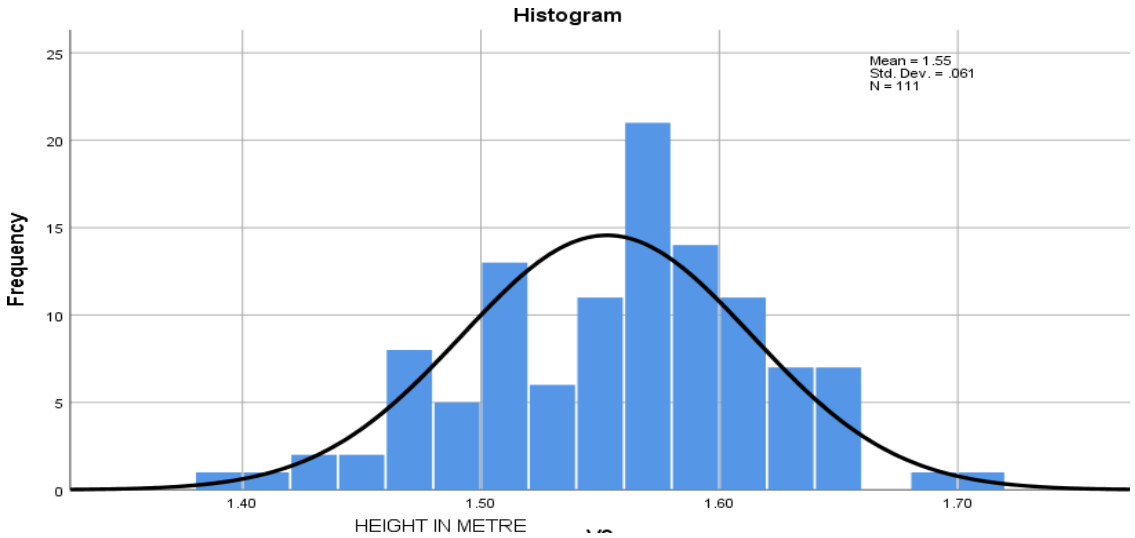
4. RELIGION:



RELIGION	FREQUENCY	PERCENTAGE
Hindu	108	97.3
Muslim	3	2.7
Grand total	**111**	**100**

There were 108(97.3%) Hindus and 3(2.7%) Muslims.

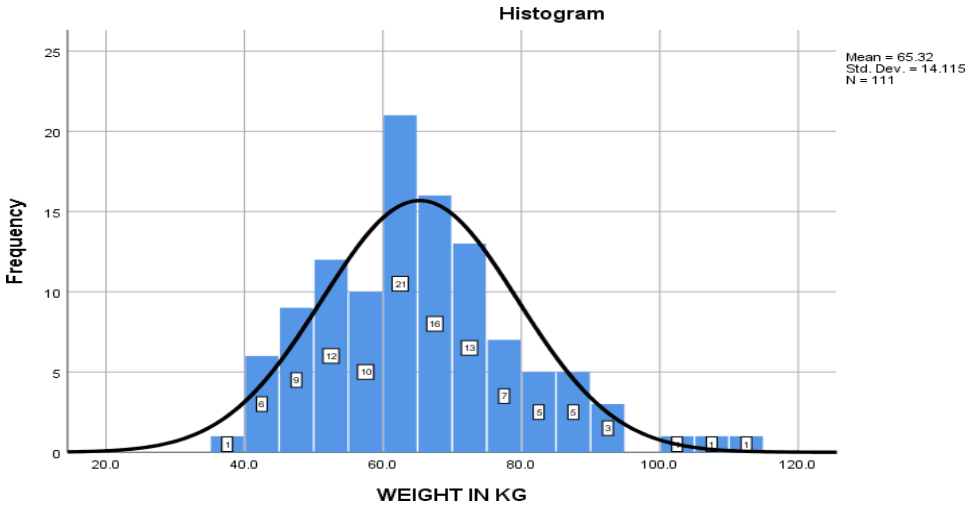
5. HEIGHT



N	111
Mean	1.5528
Median	1.5600
Mode	1.56
Std. Deviation	.06082
Variance	.004
Range	.31
Minimum	1.39
Maximum	1.70

The heights of the patients ranged from a minimum of 1.39 m to a maximum of 1.7 m with a mean of 1.55 m and a median of 1.56m.

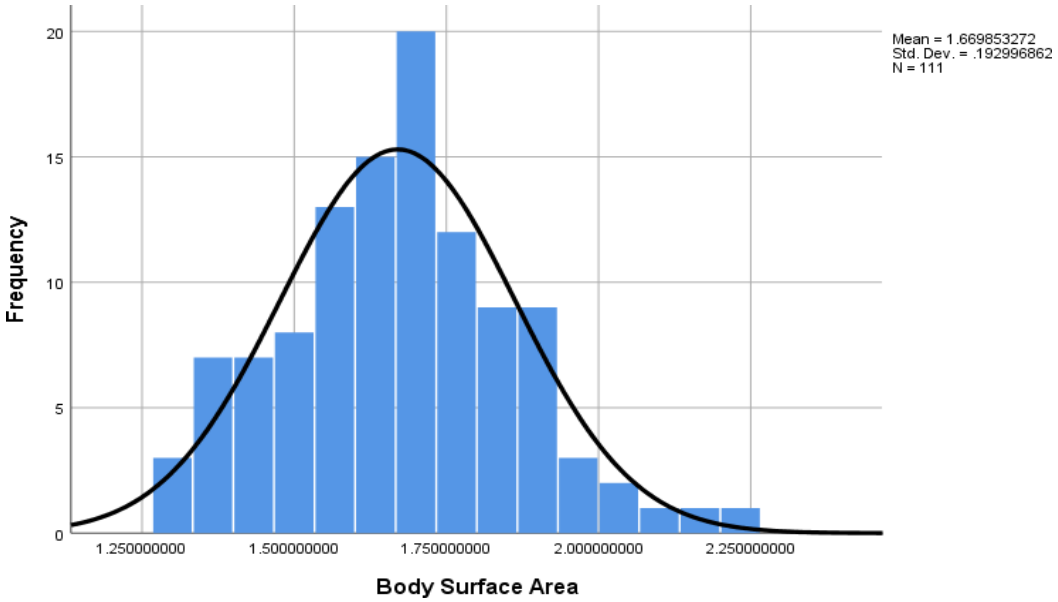
6. WEIGHT



N	111
Mean	65.320
Median	64.500
Mode	68.0
Std. Deviation	14.1154
Variance	199.245
Range	71.1
Minimum	39.0
Maximum	110.1

The weights of the patients ranged from 39kg to 110.1 kg with a mean of 65.32 kg and a median of 64.5 kg.

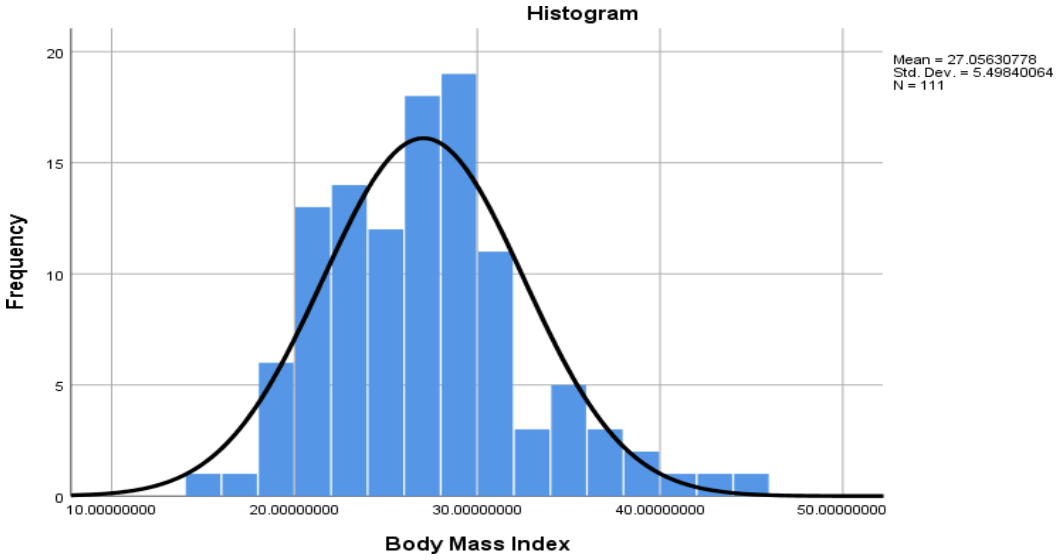
7. BODY SURFACE AREA



N	111
Mean	1.66985327168
Median	1.68000000000
Mode	1.814563002
Std. Deviation	.192996862060
Variance	.037
Range	.931076107
Minimum	1.287913903
Maximum	2.218990010

Among the 111 patients studied, the Body Surface area(BSA) ranged from a minimum of 1.27 to a maximum of 2.218 with a mean and median of 1.669 and 1.68 respectively.

8. BODY MASS INDEX



N	111
Mean	27.0563077812
Median	26.8734239200
Mode	30.63004584
Std. Deviation	5.49840063645
Variance	30.232
Range	30.57343089
Minimum	15.04571583
Maximum	45.61914672

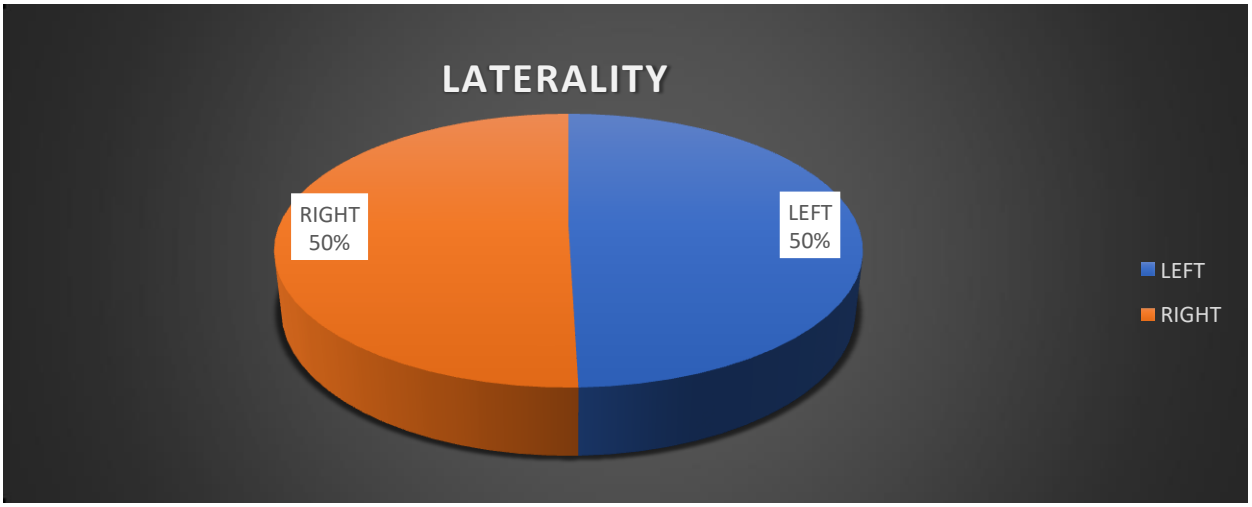
9. BMI BASED STRATIFICATION

BMI BASED STRATIFICATION	PERCENTAGE	FREQUENCY
NORMAL WEIGHT	25.45%	28
OBESE	61.82%	68
OVERWEIGHT	12.73%	14
Grand Total	**100.00%**	**110**

61.8% Patients were Obese, 12.73% were overweight with WHO Asian cut off of >25 kg/m^2 for Obesity and 23-24.9 kg/m^2 for Overweight.

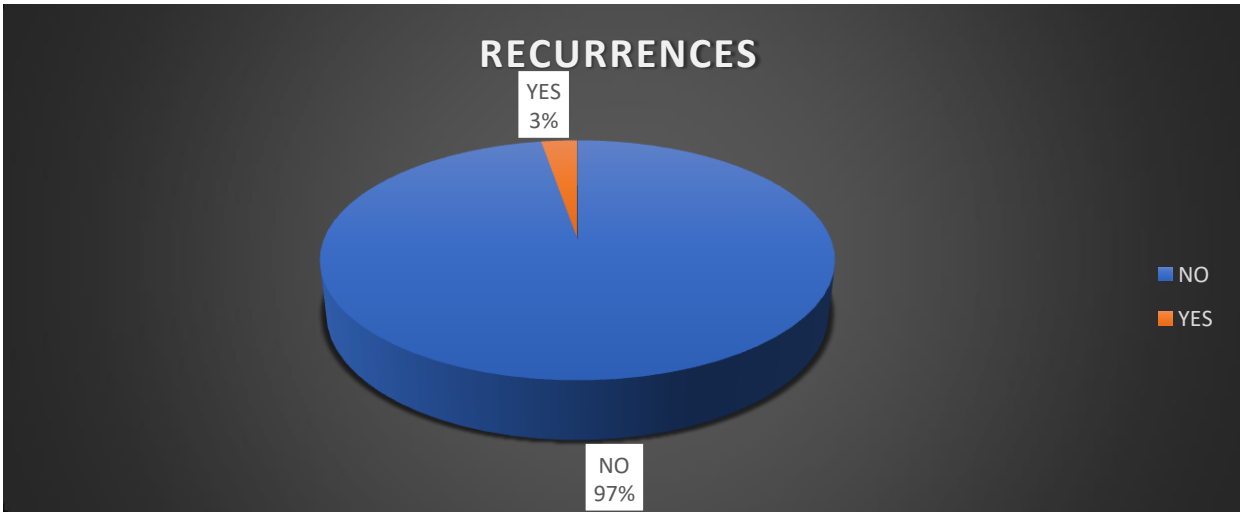
10. LATERALITY OF DISEASE(SIDE INVOLVED)

LATERALITY	COUNT OF LATERALITY
LEFT	55
RIGHT	56
Grand Total	**111**



11. RECURRENT VS NEW CASES

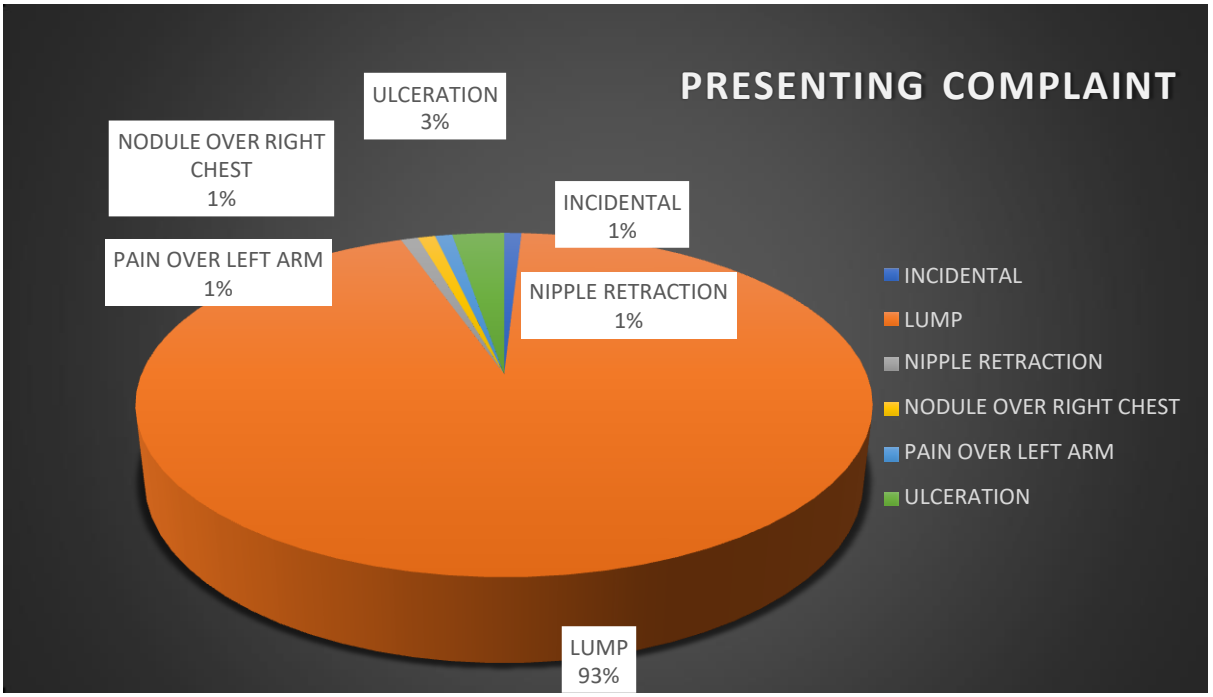
RECURRENCE?	FREQUENCY
NO	108
YES	3
Grand Total	**111**



12. CLINICAL PRESENTATION

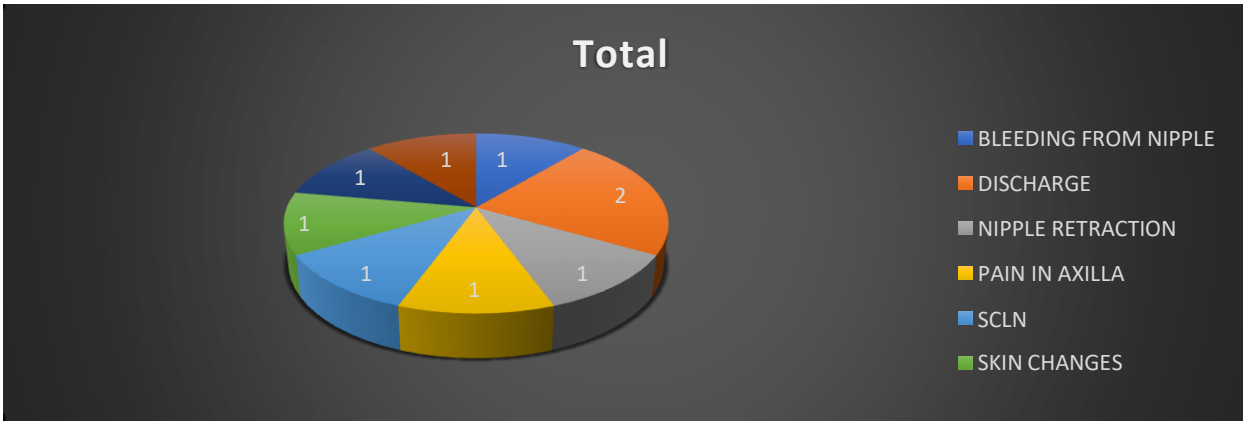
a) PRIMARY COMPLAINT

PRESENTING COMPLAINT	PERCENTAGE	FREQUENCY
INCIDENTAL	0.90%	1
LUMP	93.69%	104
NIPPLE RETRACTION	0.90%	1
NODULE OVER RIGHT CHEST	0.90%	1
PAIN OVER LEFT ARM	0.90%	1
ULCERATION	2.70%	3
Grand Total	**100.00%**	**111**



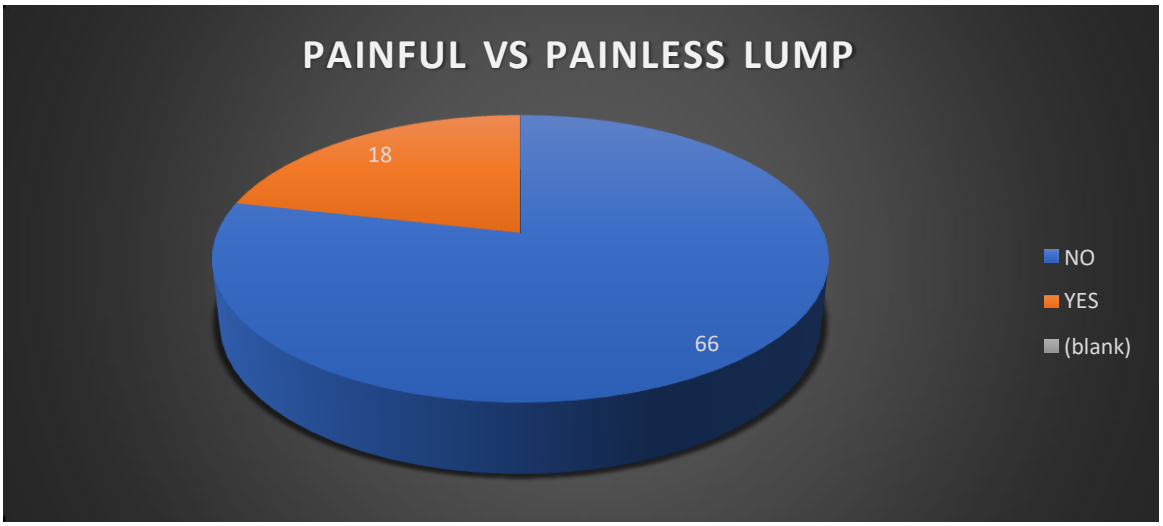
13. SECONDARY COMPLAINTS

SECONDARY SYMPTOMS	FREQUENCY
BLEEDING FROM NIPPLE	1
DISCHARGE	2
NIPPLE RETRACTION	1
PAIN IN AXILLA	1
SUPRACLAVIAN LYMPH NODE	1
SKIN CHANGES	1
BREAST ULCERATION	1
UPG IN AXILLA	1
Grand Total	9

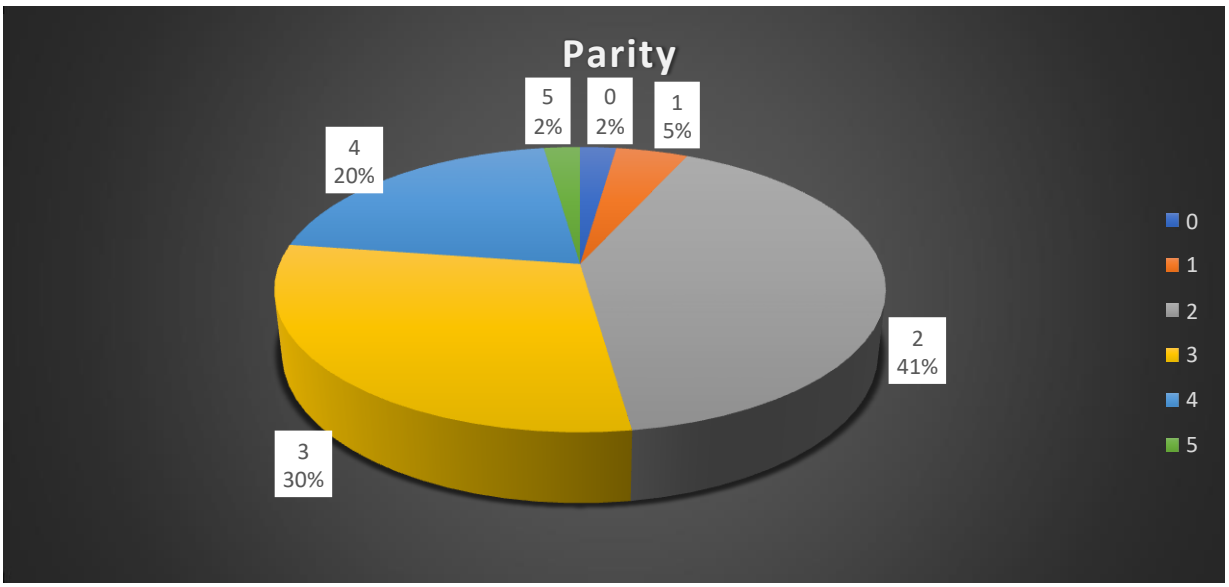


14. PAINFUL LUMP:

PRESENCE OF PAIN	FREQUENCY
NO	66
YES	18
Grand Total	84



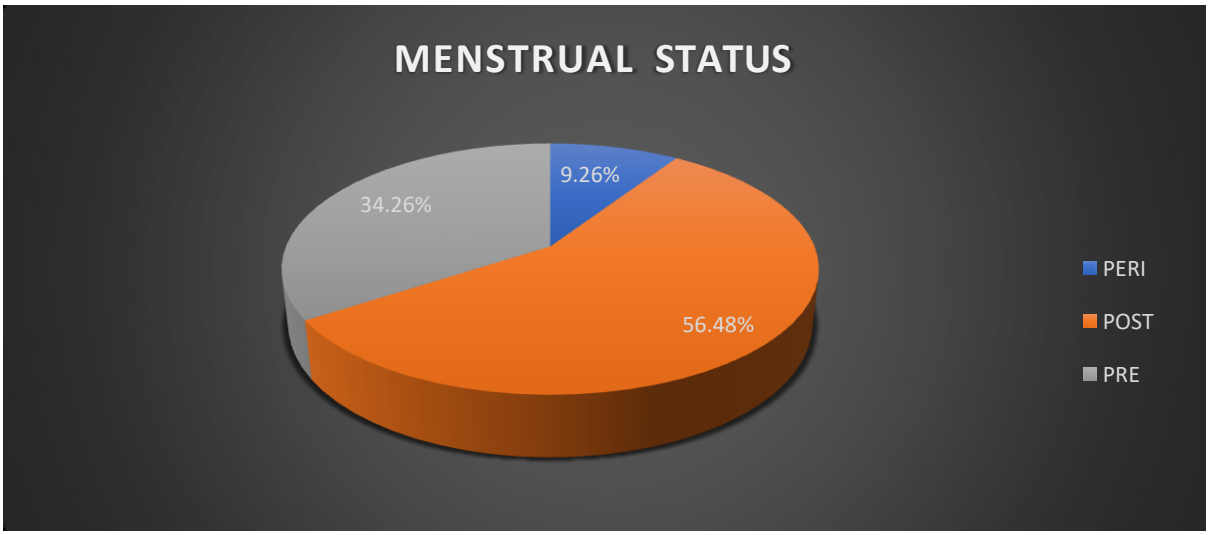
15. <u>PARITY</u>



NO: OF KIDS	FREQUENCY	PERCENTAGE
0	1	2.27%
1	2	4.55%
2	18	40.91%
3	13	29.55%
4	9	20.45%
5	1	2.27%
Grand Total	**44**	**100.00%**

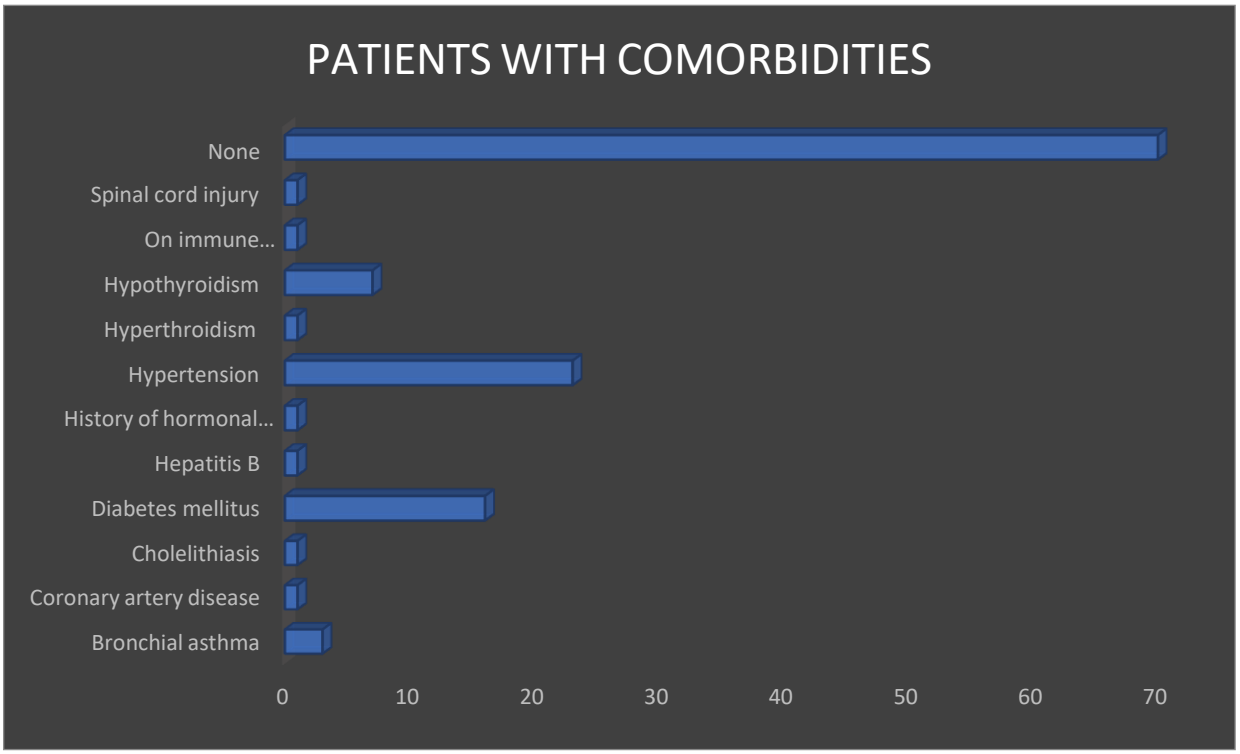
16. MENSTRUAL STATUS

MENSTRUAL STATUS	FREQUENCY	PERCENTAGE
Peri-menopausal	10	9.26%
Post-menopausal	62	56.48%
Pre- menopausal	37	34.26%
Grand Total	**110**	**100.00%**



17. COMORBIDITIES

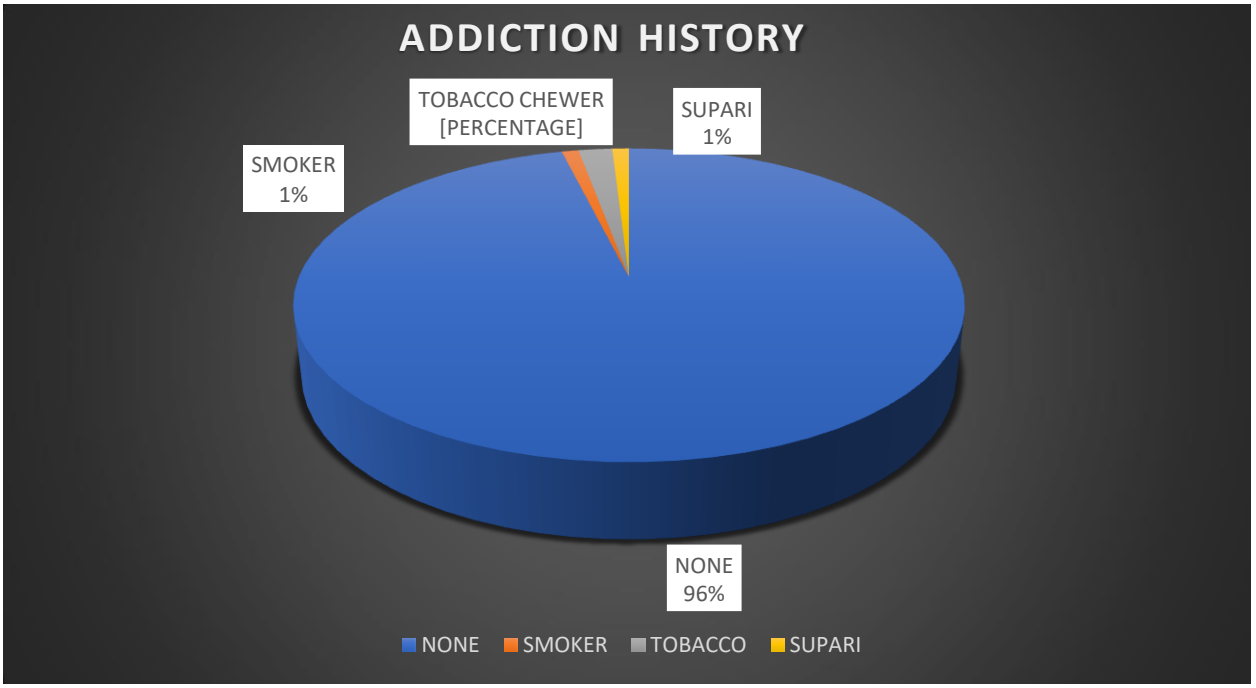
COMORBIDITY	FREQUENCY	PERCENTAGE(%)
Bronchial asthma	3	2.38095
Coronary artery disease	1	0.79365
Cholelithiasis	1	0.79365
Diabetes mellitus	16	12.6984
Hepatitis B	1	0.79365
History of hormonal therapy	1	0.79365
Hypertension	23	18.254
Hyperthroidism	1	0.79365
Hypothyroidism	7	5.55556
On immune suppressive therapy	1	0.79365
Spinal cord injury	1	0.79365
None	70	55.5556
TOTAL		**100**



Out of the 110 patients whose comorbidity history was elicited 2 patients had 3 comorbidities, 18 patients had 2 comorbidities, and the rest had 1 comorbidity. Most common comorbidities were Hypertension(18.2%) and Diabetes mellitus(12.6%).

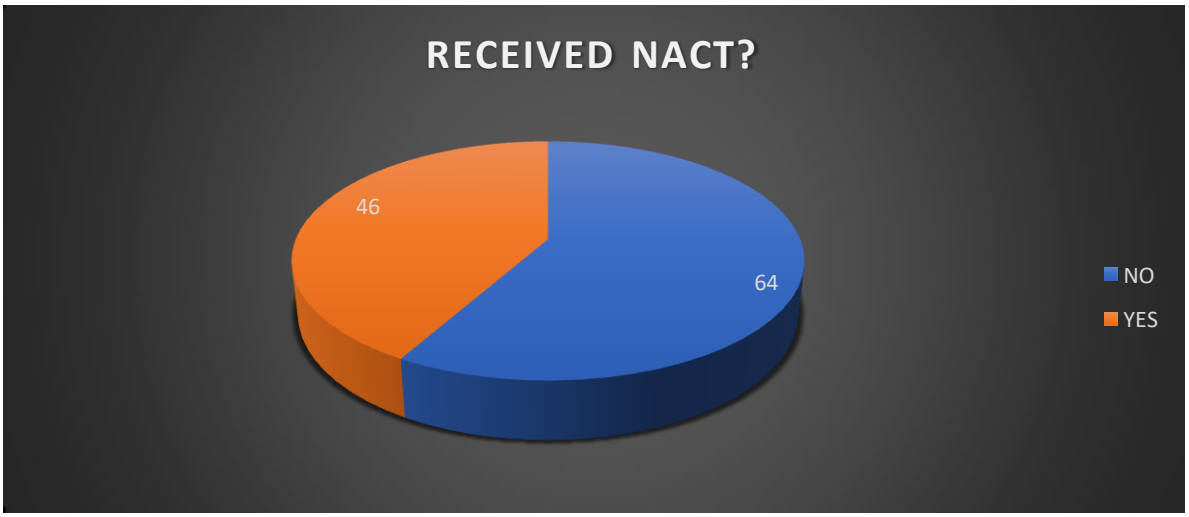
18. ADDICTION HISTORY

ADDICTION	FREQUENCY	PERCENTAGE
NONE	100	96.14%
SMOKER	1	0.96%
TOBACCO	2	1.94%
SUPARI	1	0.96%
TOTAL		**100.00%**



19. <u>DID THE PATIENT RECEIVE NEOADJUVANT CHEMOTHERAPY OR NOT?</u>

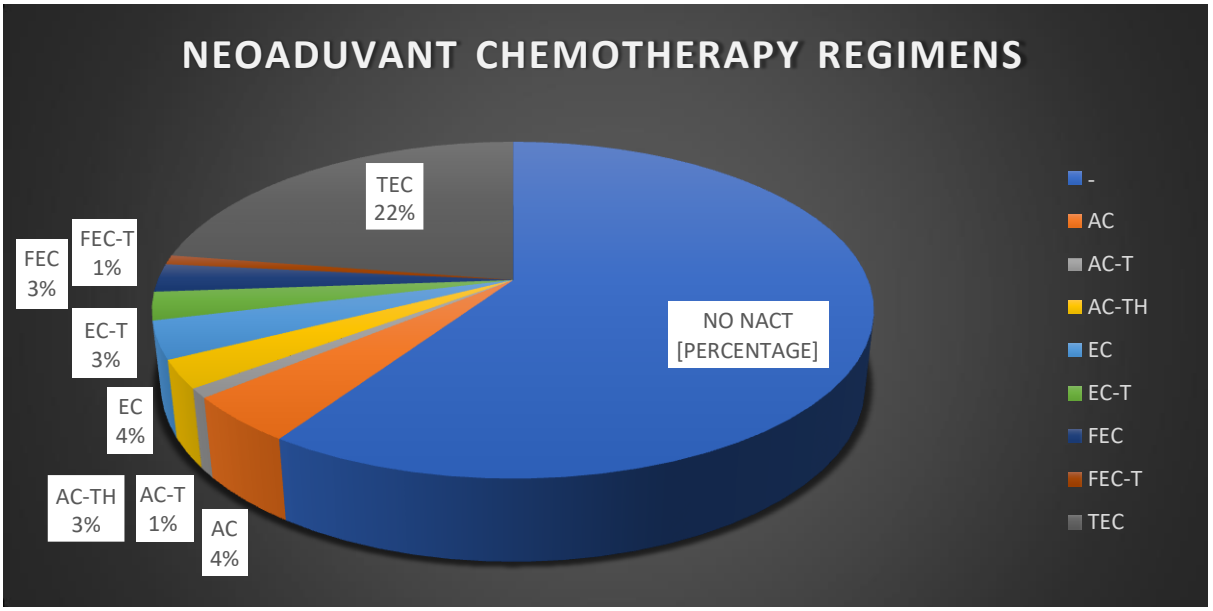
RECEIVED NACT?	FREQUENCY	PERCENTAGE
NO	64	58.18%
YES	46	41.82%
Grand Total	**110**	**100.00%**



Out of the 111 patients enrolled, 110 patients gave responses about whether or not they received NACT. 41.82% received NACT while 58.18% did not.

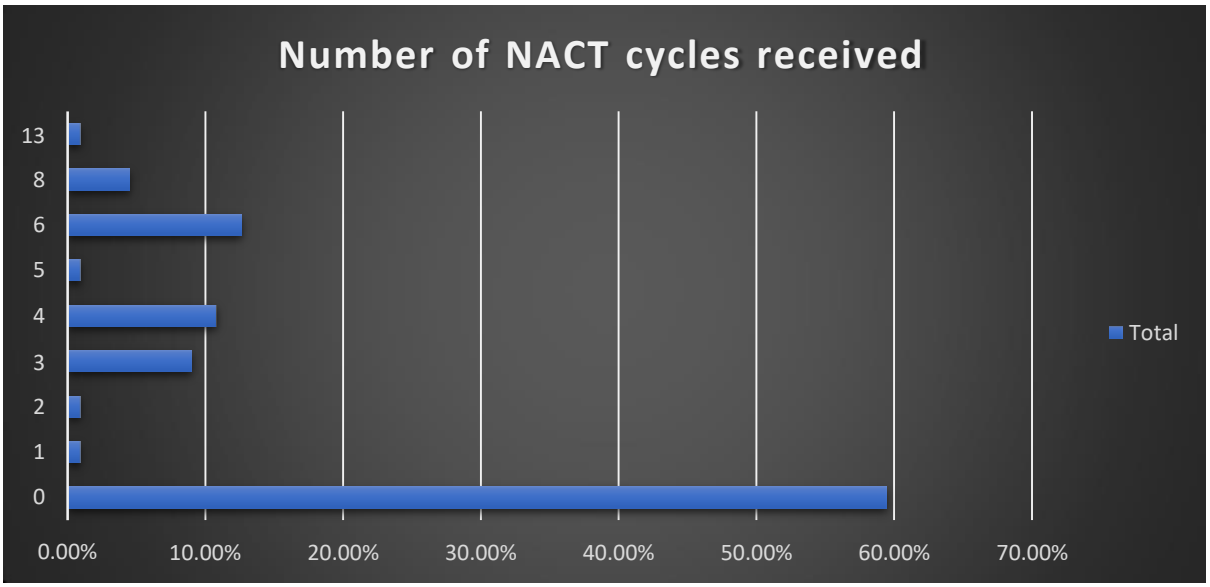
20. NEOADJUVANT CHEMOTHERAPY REGIMEN

NACT REGIMEN	FREQUENCY	PERCENTAGE
NO NACT	66	59.46%
AC	5	4.50%
AC-T	1	0.90%
AC-TH	3	2.70%
EC	4	3.60%
EC-T	3	2.70%
FEC	3	2.70%
FEC-T	1	0.90%
TEC	25	22.52%
Grand Total	**111**	**100.00%**



Out of the 111 patients, 66 did not receive NACT. Most common regimen received was TEC(22.52%) followed by AC regimen(4.5%).

21. NUMBER OF NACT CYCLES RECEIVED

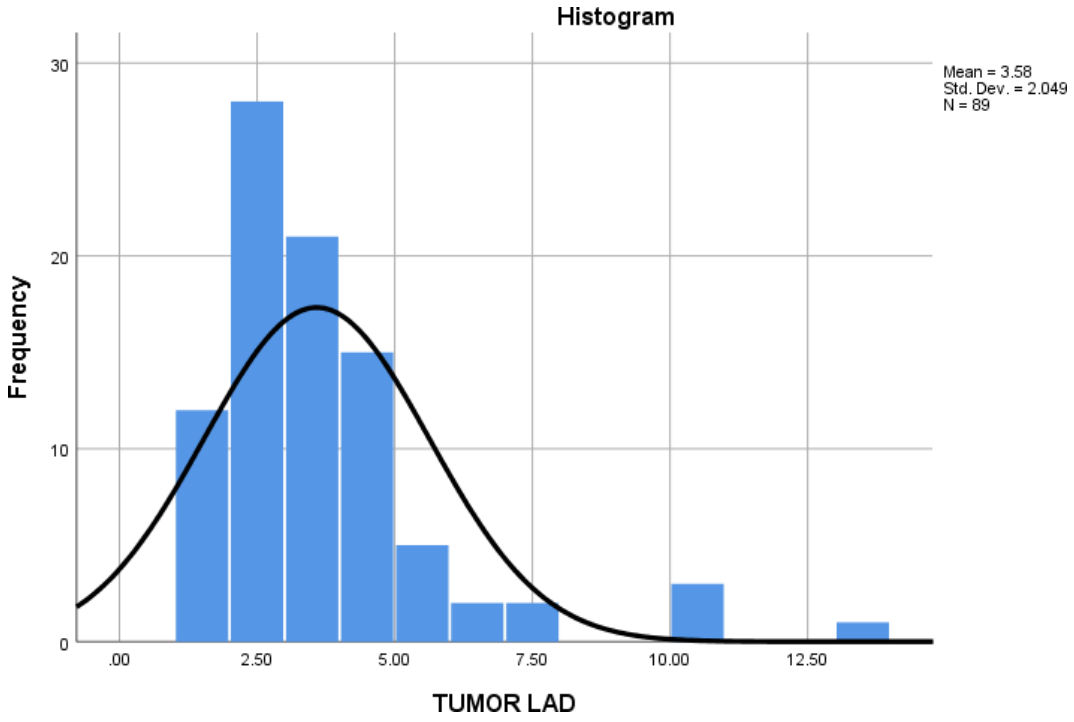


NUMBER OF CYCLES OF NACT	FREQUENCY	PERCENTAGE
0	66	59.46%
1	1	0.90%
2	1	0.90%
3	10	9.01%
4	12	10.81%
5	1	0.90%
6	14	12.61%
8	5	4.50%
13	1	0.90%
Grand Total	**111**	**100.00%**

TEC CYCLES	FREQUENCY	PERCENTAGE
1	1	4%
3	9	36%
4	3	12%
6	12	48%
Grand Total	**25**	**100.00%**

Out of the 22 patients who received TEC, 48% patients received complete NACT and 36% received 3 cycles TEC as NACT.

22. TUMOUR LONGEST AXIS DIAMETER ON IMAGING (MAMMOGRAPHY /CT SCAN)



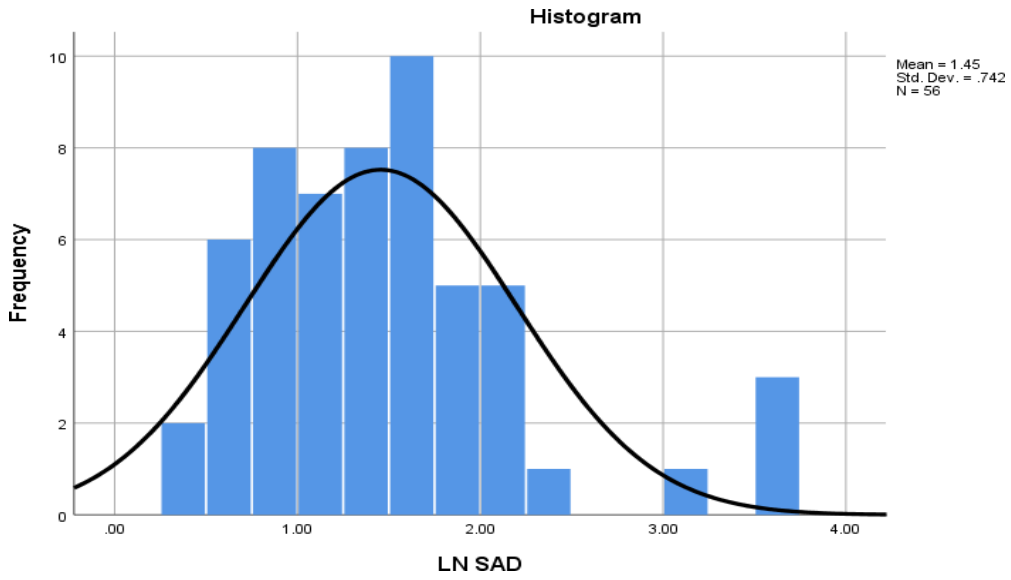
Out of the 111 patients, data of 89 patients were available and that of 22 were missing. Long axis diameters of the tumors ranged from 1cm to 13cm with a mean of 3.58cm

Statistics

TUMOR LAD

N		89
	Missing	22
Mean		3.5819
Median		3.0000
Mode		1.80[a]
Std. Deviation		2.04927
Variance		4.199
Range		12.00
Minimum		1.00
Maximum		13.00

23. LYMPH NODE SHORT AXIS DIAMETER



Statistics

LN SAD

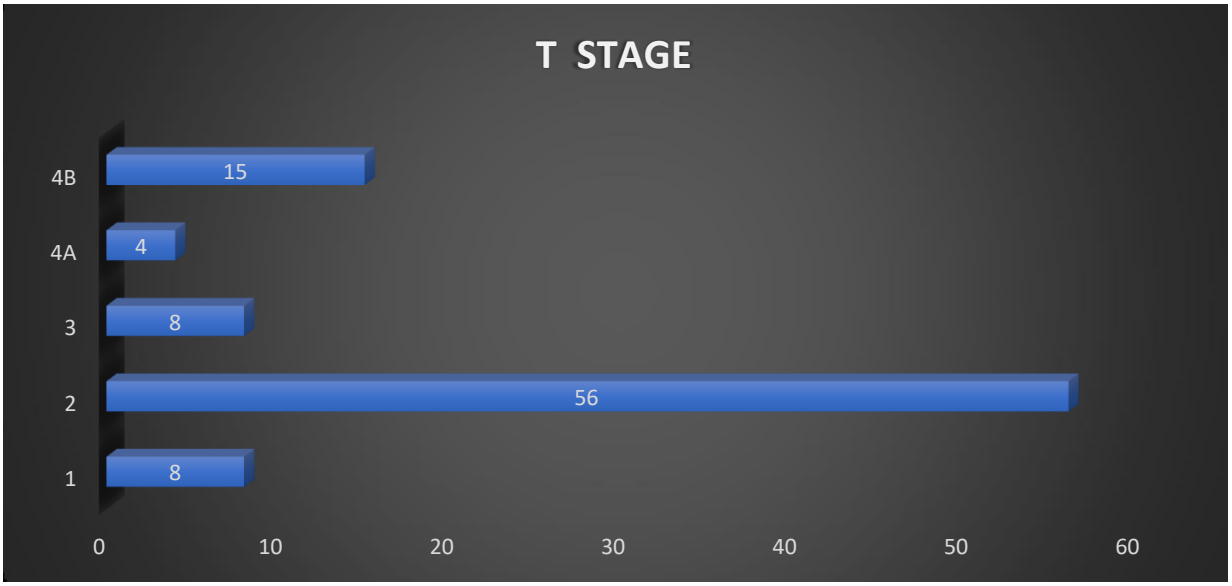
N	Valid	56
	Missing	55
Mean		1.4548
Median		1.4000
Mode		.80[a]
Std. Deviation		.74238
Variance		.551
Range		3.40
Minimum		.30
Maximum		3.70

The Lymph node SAD's were available for 56 out of 111 patients, ranging from 0.3 to 3.7 with a mean and median of 1.45 and 1.4 respectively.

24. TNM STAGING

A. TUMOUR (cT) STAGING

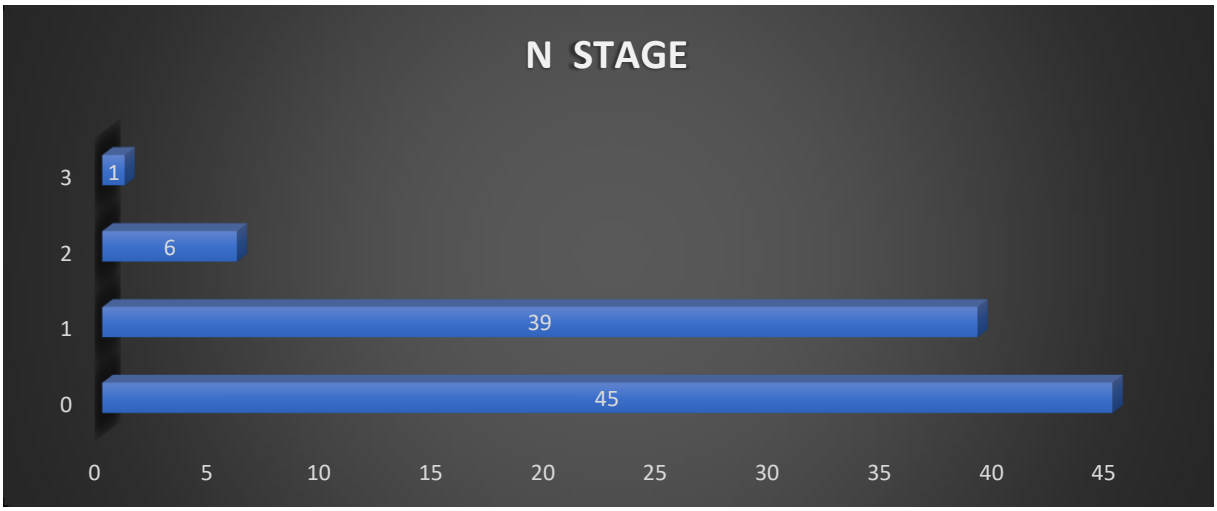
T STAGE	FREQUENCY	PERCENTAGE
1	8	8.79%
2	56	61.54%
3	8	8.79%
4A	4	4.40%
4B	15	16.48%
Grand Total	**91**	**100.00%**



TNM staging of 91 out of 111 patients were available with majority of 61.54 % patients having T2 staging followed by 16.8% patients with T4b stage.

B. NODAL(cN) STAGE

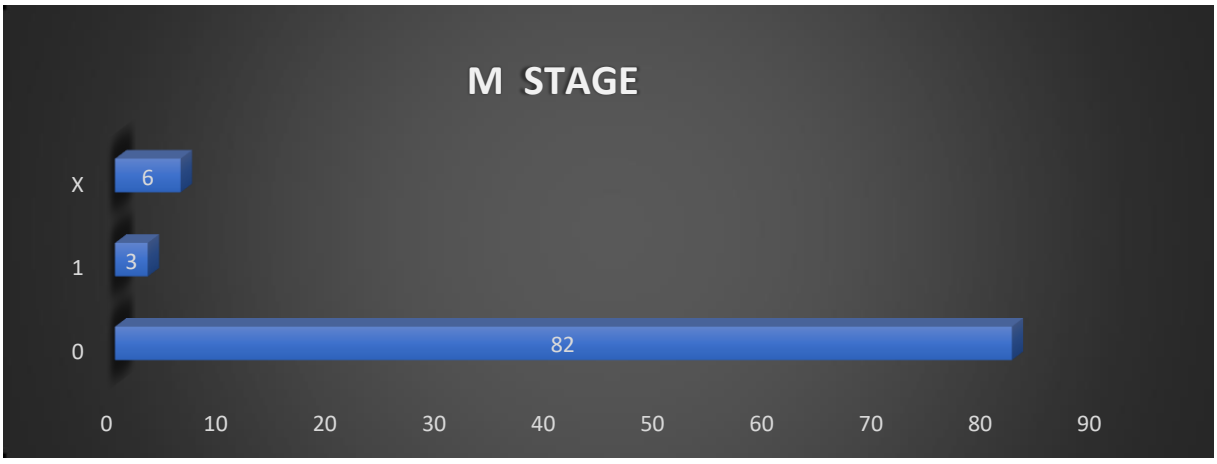
N STAGE	PERCENTAGE	FREQUENCY
N0	49.45%	45
N1	42.86%	39
N2	6.59%	6
N3	1.10%	1
Grand Total	**100.00%**	**91**



Nodal staging details of 91 patients were collected out of which a majority of 49.45% were N0 stage followed by 42.86% of N1 stage and the least from N3 stage (1.1%).

C. METASTATIC STAGING(M)

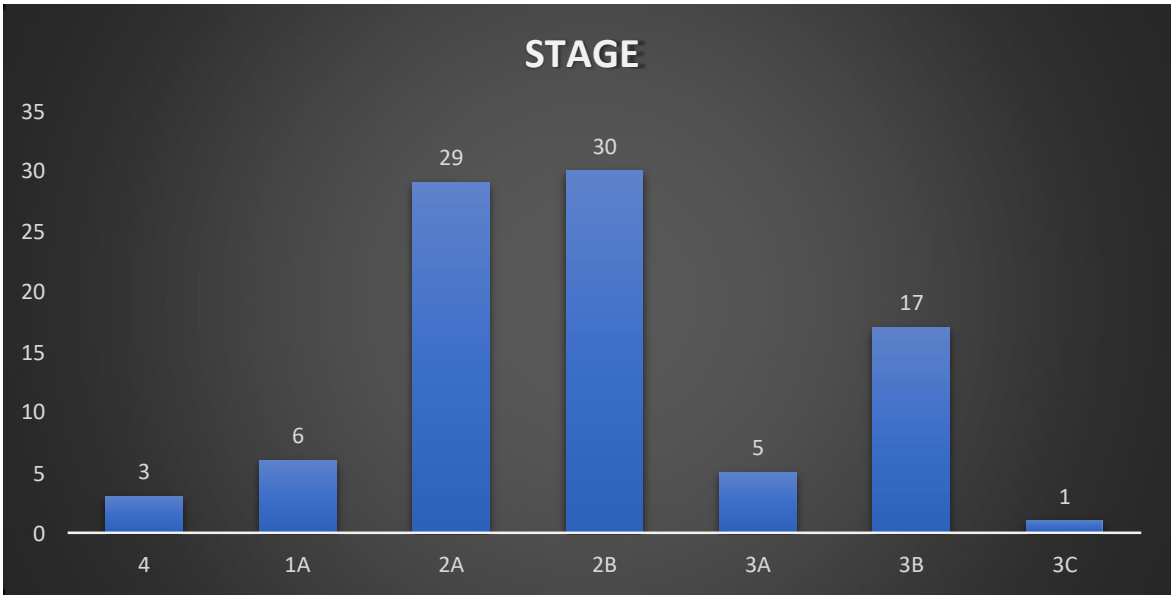
M STAGE	FREQUENCY	PERCENTAGE
0	82	90.11%
1	3	3.30%
X	6	6.59%
Grand Total	**91**	**100.00%**



Out of the 91 patients, 90.11% patients were M0, 3.30% were metastatic and the rest were not worked up for metastasis.

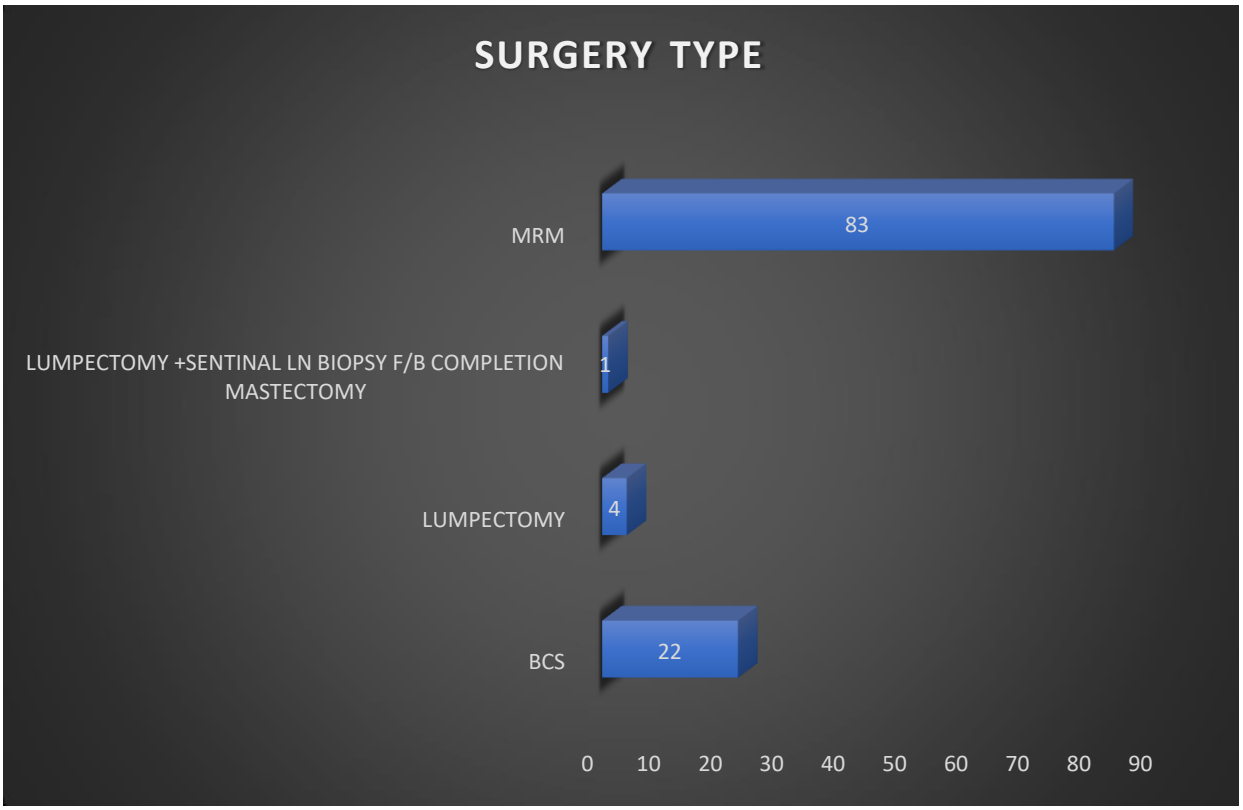
D. TNM STAGING

STAGE	FREQUENCY	PERCENTAGE
1A	6	6.59%
2A	29	31.87%
2B	30	32.97%
3A	5	5.49%
3B	17	18.68%
3C	1	1.10%
4	3	3.30%
Grand Total	**91**	100%



25. TYPE OF SURGERY DONE

SURGERY TYPE	FREQUENCY	PERCENTAGE
BREAST CONSERVATION SURGERY	22	20.00%
LUMPECTOMY	4	3.64%
LUMPECTOMY +SENTINAL LN BIOPSY F/B COMPLETION MASTECTOMY	1	0.91%
MODIFIED RADICAL MASTECTOMY	83	75.45%
Grand Total	**110**	**100.00%**

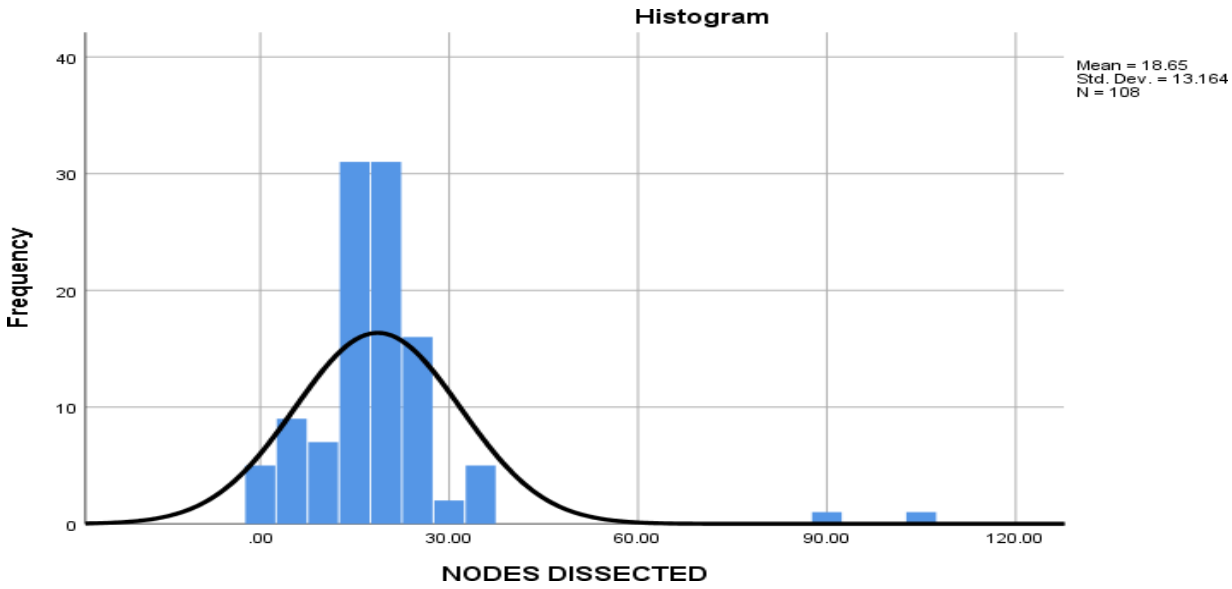


26. NUMBER OF NODES DISSECTED

Statistics

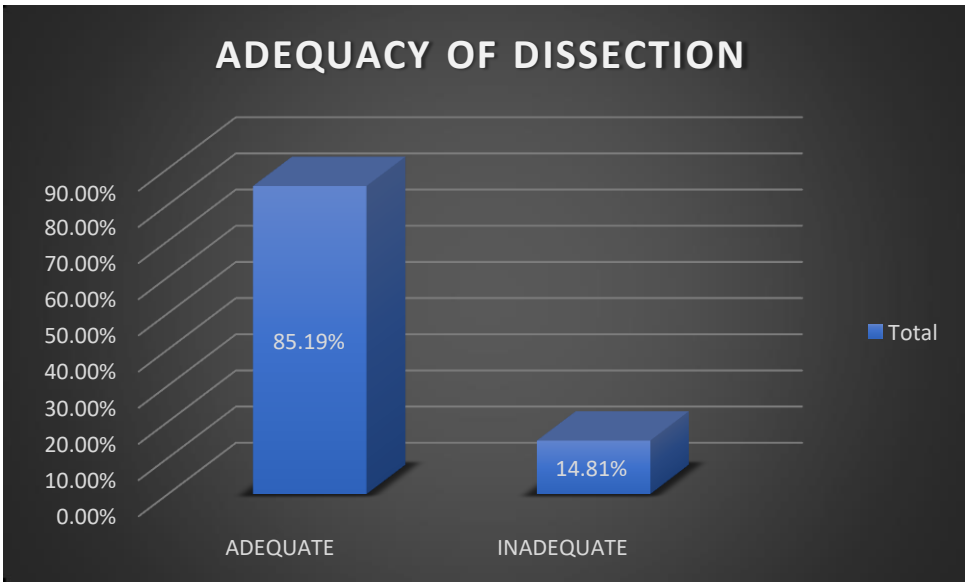
NODES DISSECTED

N	Valid	108
	Missing	4
Mean		18.6481
Median		18.0000
Mode		18.00
Std. Deviation		13.16418
Variance		173.296
Range		103.00
Minimum		.00
Maximum		103.00



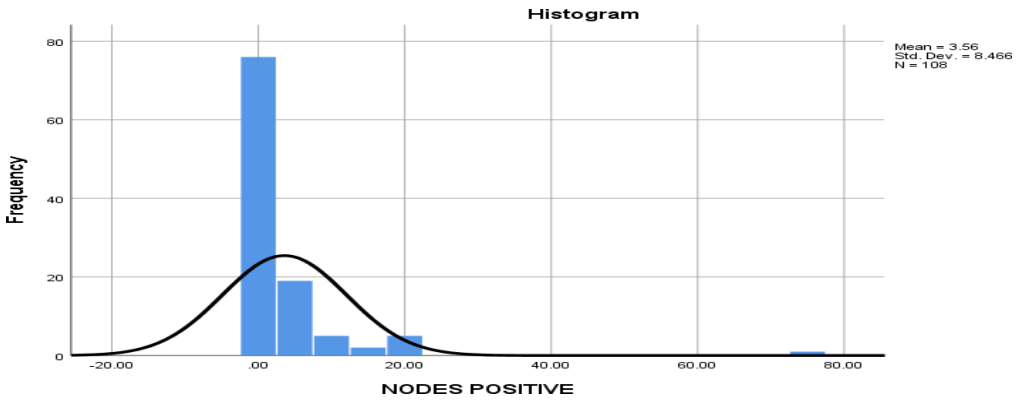
27. ADEQUACY OF DISSECTION? (>10 LN DISSECTED-ADEQUATE)

WAS DISSECTION ADEQUATE(>10 LN)?	FREQUENCY	PERCENTAGE
Adequate dissection	92	85.19%
Inadequate dissection	16	14.81%
Grand Total	**108**	**100.00%**



Out of the 108 patients, 85.19% patients had underwent adequate dissection while 14.81% patient had inadequate dissection.

28. NUMBER OF POSITIVE NODES



Statistics

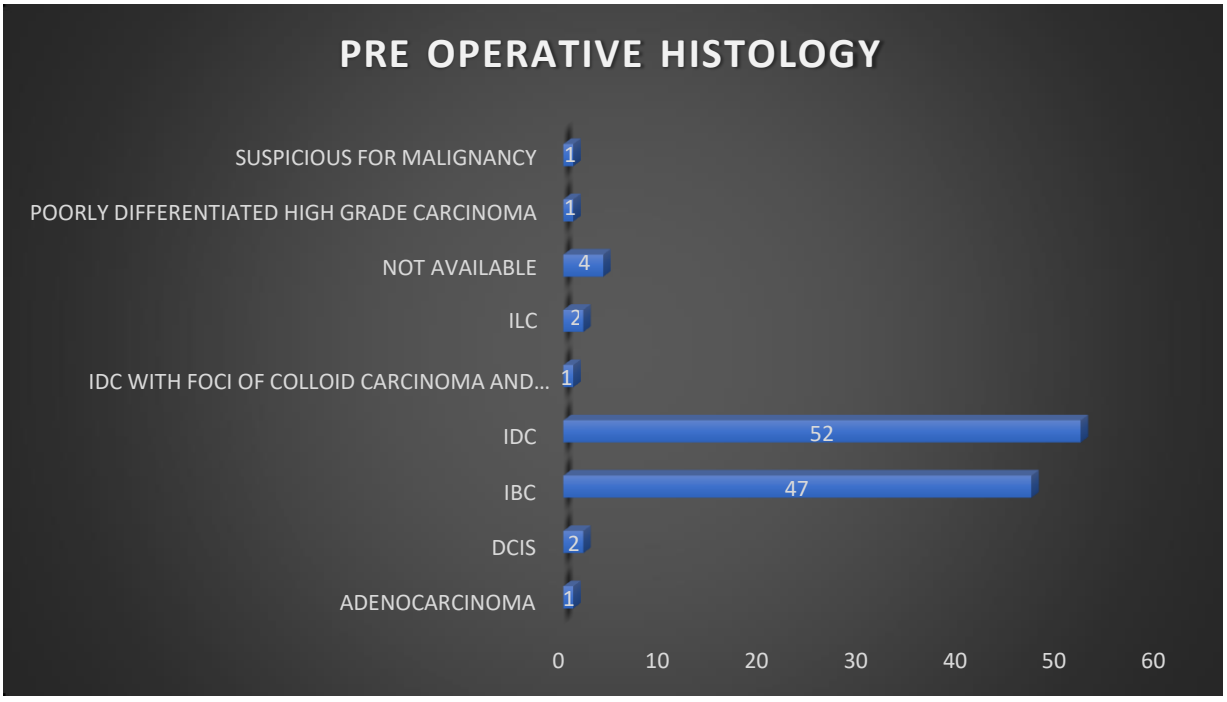
NODES POSITIVE

N	Valid	108
	Missing	4
Mean		3.5648
Median		1.0000
Mode		.00
Std. Deviation		8.46573
Variance		71.669
Range		75.00
Minimum		.00
Maximum		75.00

The node positivity data of 108 patients were collected, out of which maximum and minimum node positivity were 75 and 0 respectively with a mean of 3.56 nodes positive.

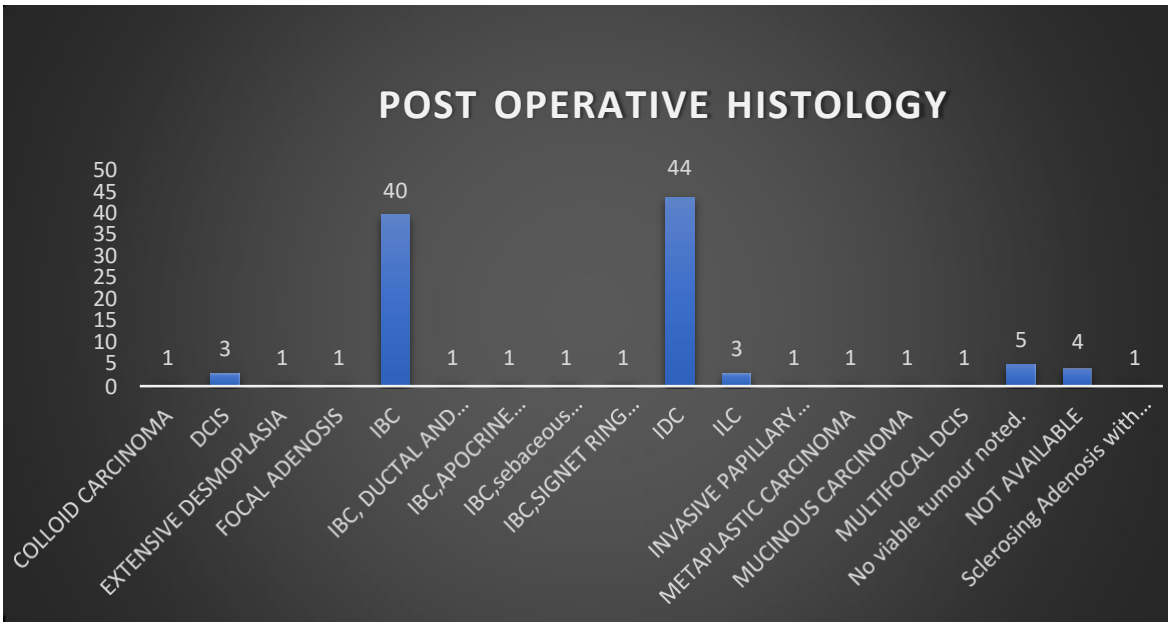
29. PRE OPERATIVE HISTOLOGY

PRE OP HISTOLOGY	FREQUENCY	PERCENTAGE
ADENOCARCINOMA	1	0.90%
DUCTAL CARCINOMA IN SITU	2	1.80%
INVASIVE BREAST CARCINOMA,NOS	47	42.34%
INVASIVE DUCTAL CARCINOMA	52	46.85%
IDC WITH FOCI OF COLLOID CARCINOMA AND MICROPAPILLARY CARCINOMA	1	0.90%
INVASIVE LOBULAR CARCINOMA	2	1.80%
NOT AVAILABLE	4	3.60%
POORLY DIFFERENTIATED HIGH GRADE CARCINOMA	1	0.90%
SUSPICIOUS FOR MALIGNANCY	1	0.90%
Grand Total	**111**	**100.00%**



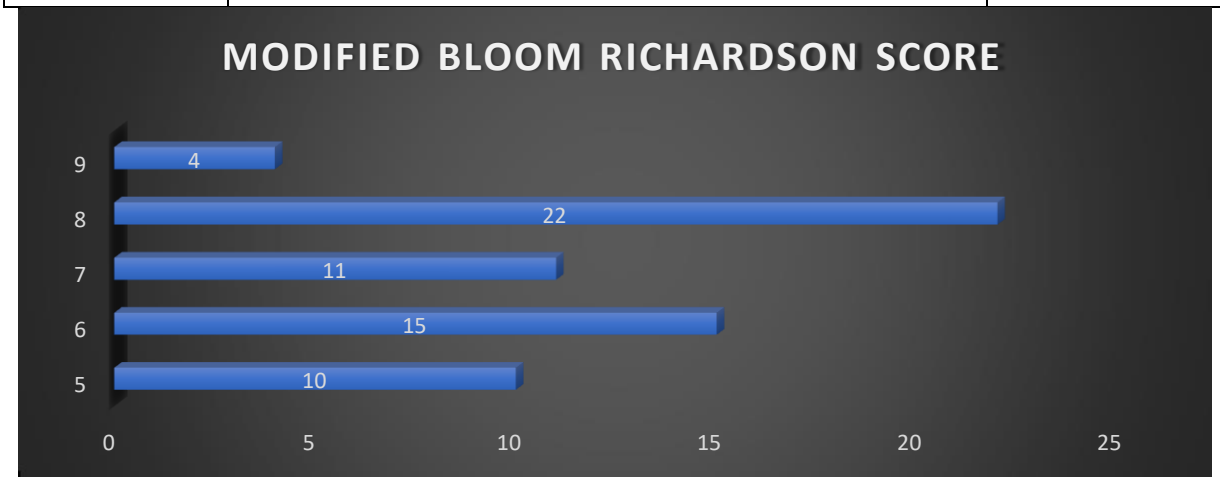
30. POST OPERATIVE HISTOPATHOLOGY

POST OP HISTOLOGY	FREQUENCY	PERCENTAGE
COLLOID CARCINOMA	1	0.90%
DCIS	3	2.70%
EXTENSIVE DESMOPLASIA	1	0.90%
FOCAL ADENOSIS	1	0.90%
INVASIVE BREAST CARCINOMA	40	36.04%
IBC, DUCTAL AND LOBULAR PATTERN	1	0.90%
IBC,APOCRINE DIFFERENTIATION	1	0.90%
IBC,SEBACEOUS DIFFERENTIATION	1	0.90%
IBC,SIGNET RING DIFFERENTIATION	1	0.90%
INVASIVE DUCTAL CARCINOMA	44	39.64%
INVASIVE LOBULAR CARCINOMA	3	2.70%
INVASIVE PAPILLARY CARCINOMA	1	0.90%
METAPLASTIC CARCINOMA	1	0.90%
MUCINOUS CARCINOMA	1	0.90%
MULTIFOCAL DCIS	1	0.90%
NO VIABLE TUMOUR NOTED.	5	4.50%
NOT AVAILABLE	4	3.60%
SCLEROSING ADENOSIS WITH FEW ATYPICAL CELLS.	1	0.90%
Grand Total	**111**	**100.00%**



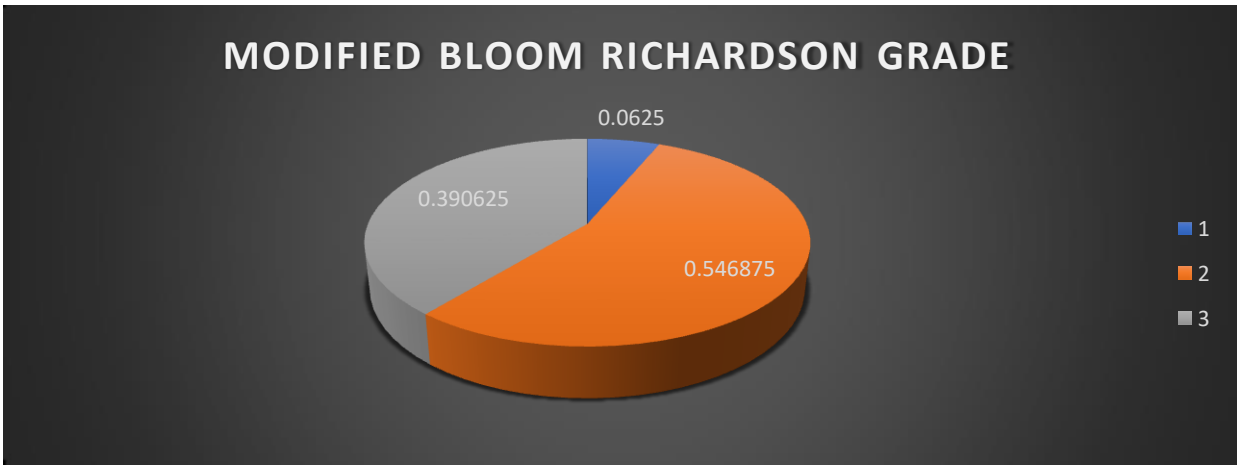
31. MODIFIED BLOOM RICHARDSON SCORE

MBR SCORE	FREQUENCY	PERCENTAGE
5	10	16.13%
6	15	24.19%
7	11	17.74%
8	22	35.48%
9	4	6.45%
Grand Total	**62**	**100.00%**



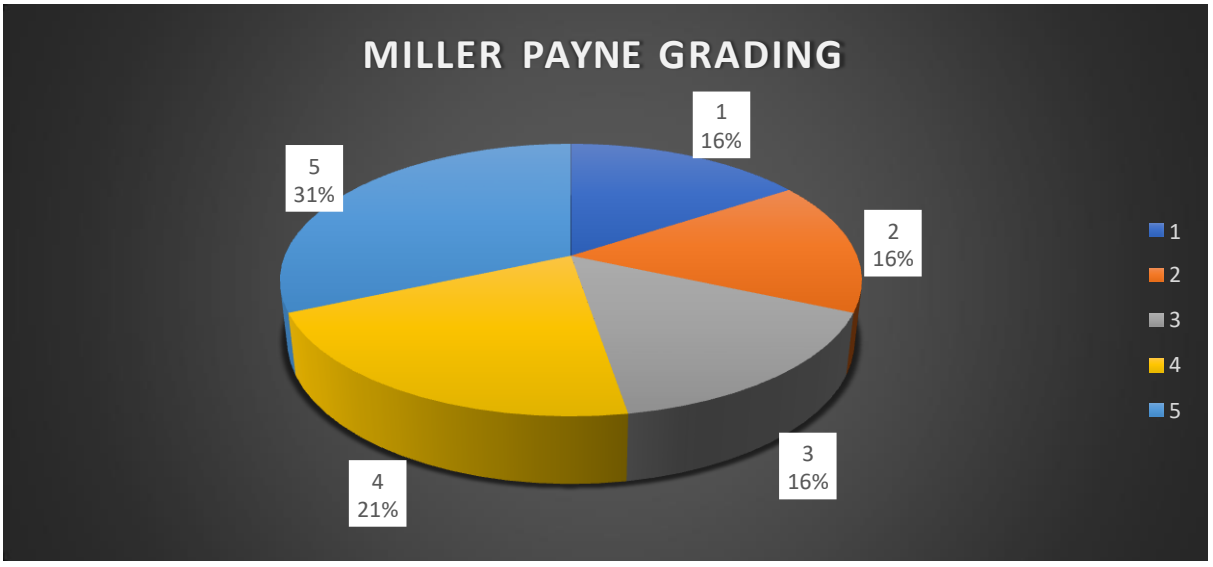
Out of the 62 patients with reported Modified Bloom Richardson Scores, the majority had a score of 8(35.48%) followed 24.19% patients with a score of 6. Only 6.45% patients had a score of 9.

32. MODIFIED BLOOM RICHARDSON GRADE



MBR GRADE	FREQUENCY	PERCENTAGE
1	4	6.25%
2	35	54.69%
3	25	39.06%
Grand Total	**64**	**100.00%**

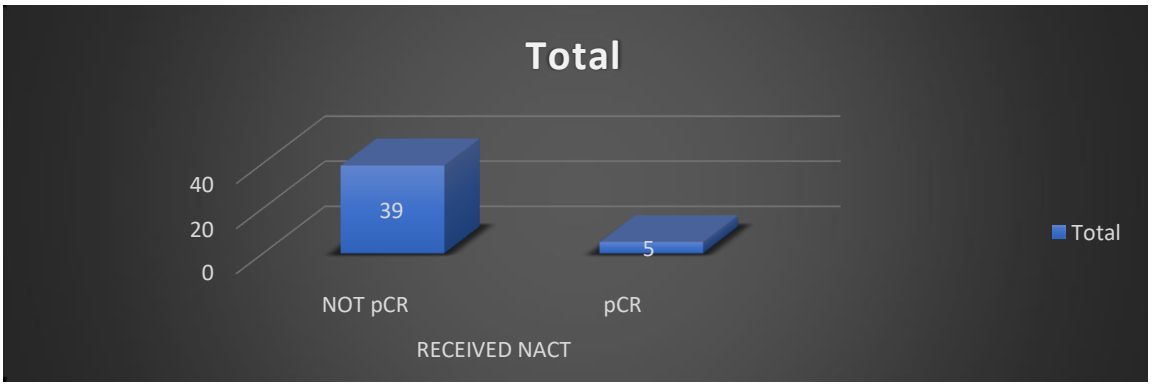
33. MILLER PAYNE GRADING



MPG	FREQUENCY	PERCENTAGE
1	3	15.79%
2	3	15.79%
3	3	15.79%
4	4	21.05%
5	6	31.58%
Grand Total	**19**	**100.00%**

Out of the 19 patients with reported Miller Payne Grading, 31.58% had grade 5 followed by 21.05% had grade 4. The other 3 grades had equal shares among the rest.

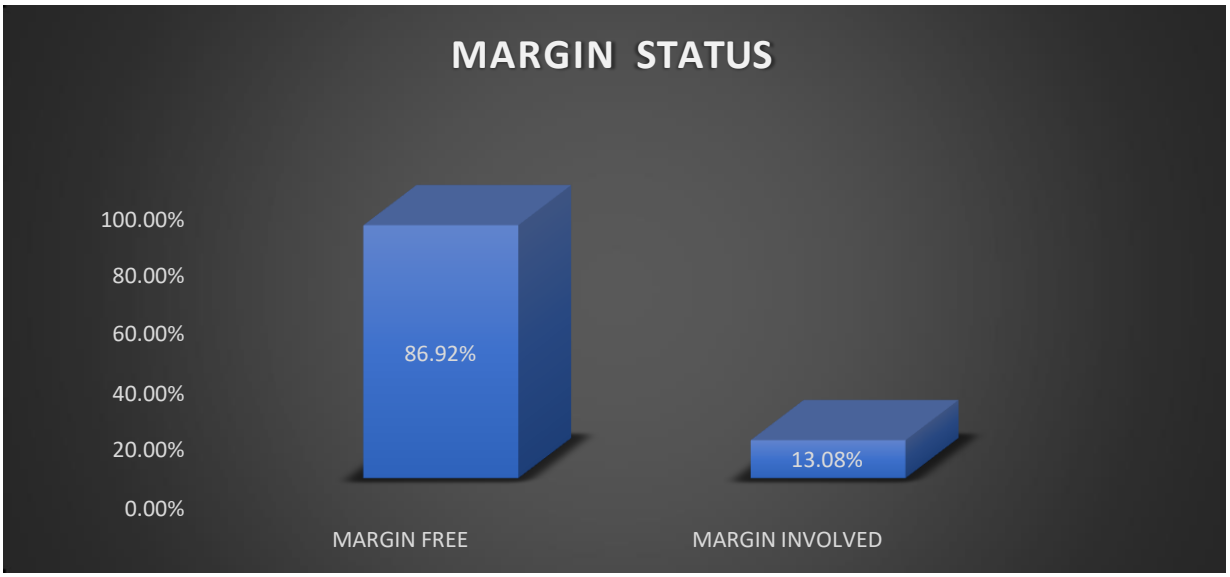
34. PATHOLOGICAL COMPLETE RESPONSE POST NACT



Row Labels	FREQUENCY
RECEIVED NACT	46
NOT pCR	40
pCR	5
UNKNOWN	1
Grand Total	**46**

35. MARGIN STATUS

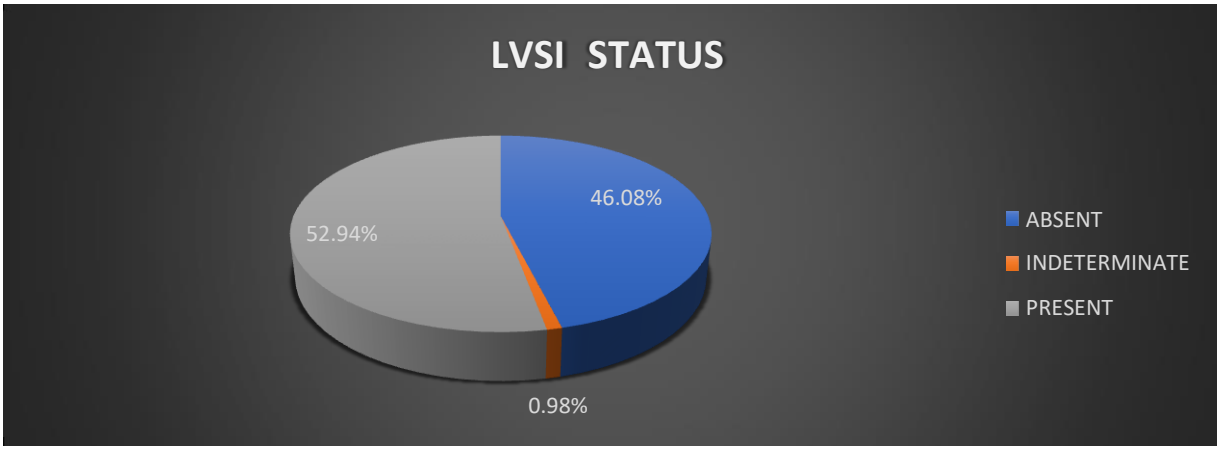
MARGIN STATUS	FREQUENCY	PERCENTAGE
MARGIN UNINVOLVED	93	86.92%
MARGIN INVOLVED	14	13.08%
Grand Total	**107**	**100.00%**



Out of the 107 patients with margin status on record, 86.92% had free margins while 13.08% patients had involved margins. Out of these except 1 , all were operated cases of MRM and 1 case of BCS.

36. LYMPHOVASCULAR SPACE INFILTRATION STATUS(LVSI)

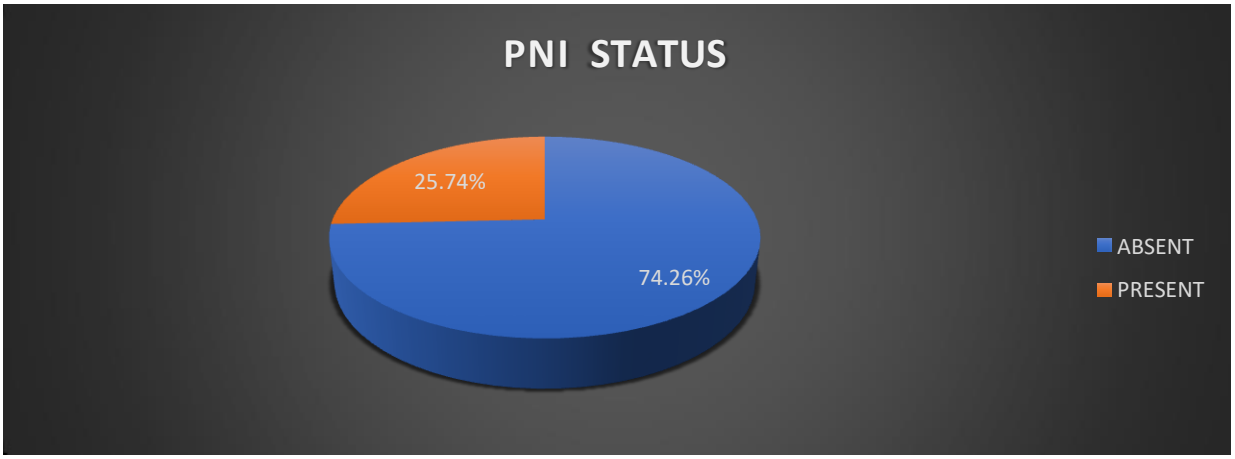
LVSI STATUS	FREQUENCY	PERCENTAGE
ABSENT	47	46.08%
INDETERMINATE	1	0.98%
PRESENT	54	52.94%
Grand Total	**102**	**100.00%**



Out of the 102 patients whose LVSI records were available, a majority of 52.94% had LVSI present and 46.08% had absent LVSI and 0.98% had an indeterminate status.

37. PERINEURAL INVASION

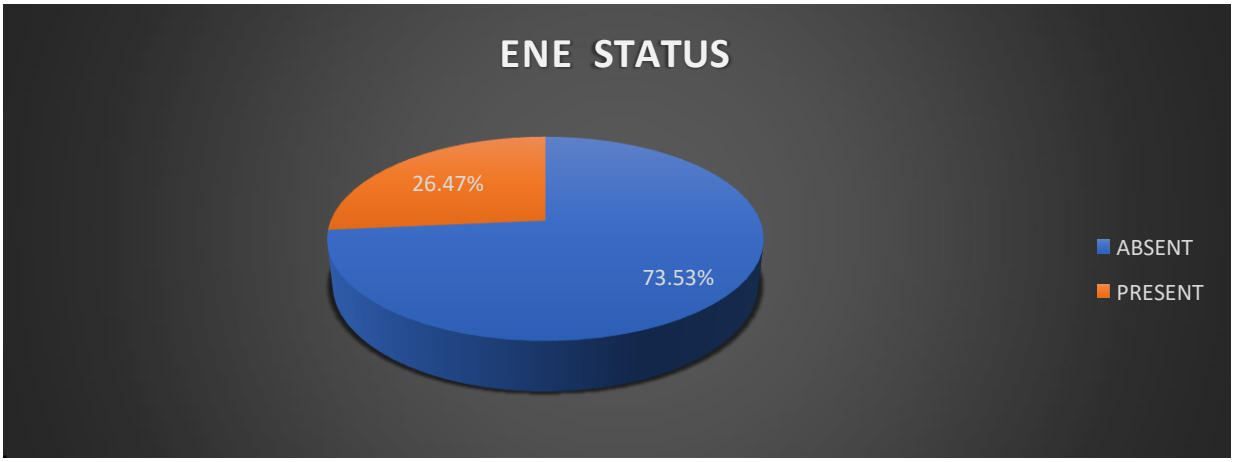
PNI STATUS	FREQUENCY	PERCENTAGE
Absent	75	74.26%
Present	26	25.74%
Grand Total	**101**	**100.00%**



Out of the 101 patients whose PNI records were available, a majority of 74.26% had PNI present and the rest had PNI absent.

38. EXTRA-NODAL EXTENSION STATUS

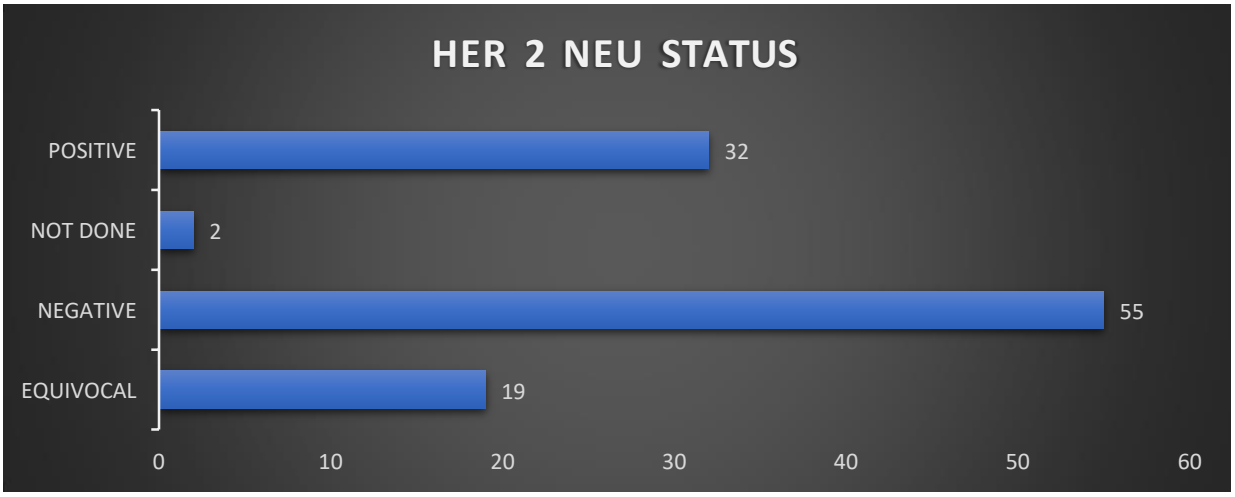
ENE STATUS	FREQUENCY	PERCENTAGE
ABSENT	75	73.53%
PRESENT	27	26.47%
Grand Total	**102**	**100.00%**



Out of the 102 patients whose ENE records were available, a majority of 73.53% had ENE present and the rest had ENE absent.

39. HER-2 NEU RECEPTOR STATUS BY IMMUNO-HISTOCHEMISTRY

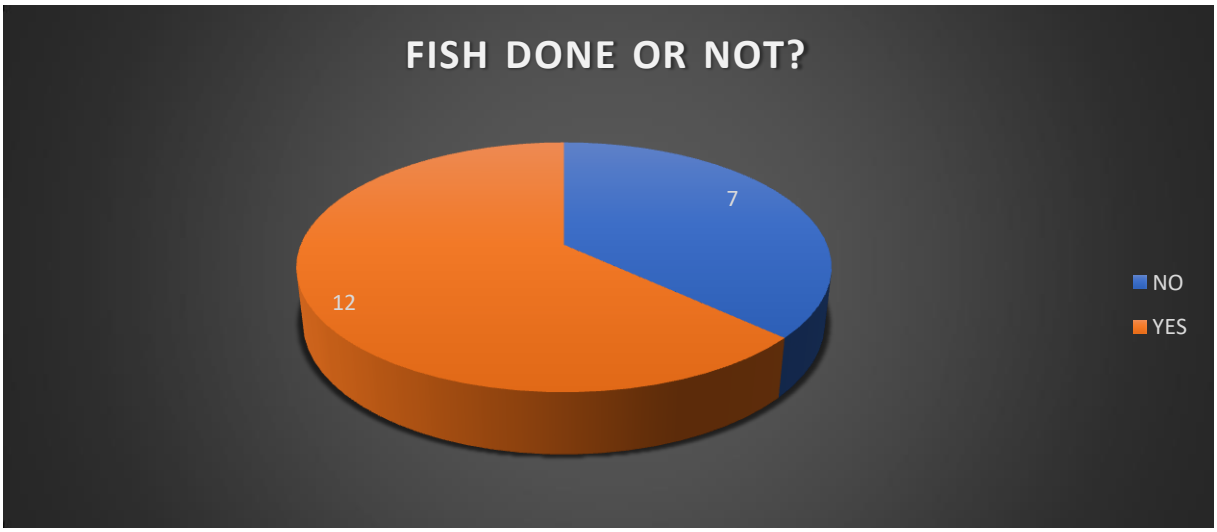
HER 2 STATUS	FREQUENCY	PERCENTAGE
EQUIVOCAL	19	17.59%
NEGATIVE	55	50.93%
NOT DONE	2	1.85%
POSITIVE	32	29.63%
Grand Total	**108**	**100.00%**



Out of the 108 patients whose Her-2 neu status records were available, a majority of 50.93% were negative, 29.63% had Her-2 neu positive , 17.59% patients had equivocal Her 2 receptor status by IHC and the rest did not have Her 2 status on record.

40. WHETHER FISH WAS DONE FOR HER-2 EQUIVOCAL PATIENTS OR NOT?

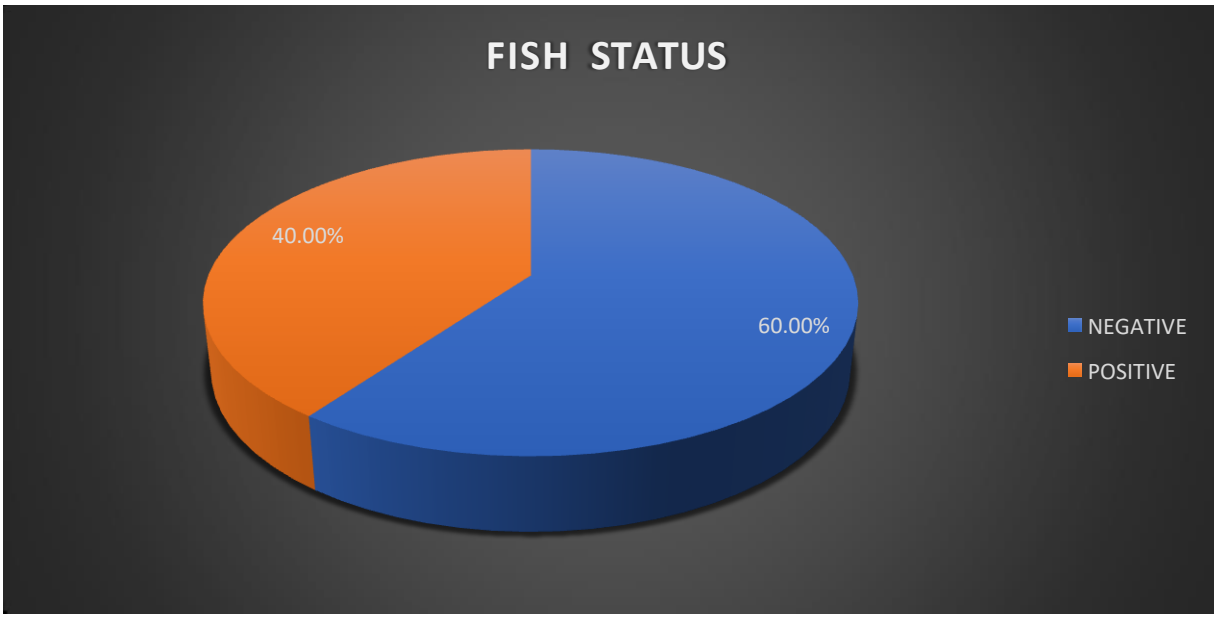
FISH DONE?	FREQUENCY	PERCENTAGE
NO	7	36.84%
YES	12	63.16%
Grand Total	**19**	**100.00%**



41. <u>HER-2 FISH STATUS?</u>

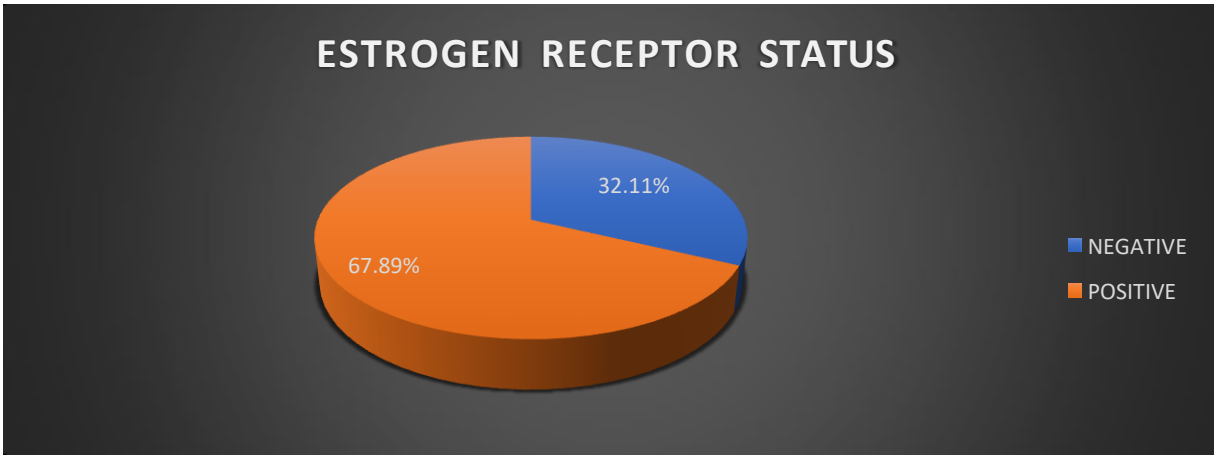
FISH STATUS	FREQUENCY	PERCENTAGE
NEGATIVE	6	60.00%
POSITIVE	4	40.00%
Grand Total	**10**	**100.00%**

10 out of 12 patients FISH reports are available which on analysis showed 60% negativity and 40% positivity.



42. ESTROGEN RECEPTOR STATUS

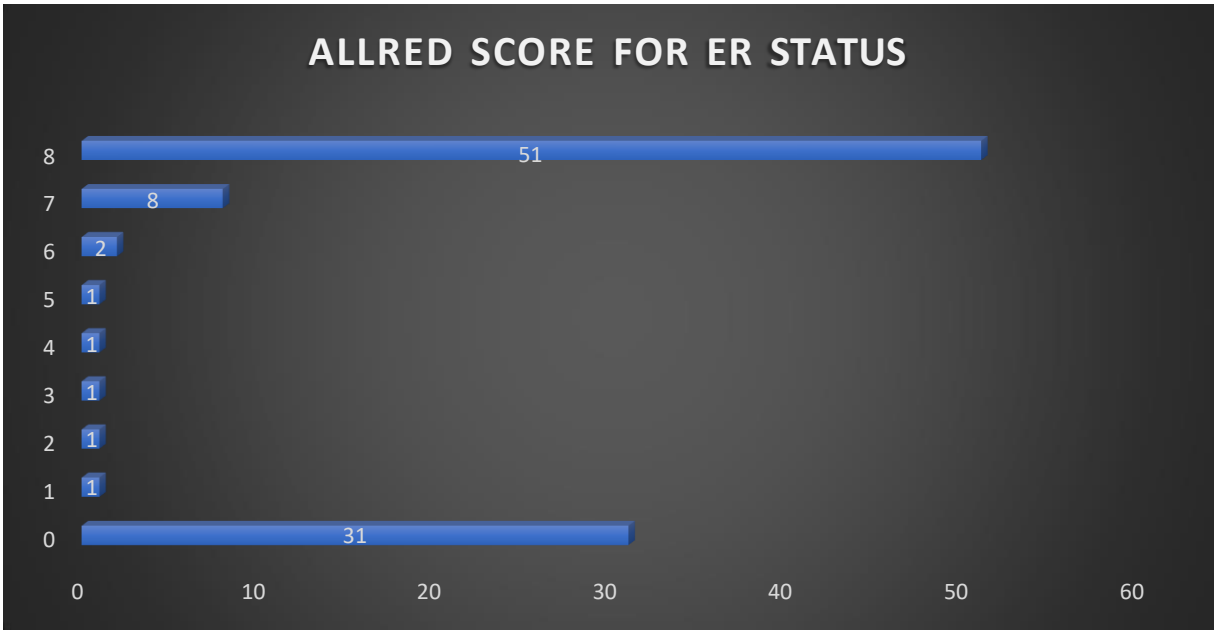
ESTROGEN RECEPTOR	FREQUENCY	PERCENTAGE
NEGATIVE	35	32.11%
POSITIVE	74	67.89%
Grand Total	**109**	**100.00%**



Out of the 109 patients whose ER status records were available, a majority of 67.89% were positive and 32.11% had ER negative.

43. ALLRED SCORE FOR ER STATUS ESTIMATION

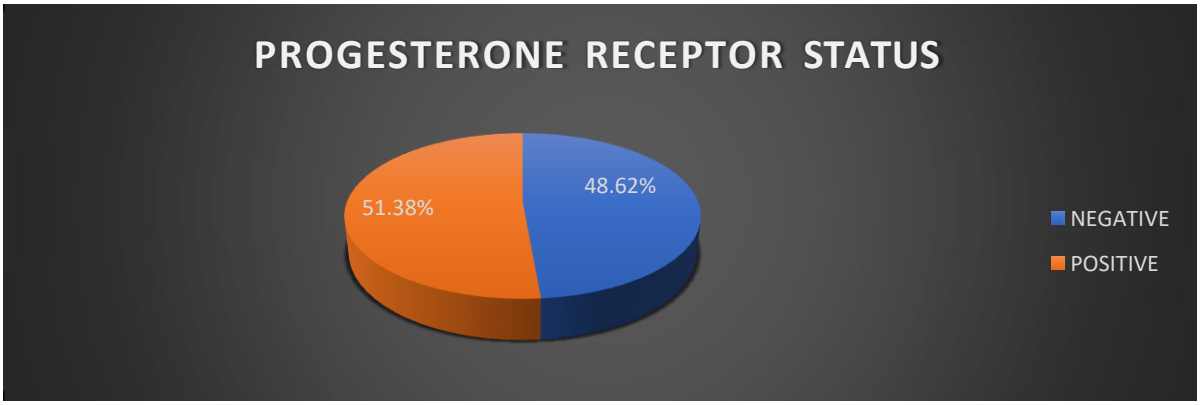
ALLRED SCORE	FREQUENCY	PERCENTAGE
0	31	31.96%
1	1	1.03%
2	1	1.03%
3	1	1.03%
4	1	1.03%
5	1	1.03%
6	2	2.06%
7	8	8.25%
8	51	52.58%
Grand Total	**97**	**100.00%**



Out of the 97 patients whose records were available a majority of 52.58% patients had a score of 8/8, followed by 31.96% patients with a score of 0.The rest had scores between 2 to 7.

44. PROGESTERONE RECEPTOR STATUS

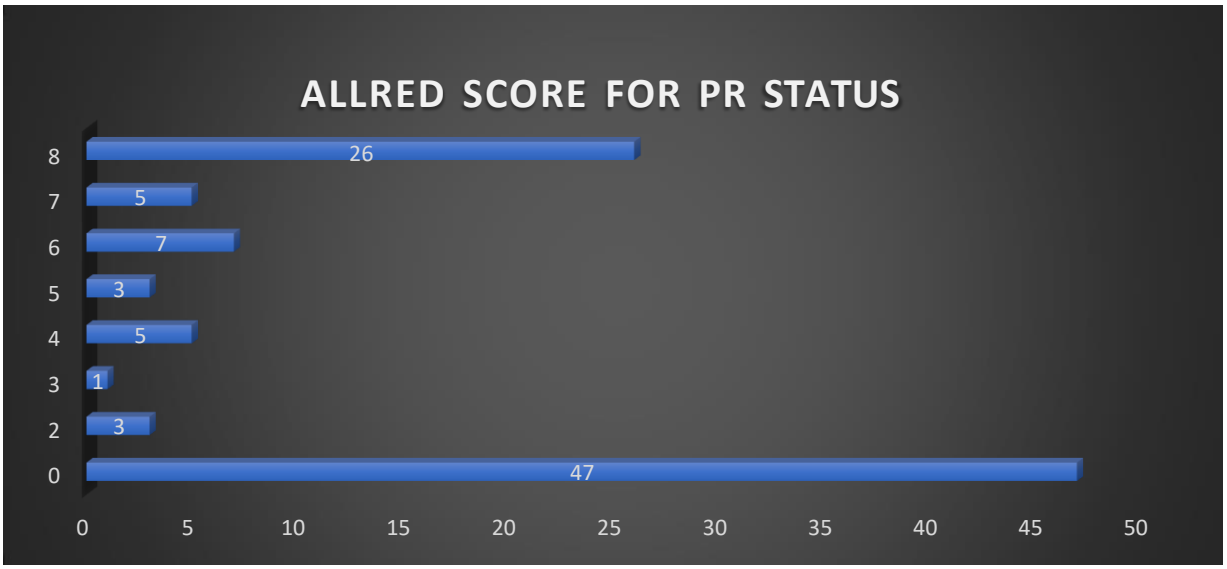
PROGESTERONE RECEPTOR STATUS	FREQUENCY	PERCENTAGE
NEGATIVE	53	48.62%
POSITIVE	56	51.38%
Grand Total	**109**	**100.00%**



Out of the 109 patients whose PR status records were available, a majority of 51.38% were PR positive and 48.62% had PR negative.

45. ALLRED SCORE FOR PROGESTERONE RECEPTOR STATUS

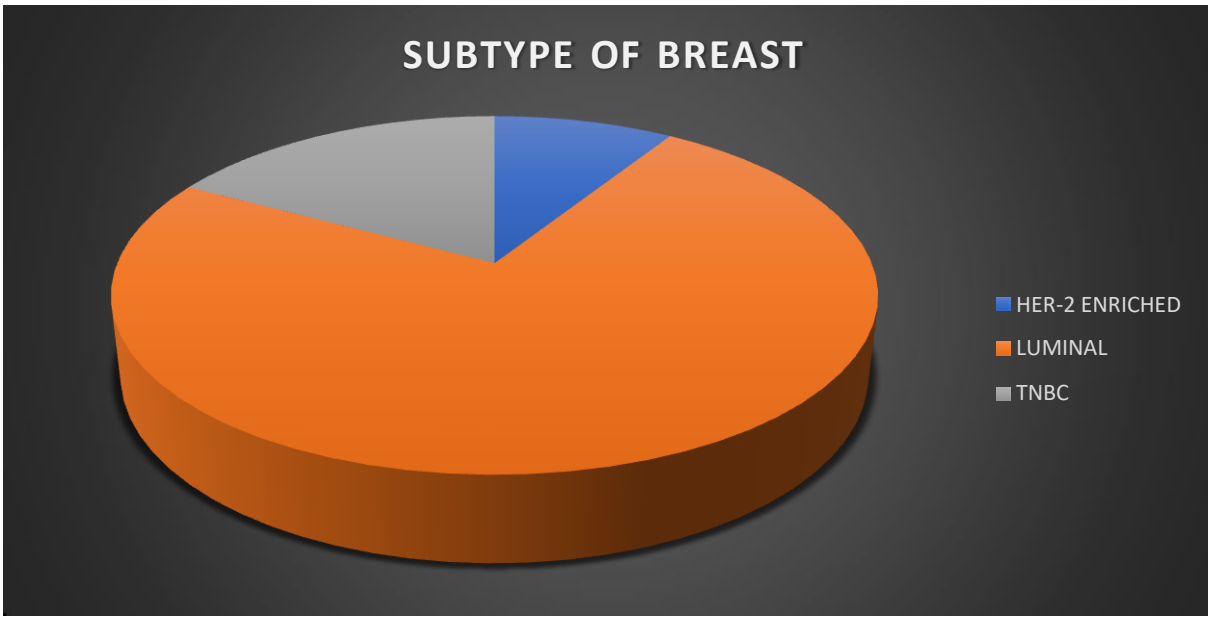
ALLRED SCORE FOR PR STATUS	FREQUENCY	PERCENTAGE
0	47	48.45%
2	3	3.09%
3	1	1.03%
4	5	5.15%
5	3	3.09%
6	7	7.22%
7	5	5.15%
8	26	26.80%
Grand Total	**97**	**100.00%**



Out of the 97 patients whose records were available a majority of 48.45% patients had a score of 0/8, followed by 26.80% patients with a score of 8/8. The rest had scores between 2 to 7.

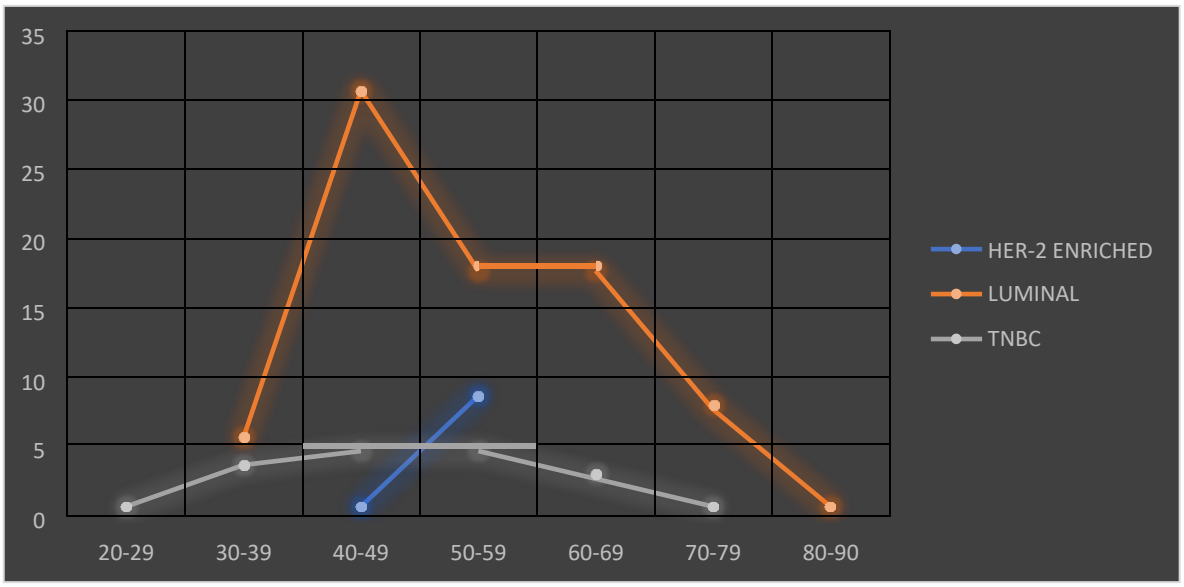
46. SUBTYPE OF BREAST CANCER

Row Labels	Count of Subtype
HER-2 ENRICHED	10
LUMINAL	82
TNBC	19
Grand Total	**111**



Out of the 111 patients assessed, 71.17% of patients were of Luminal subtype, 18.02% patients were of TNBC subtype, 9.01% patients were of Her-2 enriched subtype.

SUBTYPE	**MEAN OF AGE IN YEARS**
HER-2 ENRICHED	52.6
LUMINAL	53.64634146
TNBC	48.84210526



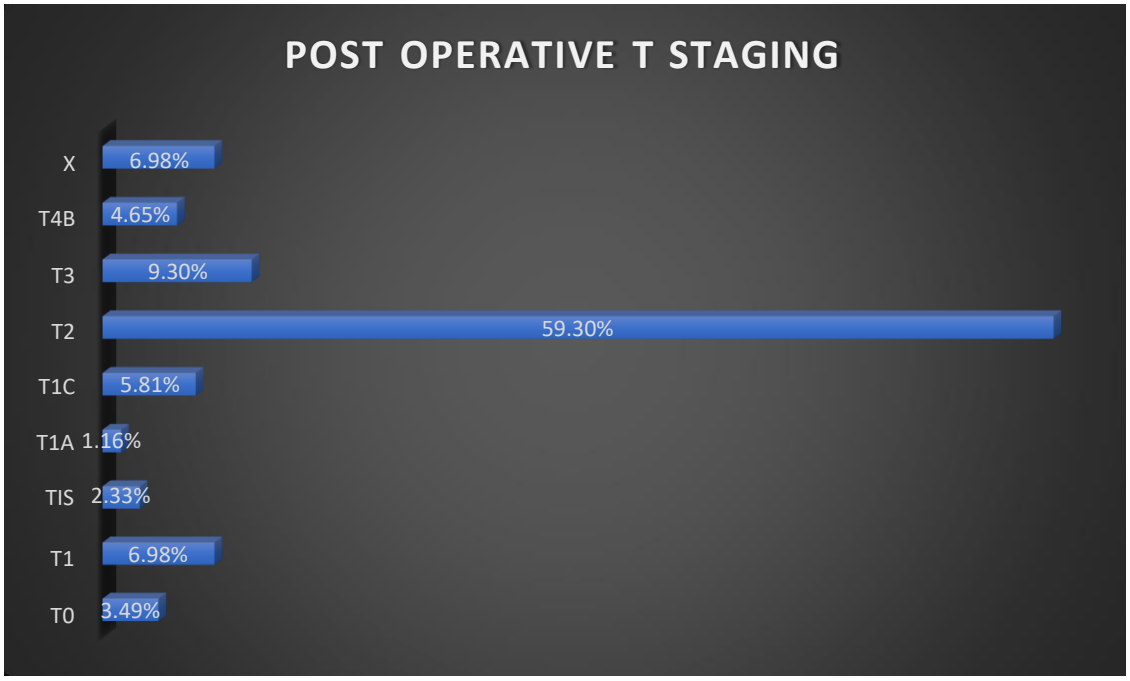
47. EFFECT OF SUBTYPE ON pCR.

ROW LABELS	FREQUENCY
RECEIVED NACT	46
HER-2 ENRICHED	2
NO	2
LUMINAL	34
NO	33
YES	1
TNBC	9
NO	5
YES	4
Grand Total	**44**

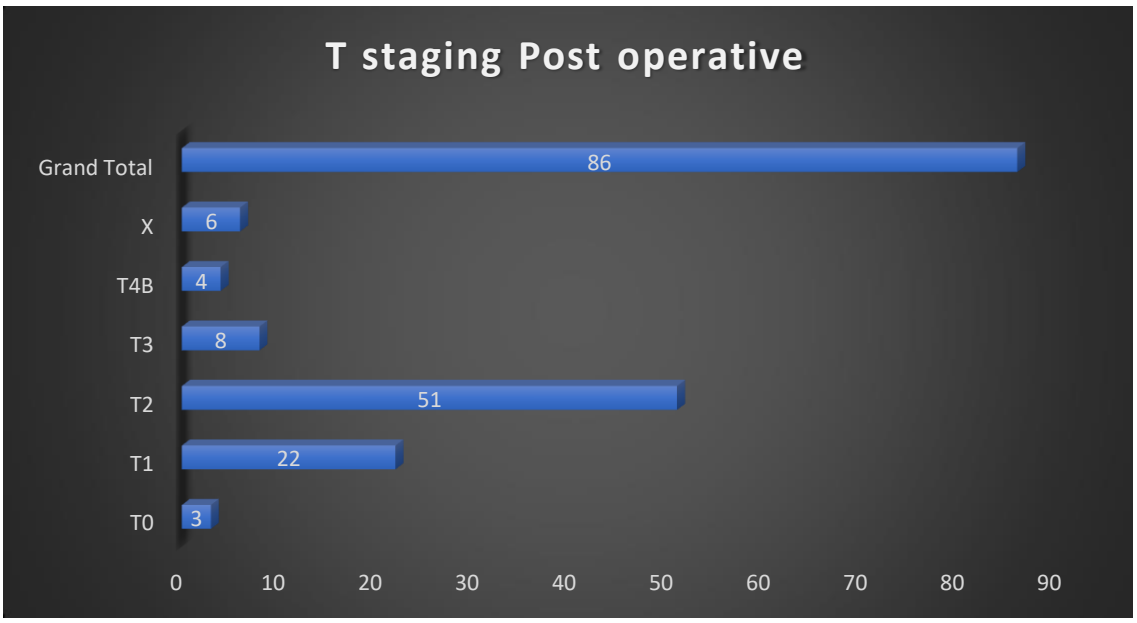
48. POST OPERATIVE HISTOPATHOLOGY

a. pT STAGING

T staging	FREQUENCY
T0	3
T1	6
TIS	2
T1A	1
T1C	5
T2	51
T3	8
T4B	4
X	6
Grand Total	**86**

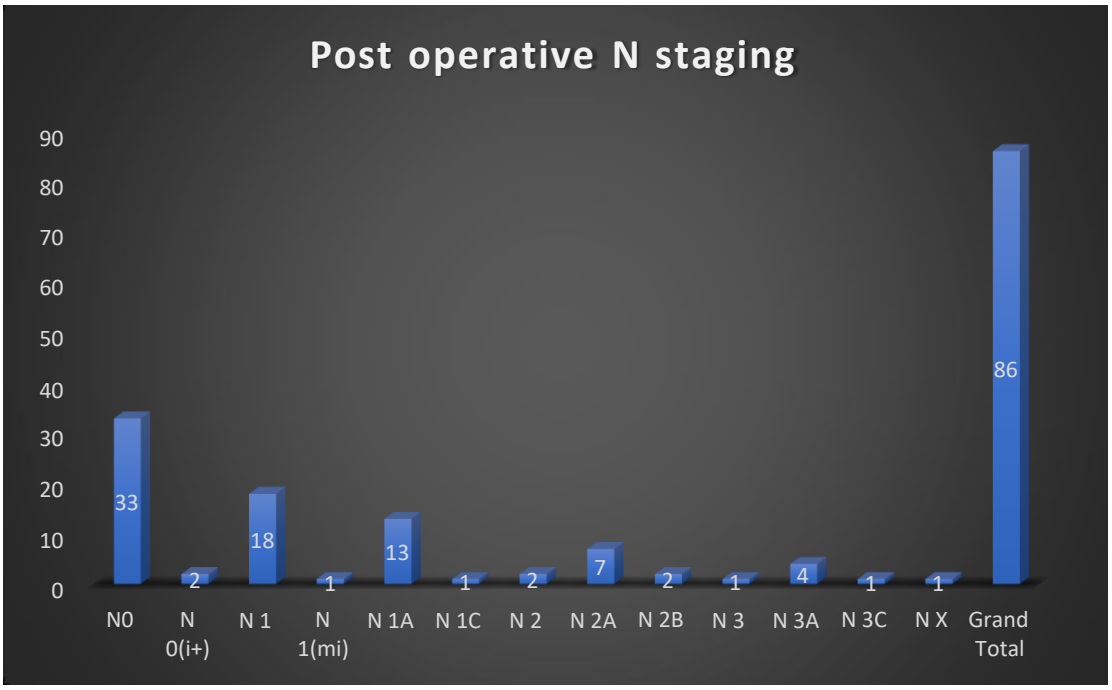


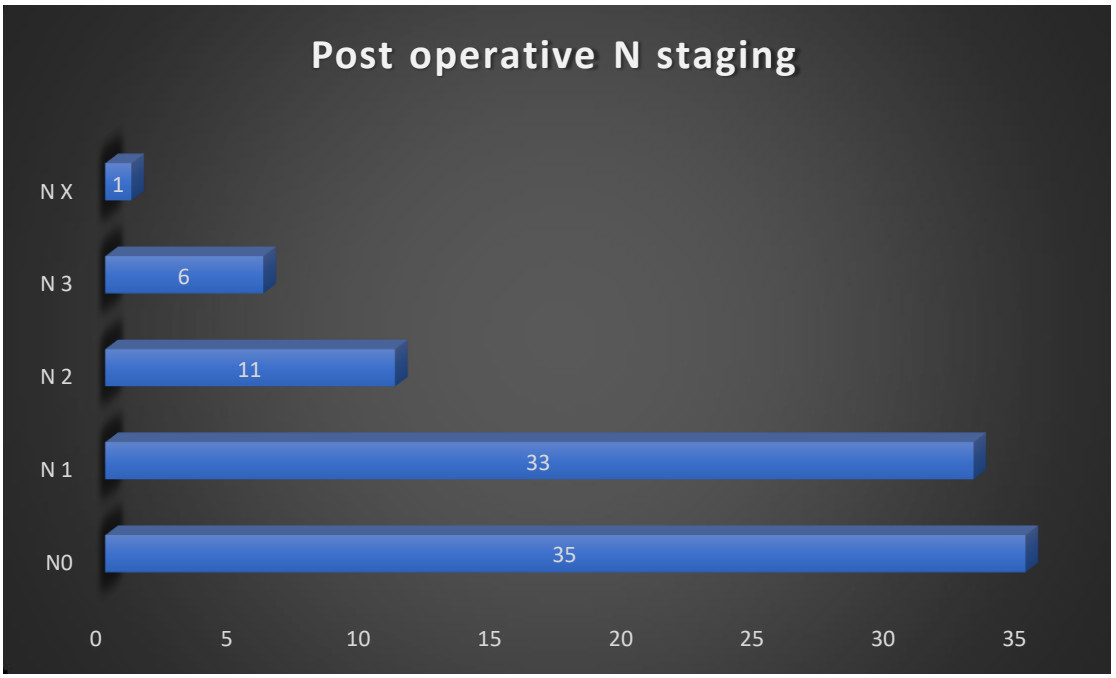
Out of 111 patients, post operative Histopathology reports of 86 patients were available. T2 staging was seen in majority of patients(59.3%) followed by 9.3% patients from T3 staging. The minimum were from T1a stage(1.16%).



b. POST OPERATIVE N STAGING

N staging	Frequency
N0	33
N 0(i+)	2
N 1	18
N 1(mi)	1
N 1A	13
N 1C	1
N 2	2
N 2A	7
N 2B	2
N 3	1
N 3A	4
N 3C	1
N X	1
Grand Total	**86**



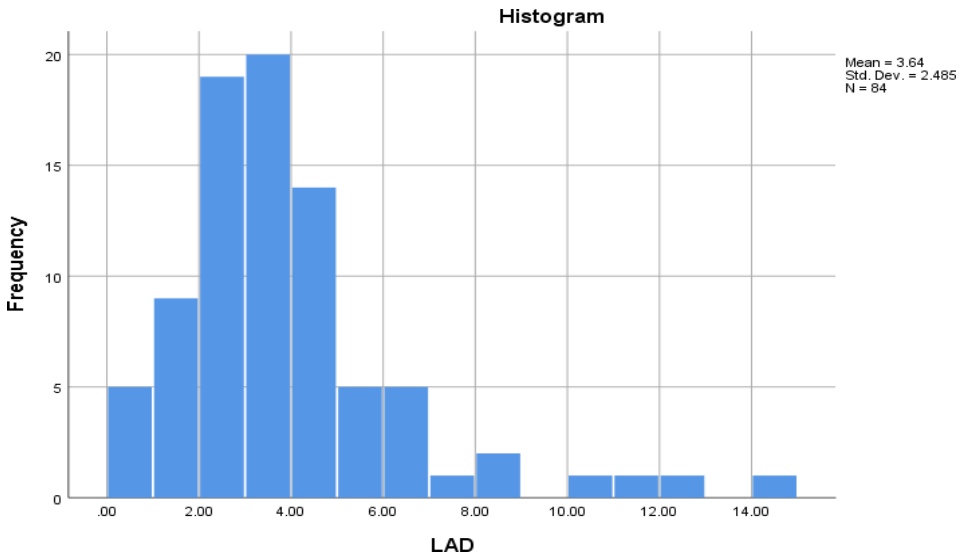


49. POST-OPERATIVE PRIMARY TUMOUR LONG AXIS DIAMETER

Statistics

LAD

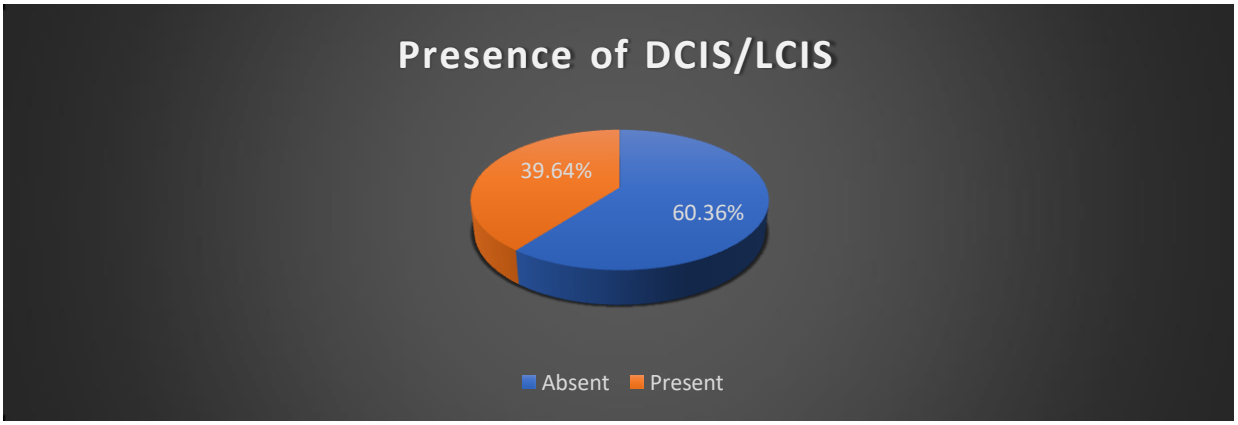
N	Valid	84
	Missing	27
Mean		3.6369
Median		3.0000
Mode		3.00
Std. Deviation		2.48522
Variance		6.176
Range		14.00
Minimum		.00
Maximum		14.00



Out of the 84 patients whose records were available, the values of Post operative tumour Long axis diameter ranged from 0 to 14cm with a mean of 3.63cm.

50. PRESENCE OR ABSENCE OF DUCTAL CARCINOMA IN SITU/LOBULAR CARCINOMA IN SITU

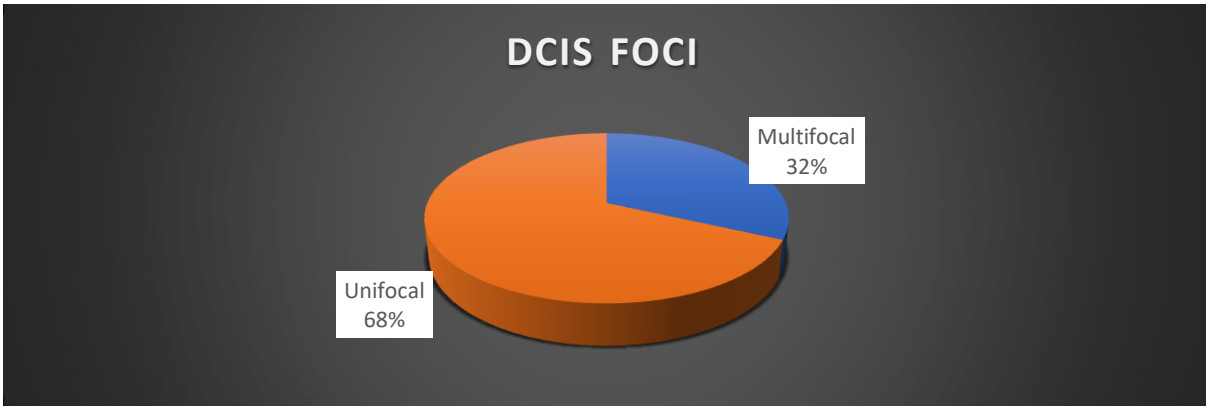
Presence of DCIS/LCIS	Frequency	Percentage
ABSENT	67	60.36%
PRESENT	44	39.64%
Grand Total	**111**	**100.00%**



Out of the 111 patients whose records were available, 60.36% patients had specimens negative for DCIS/LCIS. 39.64% were positive for DCIS/LCIS.

51. DCIS UNIFOCAL VS MULTIFOCAL?

FOCALITY OF DCIS	FREQUENCY
Multifocal	14
Unifocal	30
Grand Total	**44**

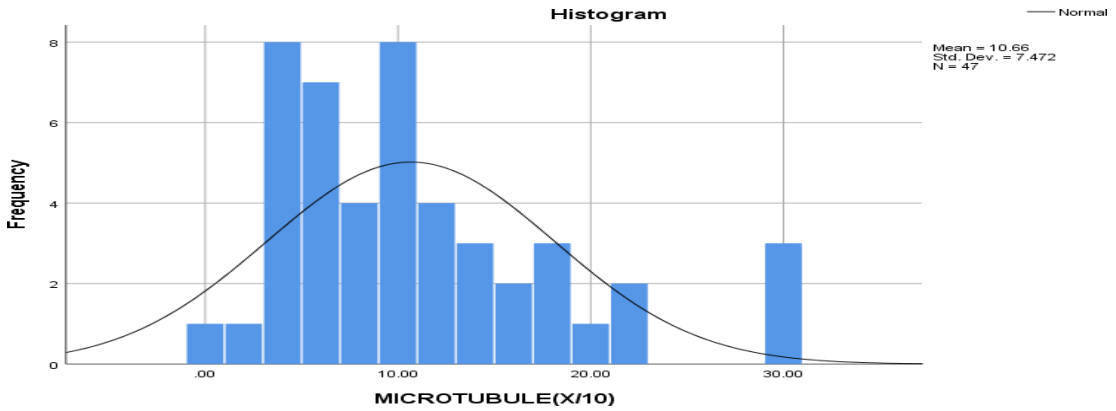


52. MITOTIC COUNT(MICROTUBULES IN X/10)

Statistics

MICROTUBULE(X/10)

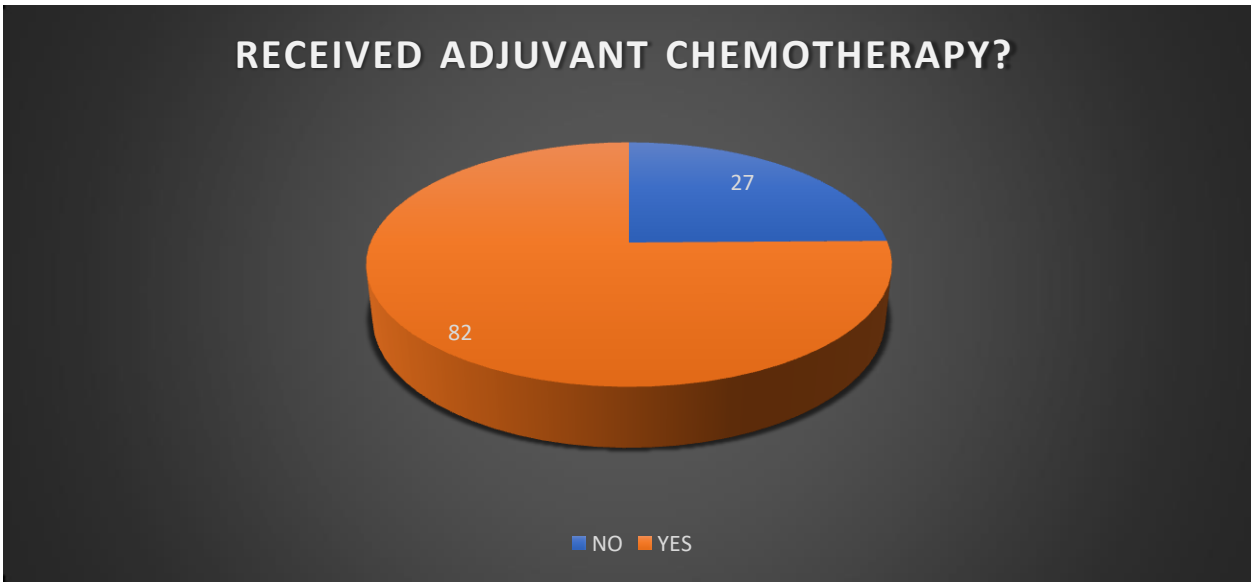
N	Valid	47
	Missing	64
Mean		10.6596
Median		9.0000
Mode		3.00
Std. Deviation		7.47249
Variance		55.838
Range		30.00
Minimum		.00
Maximum		30.00



Out of 47 patients whose data were available, their mitotic counts ranged from 0 to 30 with a mean of 10.65.

53. <u>RECEIVED ADJUVANT CHEMOTHERAPY OR NOT?</u>

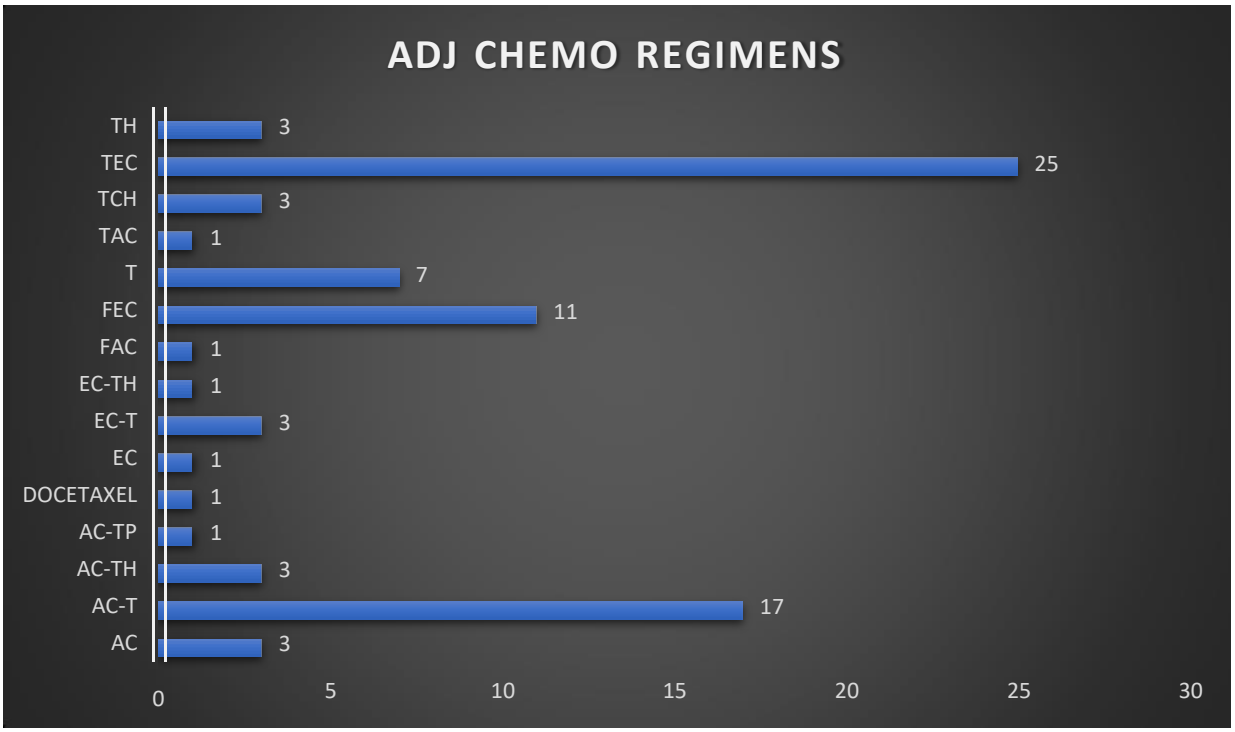
RECEIVED ADJUVANT CHEMOTHERAPY?	FREQUENCY	PERCENTAGE
NO	27	24.77%
YES	82	75.2%
Grand Total	**109**	**100.00%**



Out of the 109 patients whose data about adjuvant chemotherapy were retrieved, 75.2% had received adjuvant chemotherapy while the rest had not.

54. ADJUVANT CHEMOTHERAPY REGIMENS

ADJ CHEMO REGIMEN	FREQUENCY
AC	3
AC-T	18
AC-TH	3
AC-TP	1
DOCETAXEL	1
EC	1
EC-T	3
EC-TH	1
FAC	1
FEC	11
T	7
TAC	1
TCH	3
TEC	25
TH	3
Grand Total	**82**

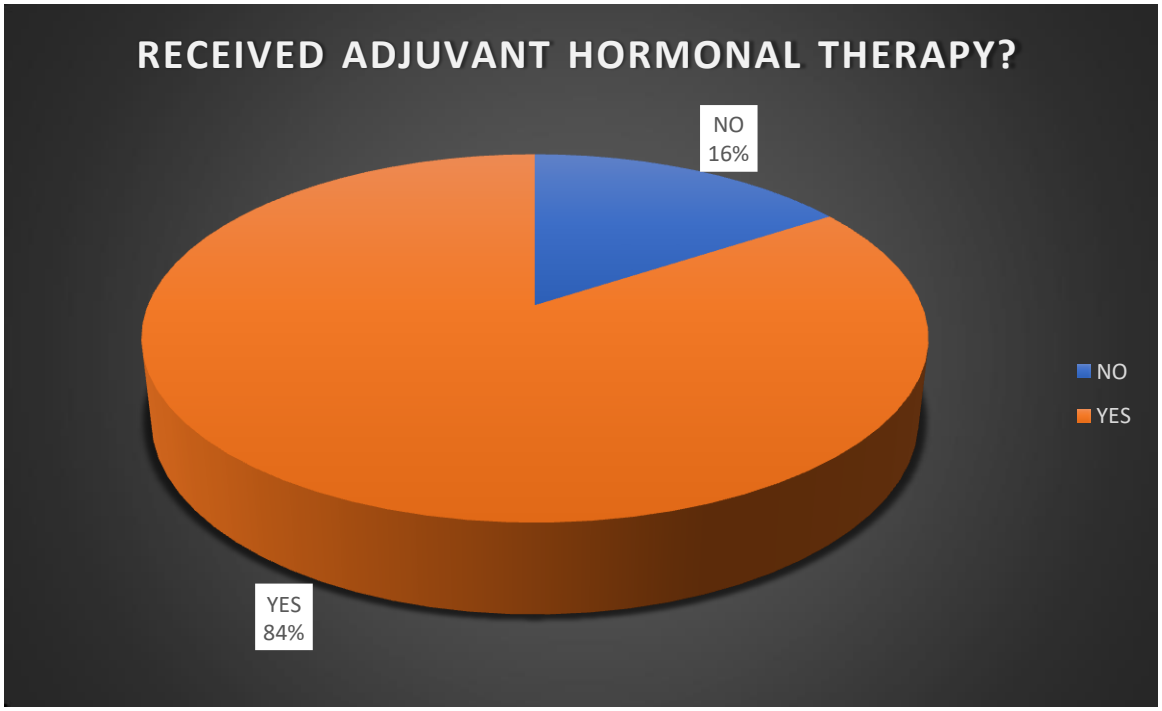


55. ADJUVANT CHEMOTHERAPY NUMBER OF CYCLES

ADJ CHEMO CYCLES	FREQUENCY
2	4
3	11
4	11
5	1
6	29
8	23
12	1
Grand Total	**81**

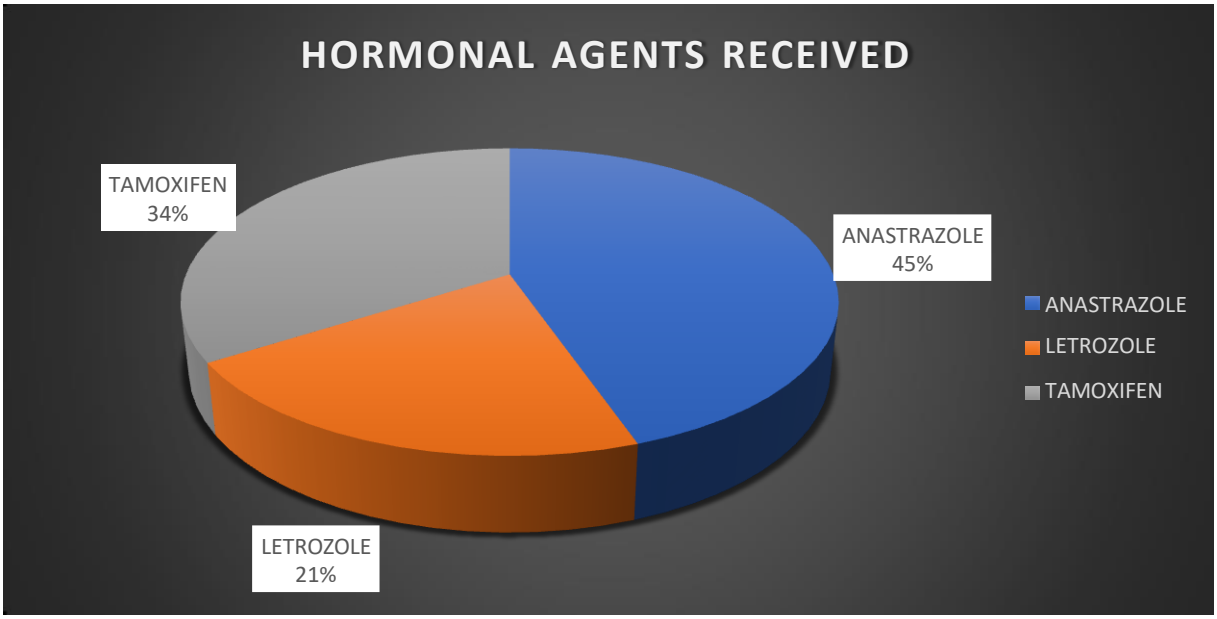
56. RECEIVED ADJUVANT HORMONAL THERAPY?

ON ADJ HT?	FREQUENCY
NO/RECORDS UNAVAILABLE	12
YES	64
Grand Total	**76**



57. HORMONAL THERAPY AGENTS

HORMONAL AGENT	FREQUENCY
ANASTRAZOLE	21
LETROZOLE	10
TAMOXIFEN	16
Grand Total	**47**



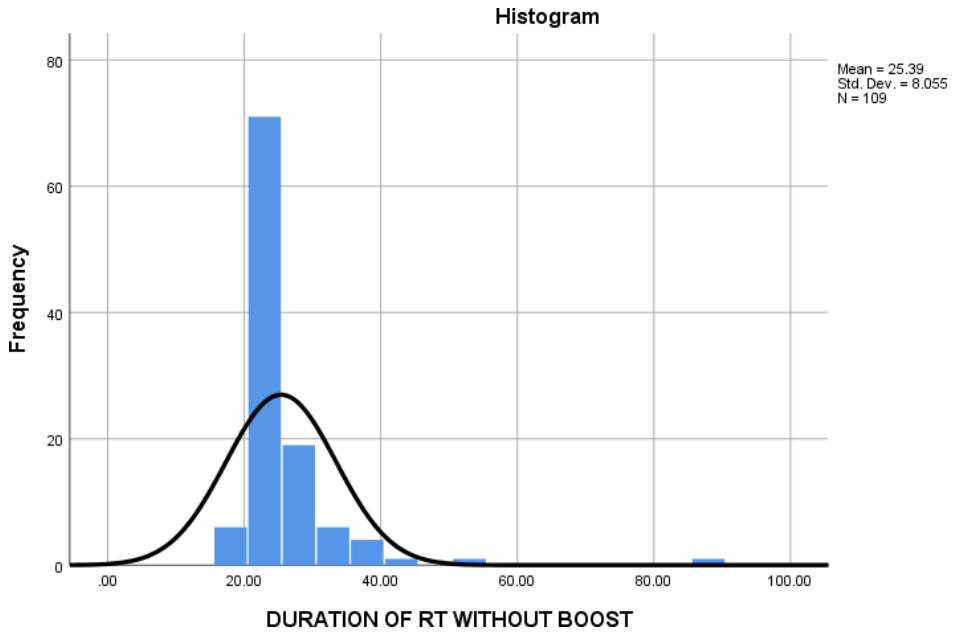
58. RADIOTHERAPY

a. DURATION OF RT WITHOUT INCLUDING DURATION OF LUMPECTOMY BOOST

Statistics

DURATION OF RT WITHOUT BOOST

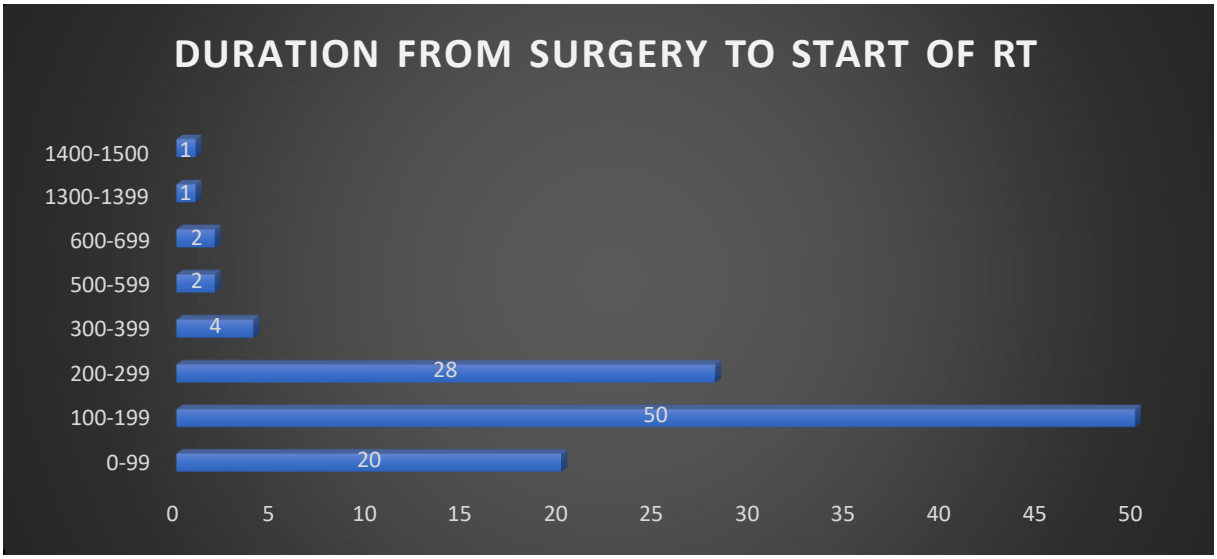
N	Valid	109
	Missing	871
Mean		25.3853
Median		22.0000
Mode		22.00
Std. Deviation		8.05526
Variance		64.887
Range		69.00
Minimum		18.00
Maximum		87.00



DURATION OF RT WITHOUT BOOST	Count
10-19	3
20-29	89
30-39	13
40-49	2
50-59	1
80-89	1
Grand Total	**109**

b. DURATION(DAYS) FROM SURGERY TO START OF RT

DURATION FROM SURGERY TO START OF RT	COUNT
10-109	30
110-209	49
210-309	21
310-409	2
510-609	2
610-709	2
1310-1409	1
1410-1509	1
Grand Total	**108**



Statistics

DURATION FROM SURGERY TO START OF RT

N	Valid	108
	Missing	4
Mean		198.1481
Median		170.5000
Mode		91.00[a]
Std. Deviation		197.21575
Range		1436.00
Minimum		26.00
Maximum		1462.00

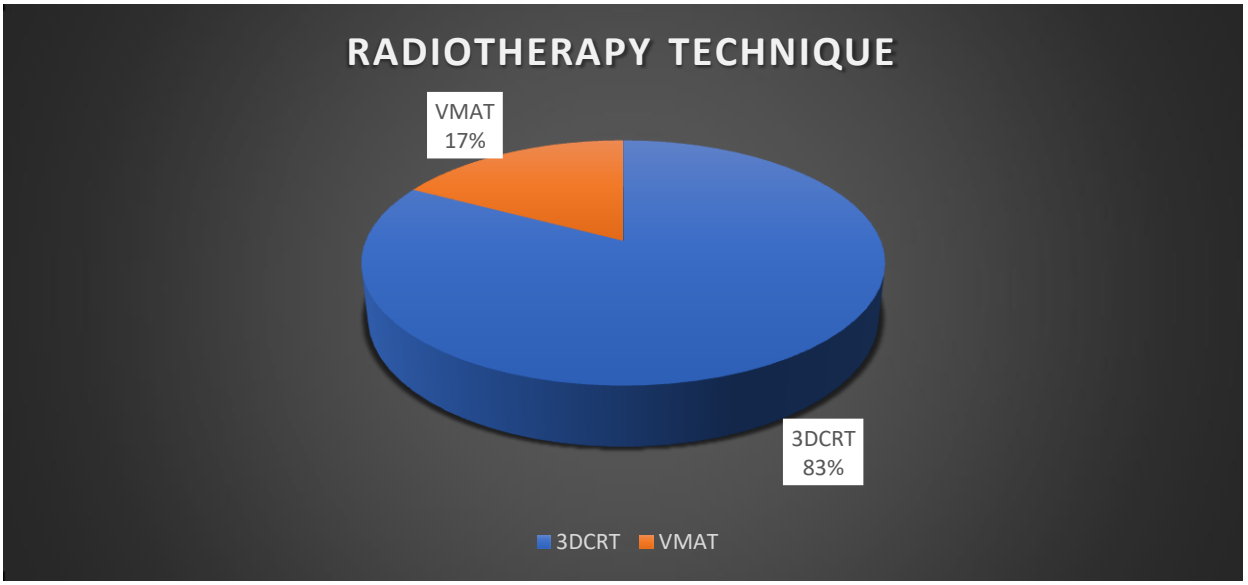
c. RADIOTHERAPY TECHNIQUE

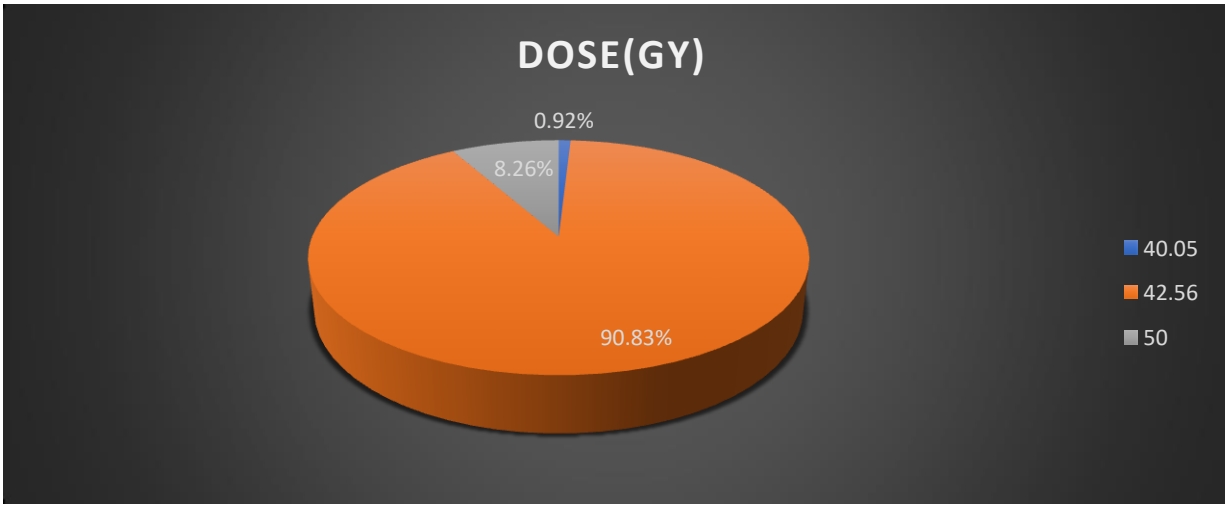
RT TECHNIQUE	**COUNT**
3DCRT	91
VMAT	19
Grand Total	**110**

82.7% of the 110 patients whose data were accrued had received RT by 3DCRT followed by 17.3 % of patients by VMAT.

d. RADIOTHERAPY DOSE REGIMENS USED(Gy)

DOSE(GY)	Count
40.05/15#	1
42.56/16#	99
50/25#	9
Grand Total	**109**

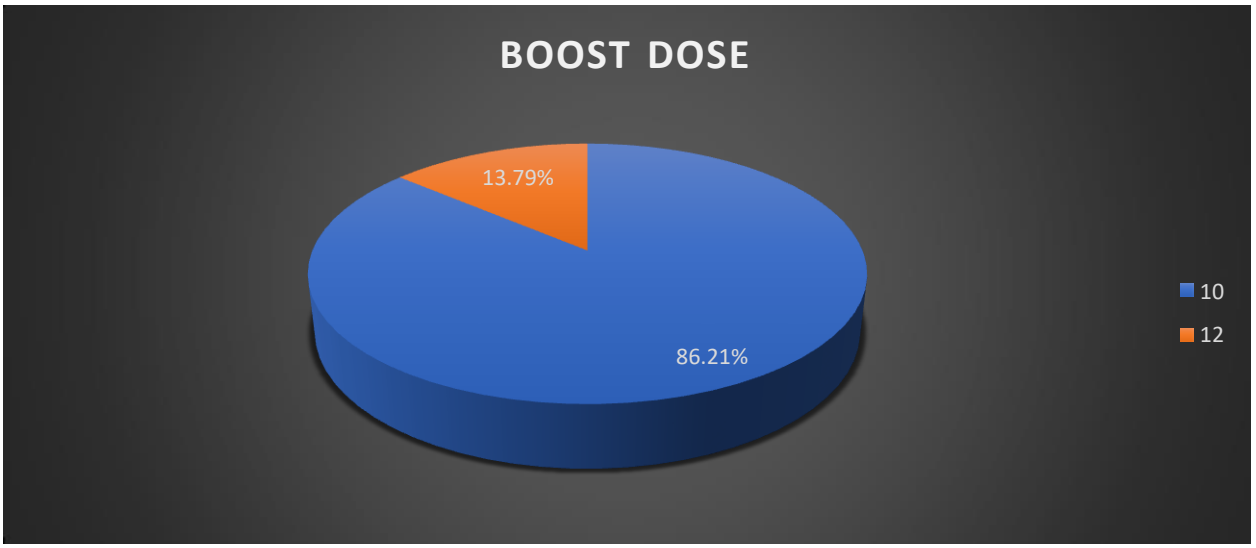




Out of the 109 patients whose data were available 90.83% patients received 42.56 Gy in 16# 8.26% patients received 50 Gy in 25 #.

e. LUMPECTOMY BOOST REGIMENS

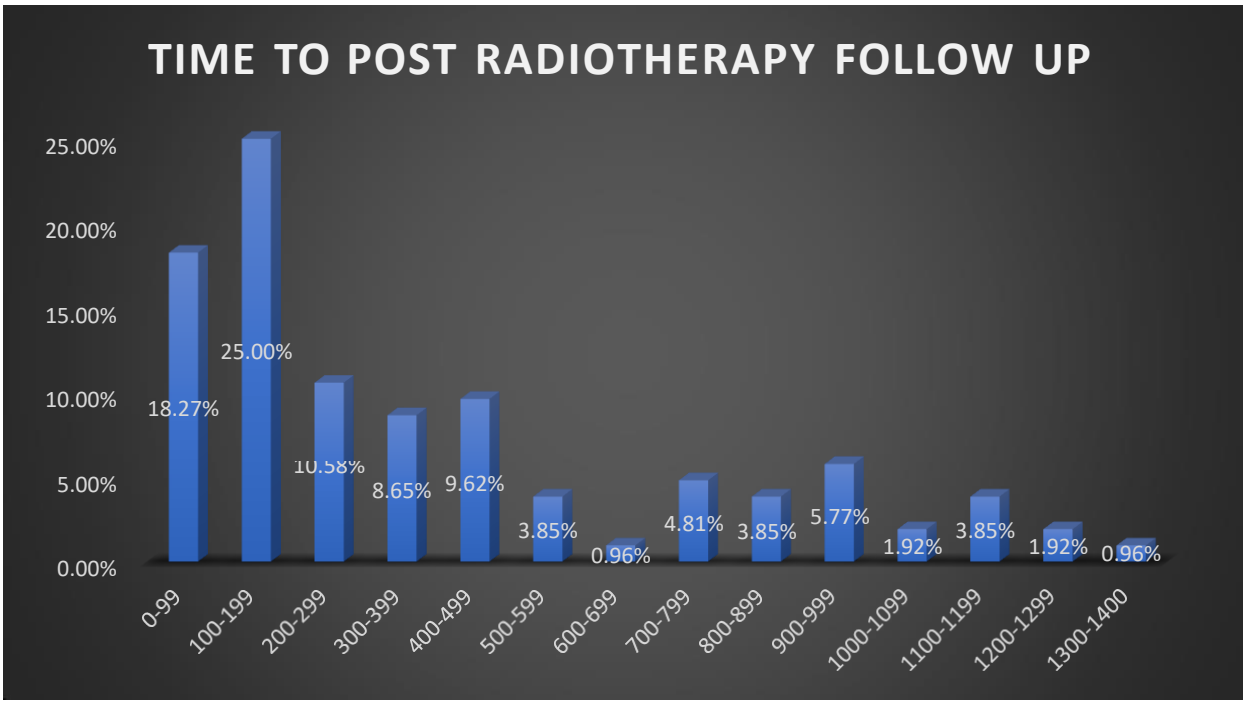
BOOST DOSE	COUNT
10Gy/5#	25
12Gy/6#	4
Grand Total	**29**



Out of the 29 patients who received lumpectomy boost, 86.21% received 10 Gy in 5 fractions while the rest received 12 Gy in 6#.

59. TIME TO POST RADIOTHERAPY RESPONSE ASSESSMENT

TIME TO POST RADIOTHERAPY FOLLOW UP	FREQUENCY
0-99	19
100-199	26
200-299	11
300-399	9
400-499	10
500-599	4
600-699	1
700-799	5
800-899	4
900-999	6
1000-1099	2
1100-1199	4
1200-1299	2
1300-1400	1
Grand Total	**104**



Out of the 104 patients, whose data on follow up was available, the mean follow up time was 402 days with a median of 253.5 days.

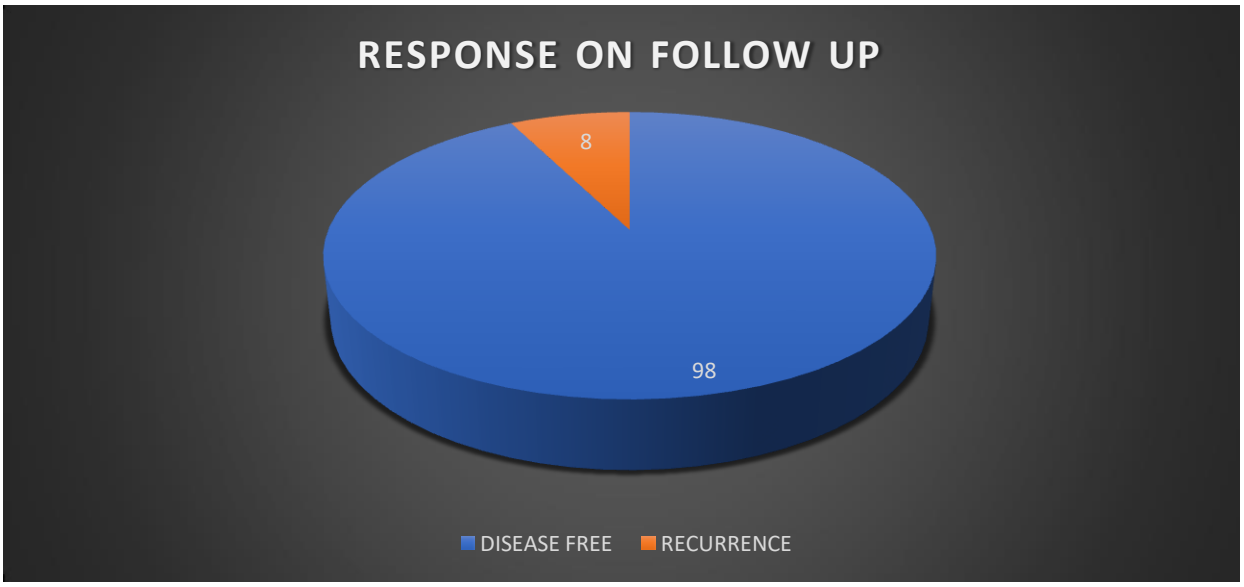
Statistics

TIME TO POST RADIOTHERAPY FOLLOW UP

N	Valid	104
	Missing	7
Mean		402.5000
Median		253.5000
Mode		92.00[a]
Std. Deviation		355.95099
Variance		126701.107
Range		1366.00
Minimum		27.00
Maximum		1393.00

60. RESPONSE ASSESSMENT POST RADIOTHERAPY

RESPONSE ASSESSMENT POST RADIOTHERAPY	Count
DISEASE FREE	98
RECURRENCE	8
Grand Total	**106**



61. DOSES TO HEART AND CARDIAC SUBSTRUCTURES IN PATIENTS WHO RECEIVED 42.56 GY/16#.

Statistics

		LAD MEAN DOSE(cGY)	LAD V25	LAD V45	LCX MEAN DOSE(cGY)	LC MEAN DOSE(cGY)	HEART MEAN DOSE(cGY)
N	Valid	33	33	33	33	33	51
	Missing	79	79	79	79	79	61
Mean		1255.5212	.8183	.0174	167.7424	260.5879	644.6235
Median		308.3000	.0000	.0000	120.0000	123.8000	535.8000
Mode		9.40[a]	.00	.00	10.60[a]	10.10[a]	12.40[a]

Std. Deviation		1450.28156	1.16053	.09329	211.22634	447.03722	585.06239
Variance		2103316.604	1.347	.009	44616.565	199842.272	342297.995
Range		4185.30	3.44	.54	1043.20	2375.90	1972.60
Minimum		9.40	.00	.00	10.60	10.10	12.40
Maximum		4194.70	3.44	.54	1053.80	2386.00	1985.00
Percentiles	10	22.4200	.0000	.0000	19.4600	19.5400	79.9000
	20	76.4200	.0000	.0000	47.3200	75.5000	116.7200
	30	129.0600	.0000	.0000	58.7600	92.7200	135.6600
	40	177.8200	.0000	.0000	75.0000	99.8400	351.8600
	50	308.3000	.0000	.0000	120.0000	123.8000	535.8000
	60	1031.8400	.5044	.0000	151.5200	192.4800	618.4600
	70	2132.0200	1.2178	.0000	173.3400	209.3000	740.6400
	80	3188.7800	2.0254	.0000	208.7800	279.8200	1385.4000
	90	3544.9400	3.0474	.0024	456.3400	536.3600	1659.1800

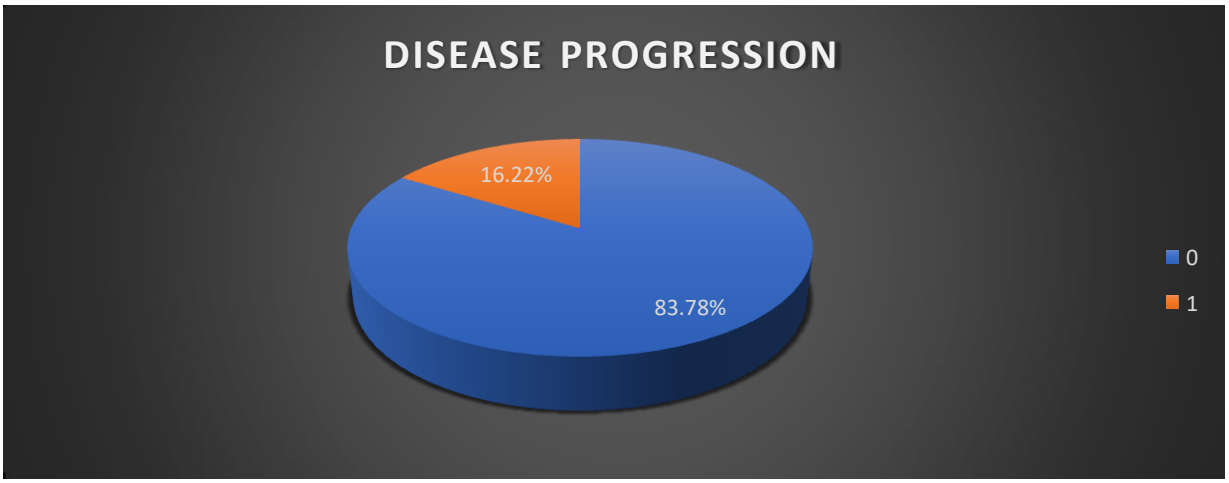
a. Multiple modes exist. The smallest value is shown

62. EFFECT OF LATERALITY ON CARDIAC DOSES

LATERALITY	LEFT	RIGHT
AVERAGE OF LAD MEAN DOSE(CGY)	2299.482353	146.3125
AVERAGE OF LAD V45	0.033823529	0
AVERAGE OF LAD V25	1.588470588	0
AVERAGE OF LCX MEAN DOSE(CGY)	257.2705882	72.61875
AVERAGE OF LC MEAN DOSE(CGY)	413.9647059	97.625
AVERAGE OF HEART MEAN DOSE(CGY)	797.0705882	243.99375

63. DISEASE PROGRESSION/RECURRENCE

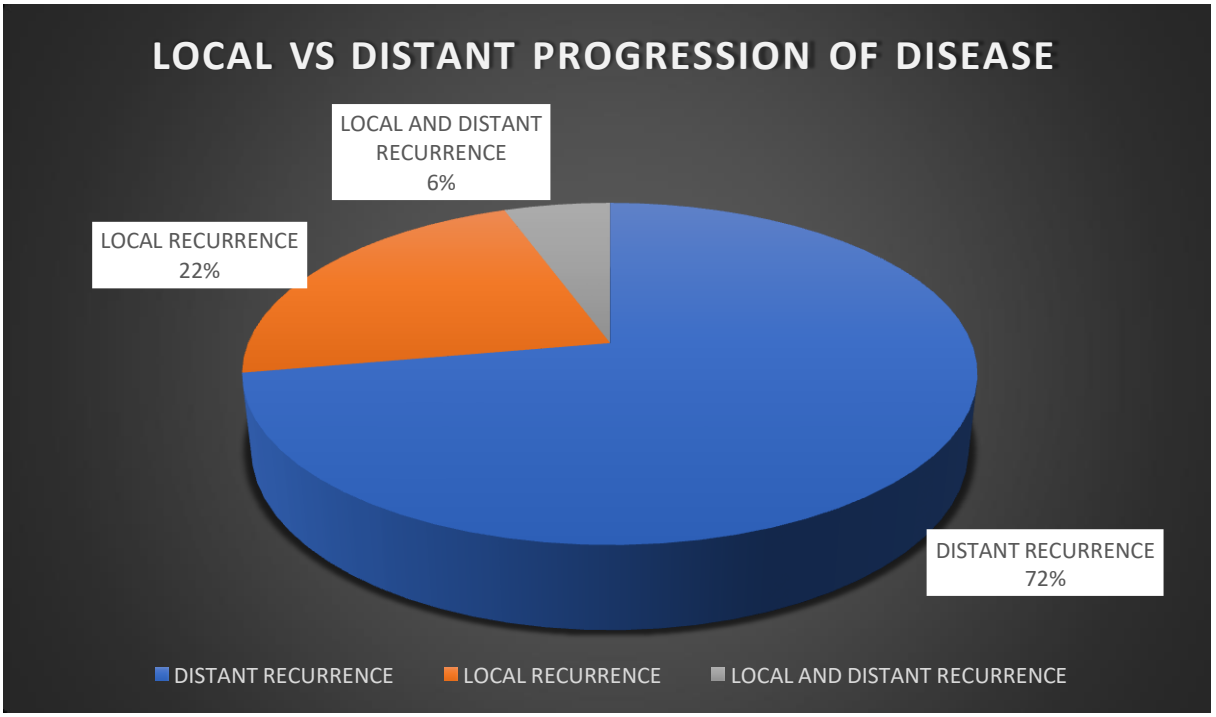
DISEASE PROGRESSION	Count
DISEASE FREE (0)	93
RECURRENT/ PROGRESSIVE DISEASE(1)	18
Grand Total	**111**



Out of the 111 patients, nearly 16% patients had disease progression on last follow up

LOCAL OR DISTANT RECURRENCE?

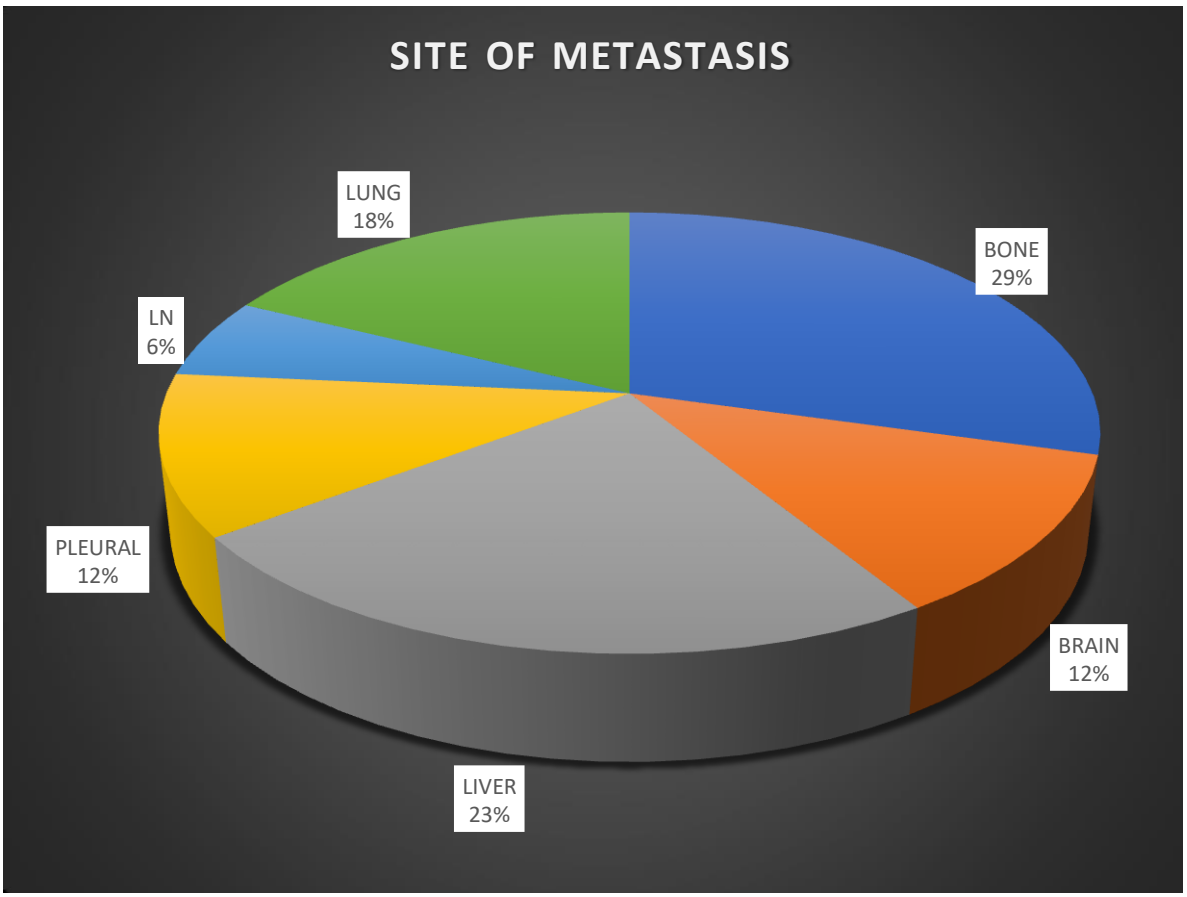
LOCAL OR DISTANT RECURRENCE?	COUNT
DISTANT RECURRENCE	13
LOCAL RECURRENCE	4
LOCAL AND DISTANT RECURRENCE	1
Grand Total	**18**



Amongst the 18 patients with documented recurrence, 72% had distant recurrences, 22% had local recurrences and the remaining had both local as well as distant recurrence.

64. SITE OF DISTANT METASTASIS?

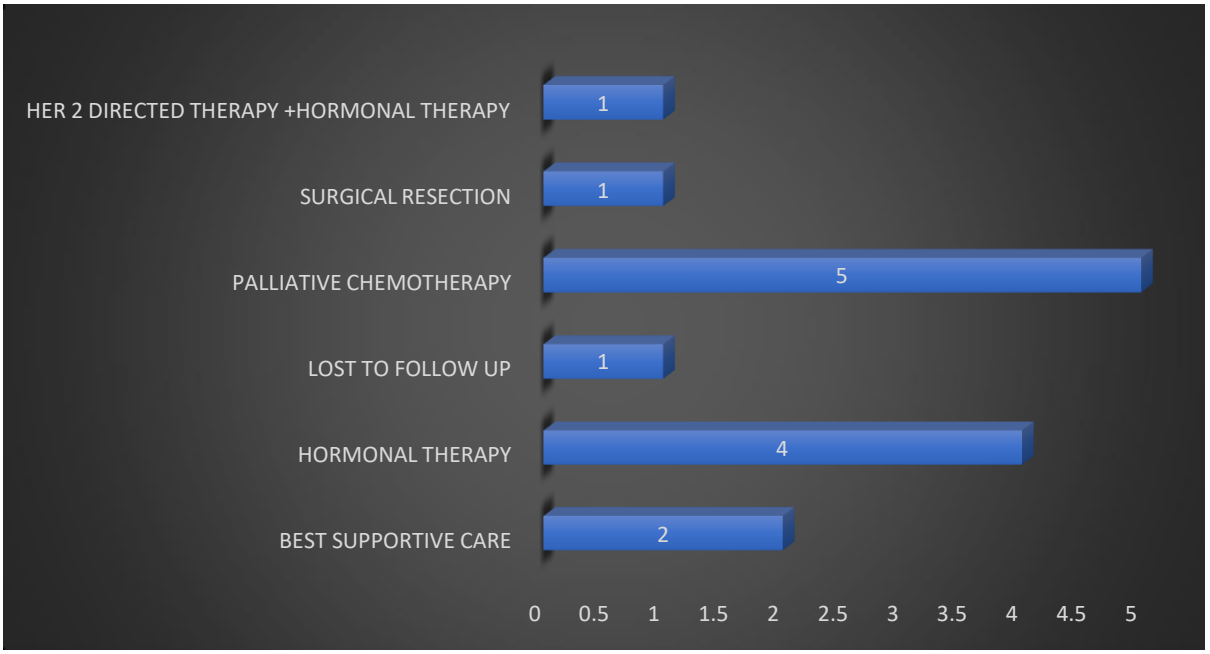
SITE OF METS	Count
BONE	5
BRAIN	2
LIVER	4
PLEURAL	2
LYMPH NODAL	1
LUNG	3



A majority of 29% patients had one metastasis followed by 23% patients with Liver metastasis.

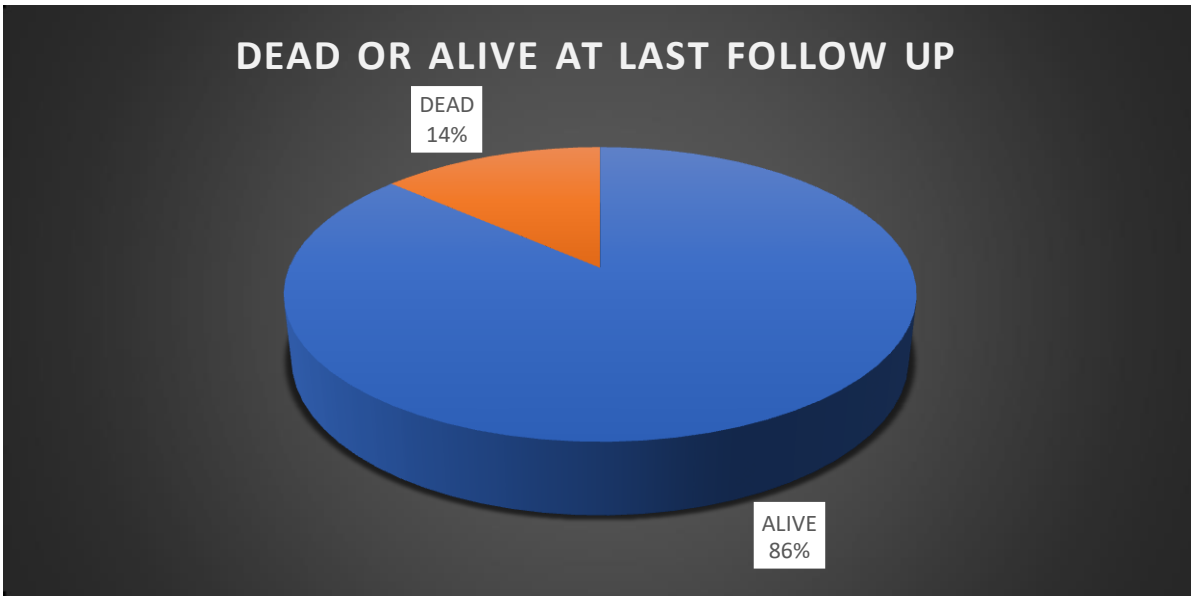
65. TREATMENT RECEIVED FOR RECURRENCE

Row Labels	Count
BEST SUPPORTIVE CARE	2
HORMONAL THERAPY	4
LOST TO FOLLOW UP	1
PALLIATIVE CHEMOTHERAPY	5
SURGICAL RESECTION	1
HER 2 DIRECTED THERAPY +HORMONAL THERAPY	1



66. SURVIVAL STATUS AT LAST FOLLOW UP

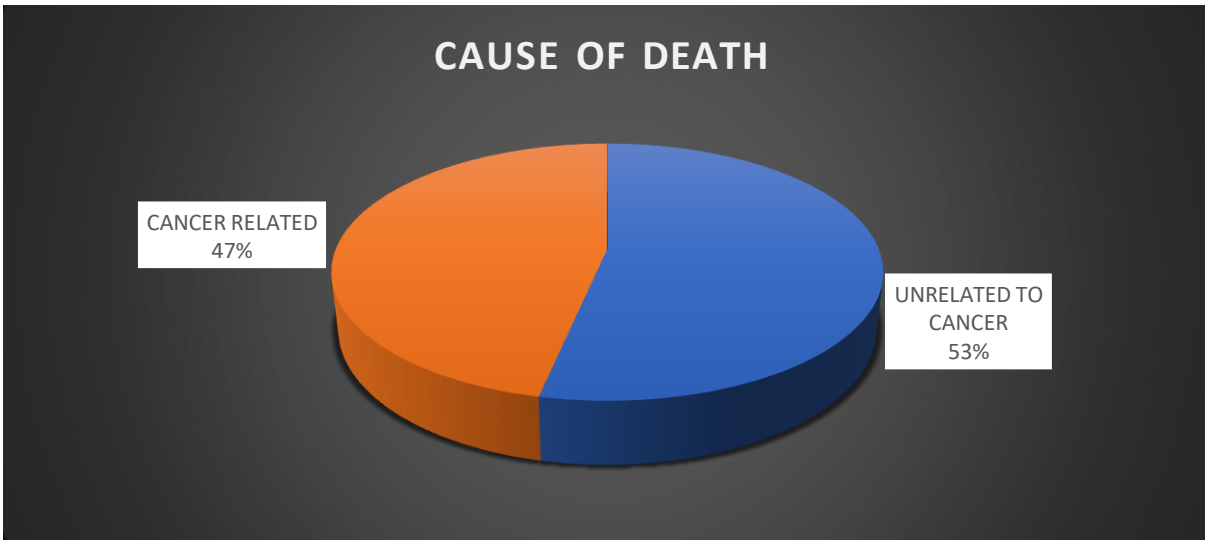
DEAD OR ALIVE AT LAST FOLLOW UP	COUNT
ALIVE	96
DEAD	15
Grand Total	**111**



Out of the 111 patients with accrued data, 86% were alive at last follow up and 14% had passed away.

67. CAUSE OF DEATH

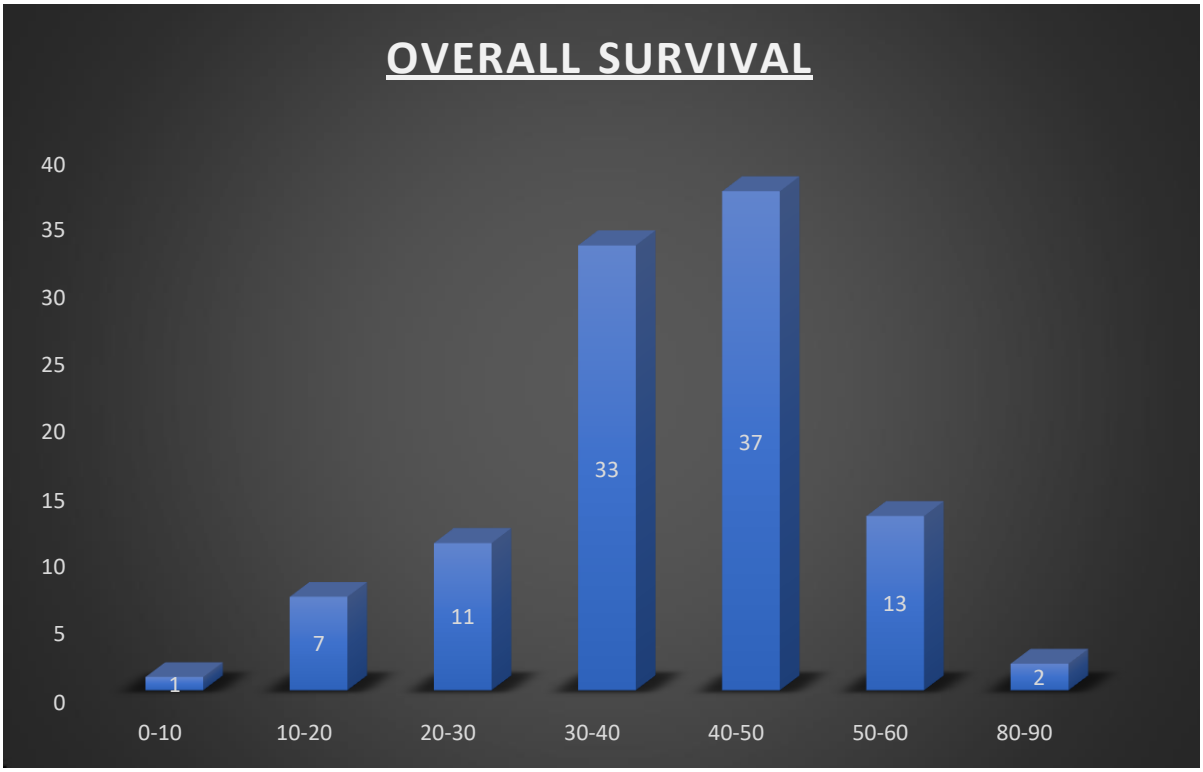
CAUSE OF DEATH	Count
UNRELATED TO CANCER	8
CANCER RELATED	7
Grand Total	**15**



53% of the deaths by the time of last follow up were unrelated to cancer and 47% were cancer related deaths.

68. OVERALL SURVIVAL

OS IN MONTHS	COUNT
0-10	1
10-20	7
20-30	11
30-40	33
40-50	37
50-60	13
80-90	2
Grand Total	**104**



Statistics

os in months

N	Valid	104
	Missing	7
Mean		38.9788
Median		39.9833
Mode		33.07[a]
Std. Deviation		12.05476
Variance		145.317
Range		77.83
Minimum		8.07
Maximum		85.90

Median survival could not be calculated because survival curve does not cross 50%.

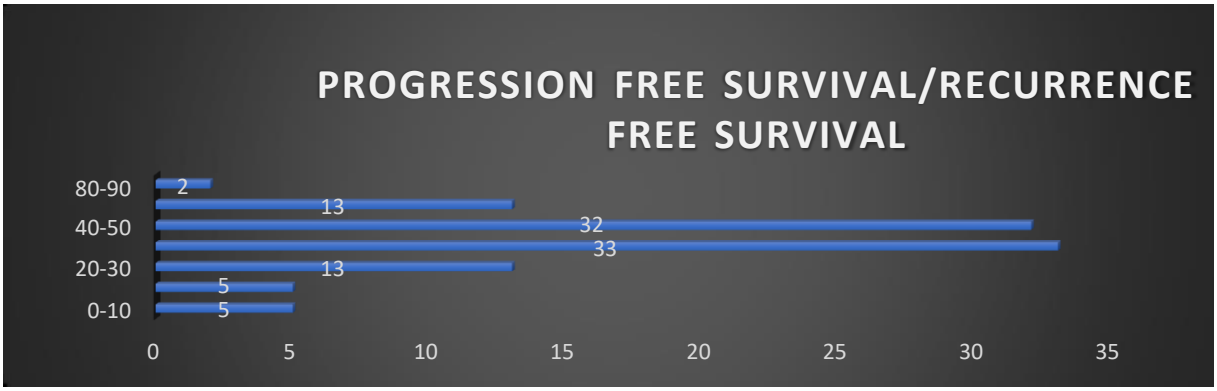
69. <u>SITE WISE OS</u>

ROW LABELS	COUNT OF EXAMINATION SITE OF PRIMARY	AVERAGE OF OS IN MONTHS	AVERAGE OF PFS/RFS IN MONTHS	AVERAGE OF DFS IN MONTHS
LOWER INNER QUADRANT	3	31.25555556	22.32222222	18.65555556
RETRO AREOLAR	13	33.08461538	31.27435897	26.71025641
LEFT OUTER QUADRANT	7	34.62777778	32.89333333	23.88333333
AXILLARY TAIL	2	37.4	37.4	33.31666667
UPPER OUTER QUADRANT	37	38.64504505	38.38828829	31.94414414
CHEST WALL	2	40.05	40.05	34.05

ALL QUADRANT	3	46.56666667	40.87777778	33.91111111
UPPER INNER QUADRANT	15	49.2	44.15	30.94444444
INFRA MAMMARY FOLD	1	51.36666667	51.36666667	44.16666667
AXILLA	1	52.26666667	52.26666667	45.03333333
Grand Total	**84**	**39.37666667**	**37.58649789**	**30.31791667**

70. PROGRESSION FREE SURVIVAL/RECURRENCE FREE SURVIVAL

PFS/RFS IN MONTHS	Count
0-10	5
10-20	5
20-30	13
30-40	33
40-50	32
50-60	13
80-90	2
Grand Total	**103**



Statistics

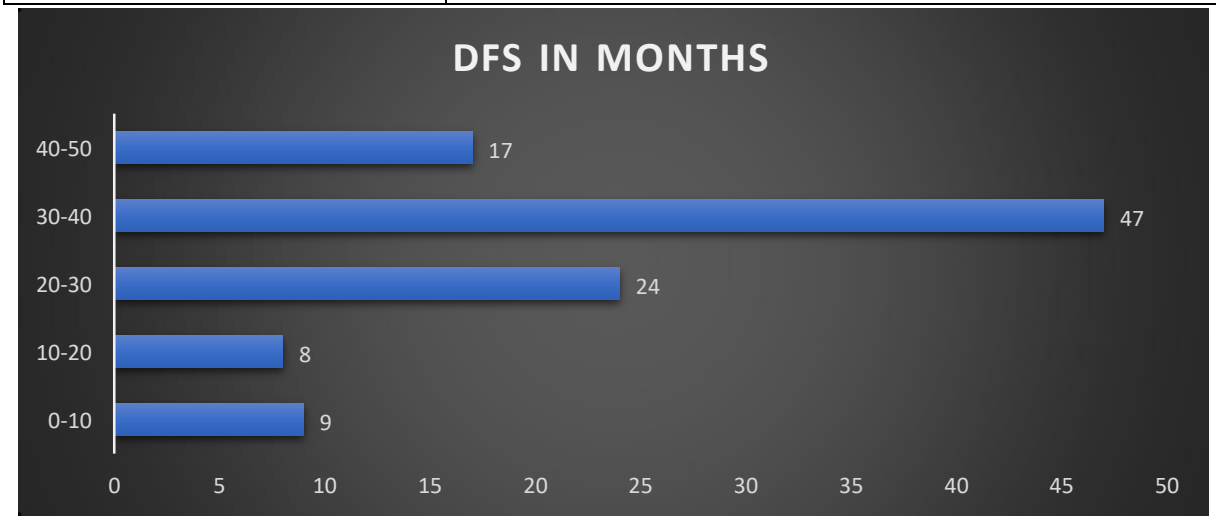
PFS/RFS IN MONTHS

N	Valid	103
	Missing	8
Mean		37.5799
Median		39.1000
Mode		23.03[a]
Std. Deviation		13.57942
Variance		184.401
Range		85.53
Minimum		.37
Maximum		85.90

Out of 103 patients, the mean and median progression free survival/recurrence free survival was 37.5 months and 39.1 months respectively and ranging from 85.9 to 0.37 months.

71. DISEASE FREE SURVIVAL

DFS	Count
0-10	9
10-20	8
20-30	24
30-40	47
40-50	17
Grand Total	**105**



Statistics

DFS IN MONTHS

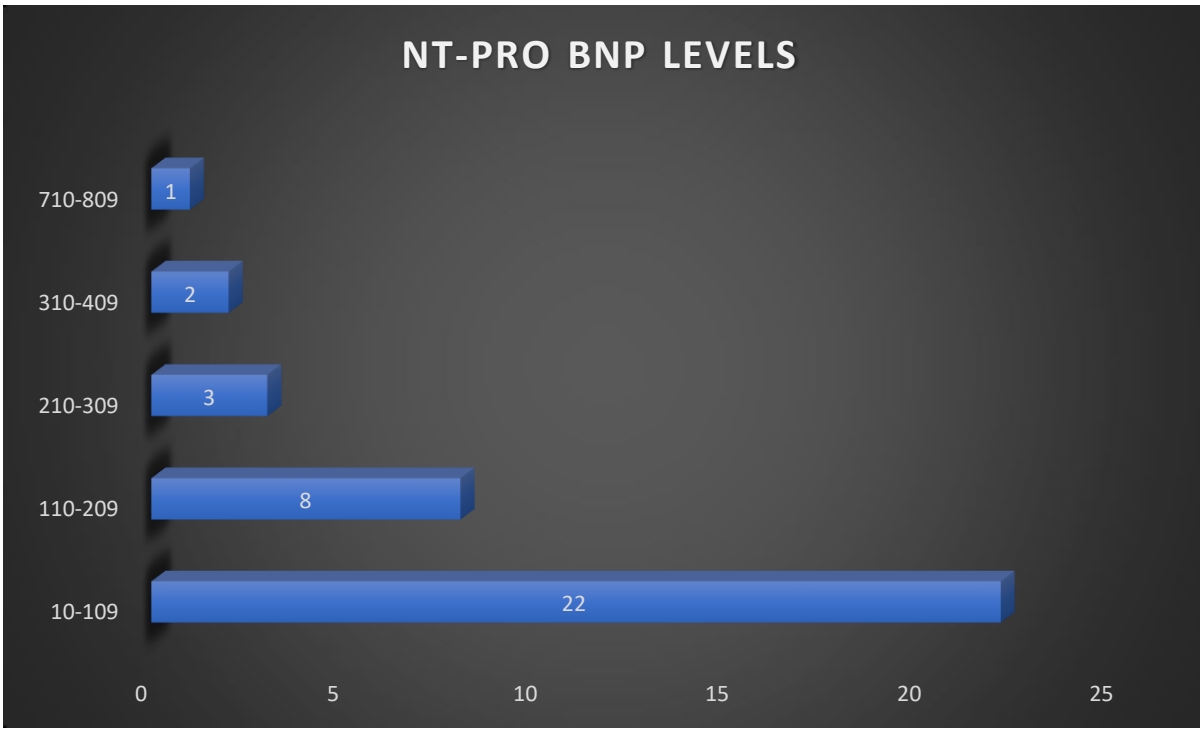
N	Valid	105
	Missing	6
Mean		30.5854
Median		33.1667
Mode		34.03[a]
Std. Deviation		11.01005
Variance		121.221
Range		45.00
Minimum		3.03
Maximum		48.03

Out of 103 patients, the mean and median Disease free survival was 30.5 months and 33.1 months respectively and ranging from 3.03 to 48.03 months.

72. CARDIAC WORKUP POST TREATMENT

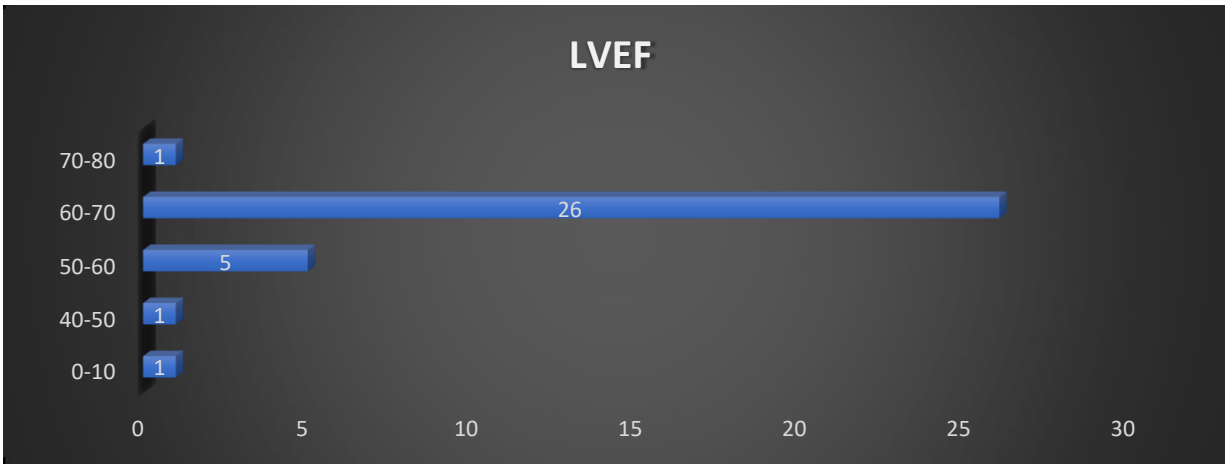
a. NT-PRO NP LEVELS

NT PRO BNP	Count
10-109	22
110-209	8
210-309	3
310-409	2
710-809	1
Grand Total	**36**



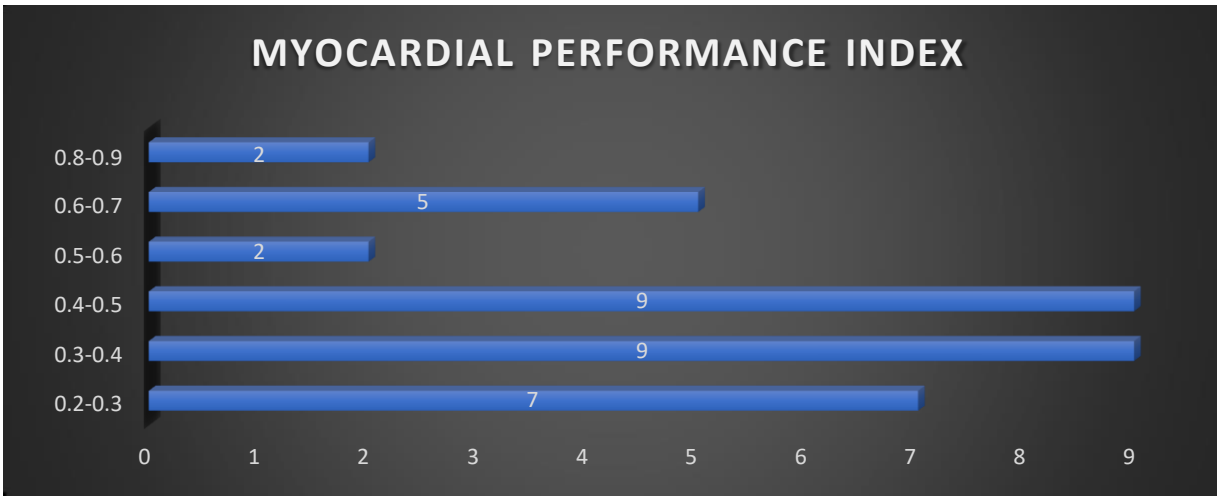
b. EJECTION FRACTION AT FOLLOW UP

EJECTION FRACTION(%)	Count
0-10	1
40-50	1
50-60	5
60-70	26
70-80	1
Grand Total	**34**



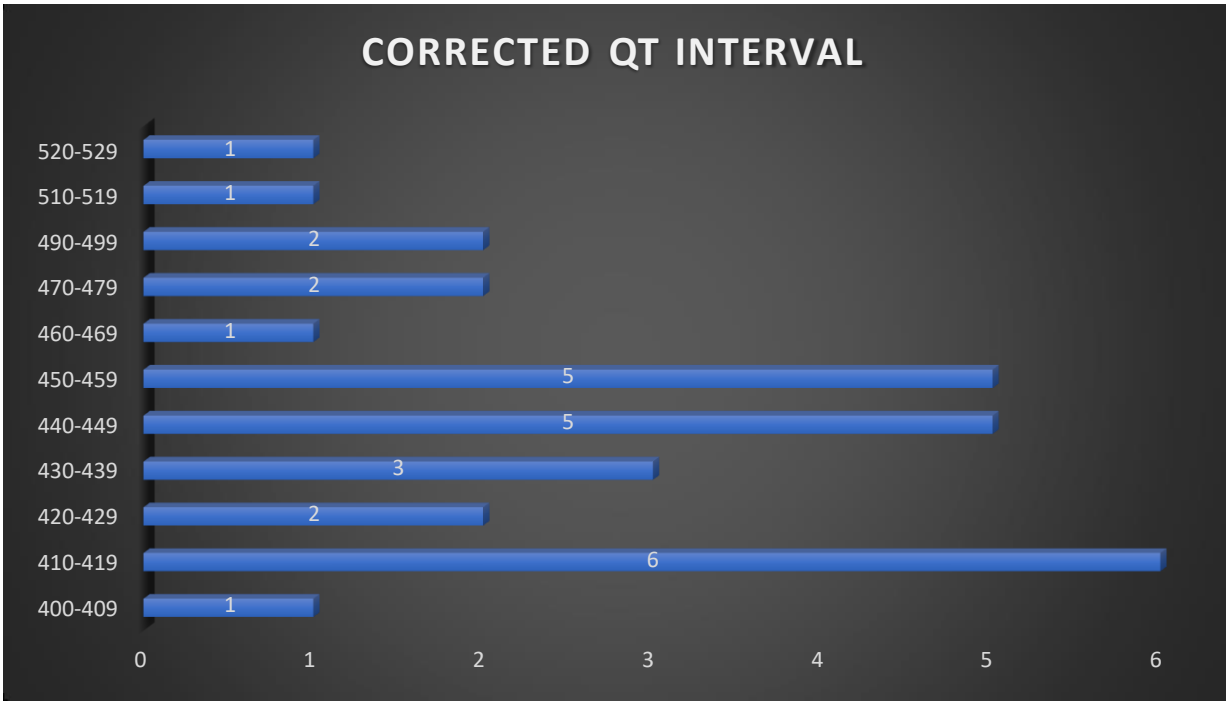
c. MYOCARDIAL PERFORMANCE INDEX

Row Labels	Count of MPI
0.2-0.3	7
0.3-0.4	9
0.4-0.5	9
0.5-0.6	2
0.6-0.7	5
0.8-0.9	2
Grand Total	**34**



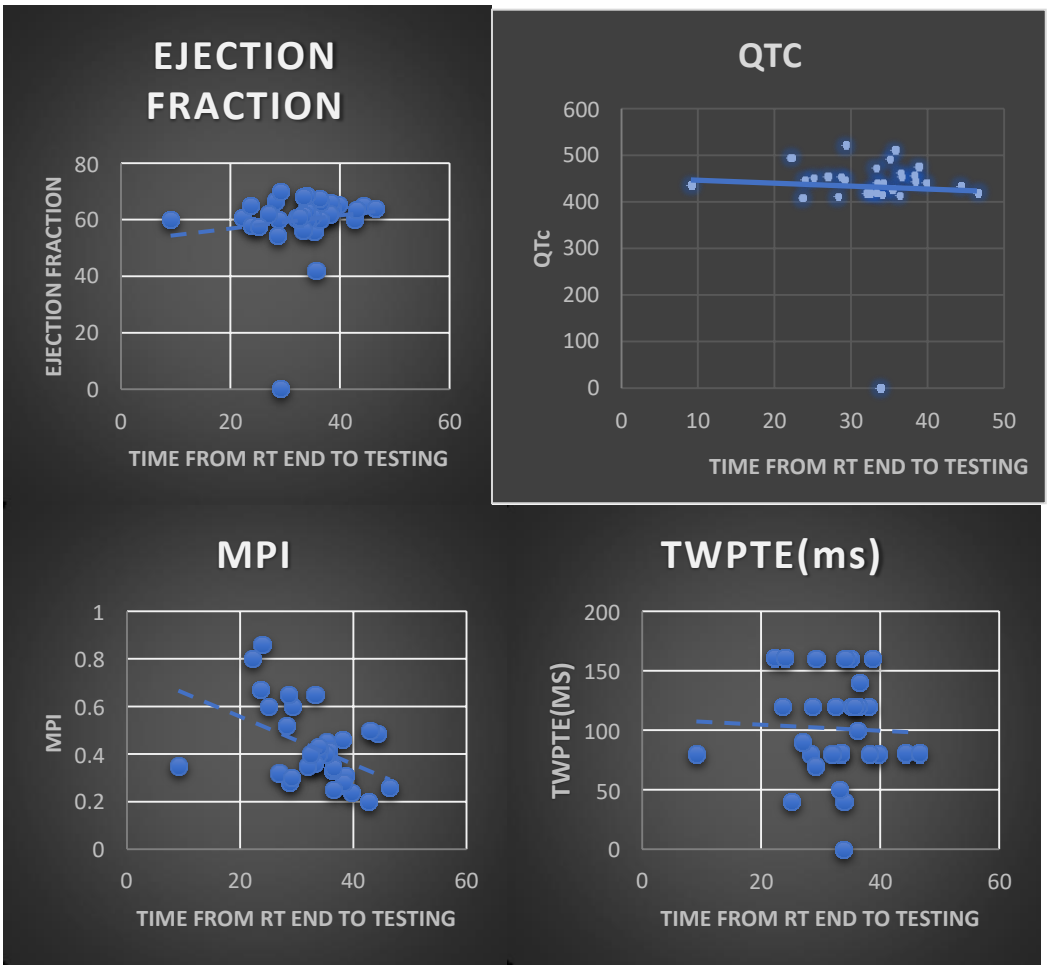
d. CORRECTED QT SEGMENT INTERVAL

Row Labels	Count of QTC
400-409	1
410-419	6
420-429	2
430-439	3
440-449	5
450-459	5
460-469	1
470-479	2
490-499	2
510-519	1
520-529	1
Grand Total	**29**



		NT PRO BNP	EJECTION FRACTION	MPI	QTC	TWPTE(ms)
N	Valid	36	33	34	29	29
Mean		137.9167	61.7606	.4267	447.2069	105.1724
Median		103.5000	62.0000	.4000	444.0000	100.0000
Mode		30.00[a]	60.00	.40	419.00[a]	80.00
Std. Deviation		134.60745	5.16478	.16137	29.33109	37.57095
Variance		18119.164	26.675	.026	860.313	1411.576
Range		717.00	28.00	.66	111.00	120.00
Minimum		25.00	42.00	.20	409.00	40.00
Maximum		742.00	70.00	.86	520.00	160.00

73. ANALYSIS OF TIME FOR END OF RADIOTHERAPY AND RELATION WITH MARKERS OF SUCLINICAL CARDIOTOXICITY.



74. MEDIAN DURATION OF FOLLOW UP BY REVERSE KAPLAN MEIER ANALYSIS

Means and Medians for Survival Time

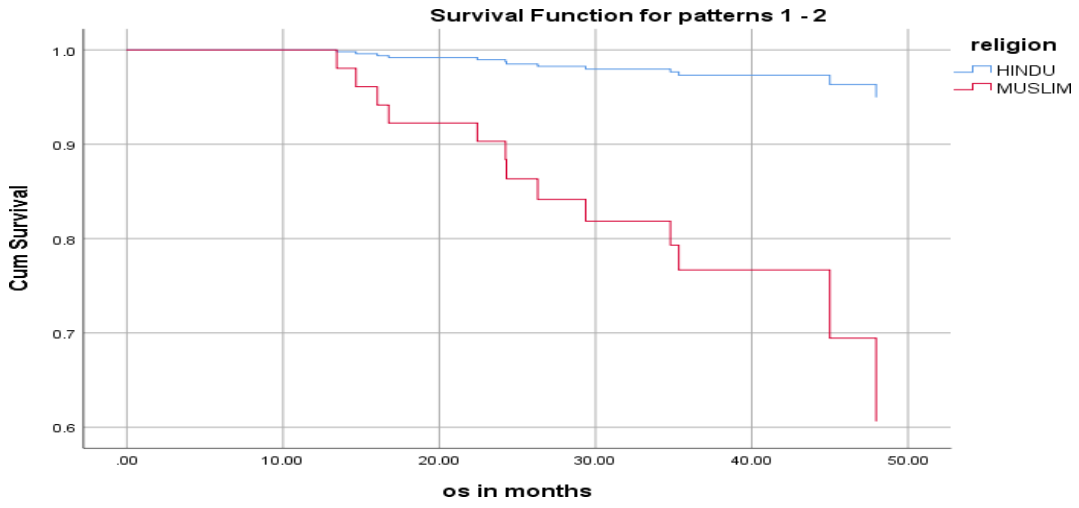
	Mean[a]				Median			
		95% Confidence Interval				95% Confidence Interval	
Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
41.301	1.176	38.996	43.606	40.700	.540	39.642	41.758

a. Estimation is limited to the largest survival time if it is censored.

75. SURVIVAL ANALYSIS-DEMOGRAPHIC VARIABLES COX REGRESSION SURVIVAL ANALYSIS

Variables in the Equation

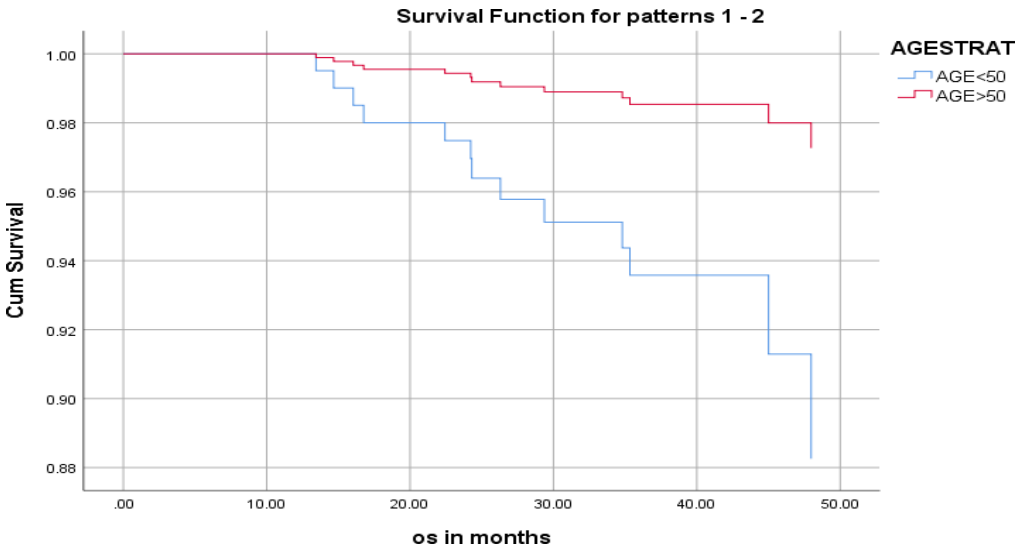
	B	SE	Wald	df	P value	Hazard ratio	95.0% CI for Exp(B) Lower	Upper
RELIGION	-2.280	.934	5.962	1	.015	.102	.016	.638
AGE</>50	1.506	.950	2.514	1	.113	4.507	.701	28.985
OBESE			1.451	2	.484			
OVERWEIGHT	-.828	.695	1.418	1	.234	.437	.112	1.707
NORMAL WEIGHT	-.276	.895	.095	1	.758	.759	.131	4.382
ANY COMORBIDITY	1.678	1.148	2.138	1	.144	5.357	.565	50.808
PREMENSTRUAL			3.510	2	.173			
POSTMENSTRUAL	9.079	112.879	.006	1	.936	8771.082	.000	1.060E+100
PERIMENSTRUAL	10.871	112.879	.009	1	.923	52629.232	.000	6.368E+100



Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
religion	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
HINDU	76.000	2.884	70.347	81.652	.	.	.	.
MUSLIM	30.444	3.181	24.209	36.679	29.367	4.137	21.258	37.475
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

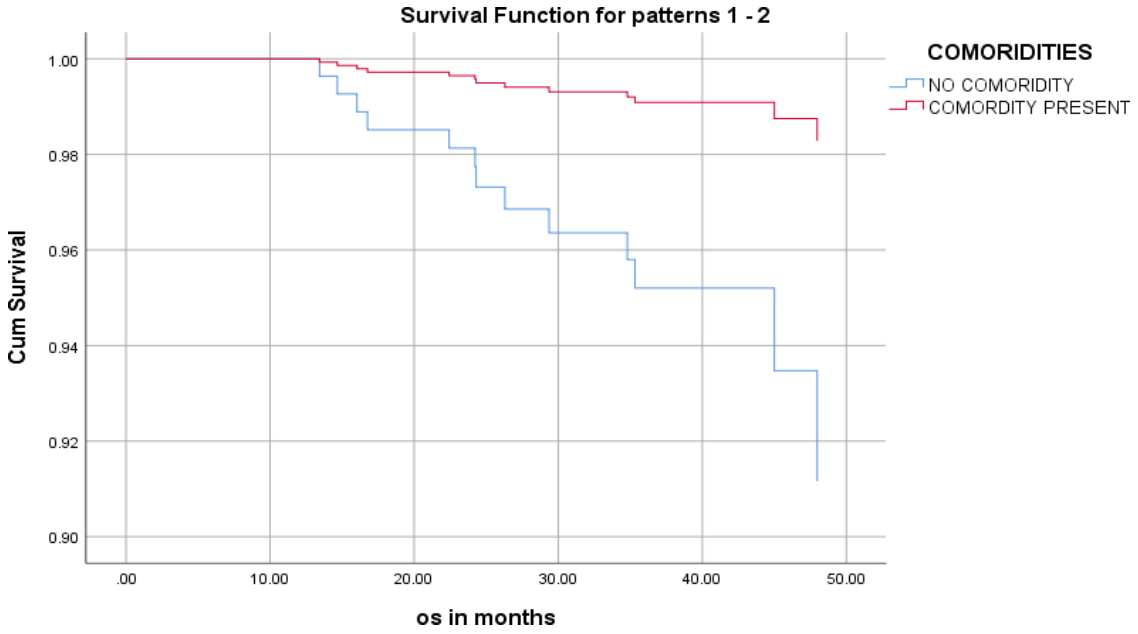


Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
AGESTRAT	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
<50	51.163	1.886	47.466	54.860	.	.	.	.
>50	76.119	3.701	68.865	83.374	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

P=0.667



Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
COMORIDITIES	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
NO COMORBIDITY	51.642	1.739	48.234	55.051	.	.	.	.
WITH COMORBIDITY	83.492	2.350	78.886	88.098	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3.742	1	.053

The vector of trend weights is -1, 1. This is the default.

EFFECT OF BMI ON OS:

Means and Medians for Survival Time

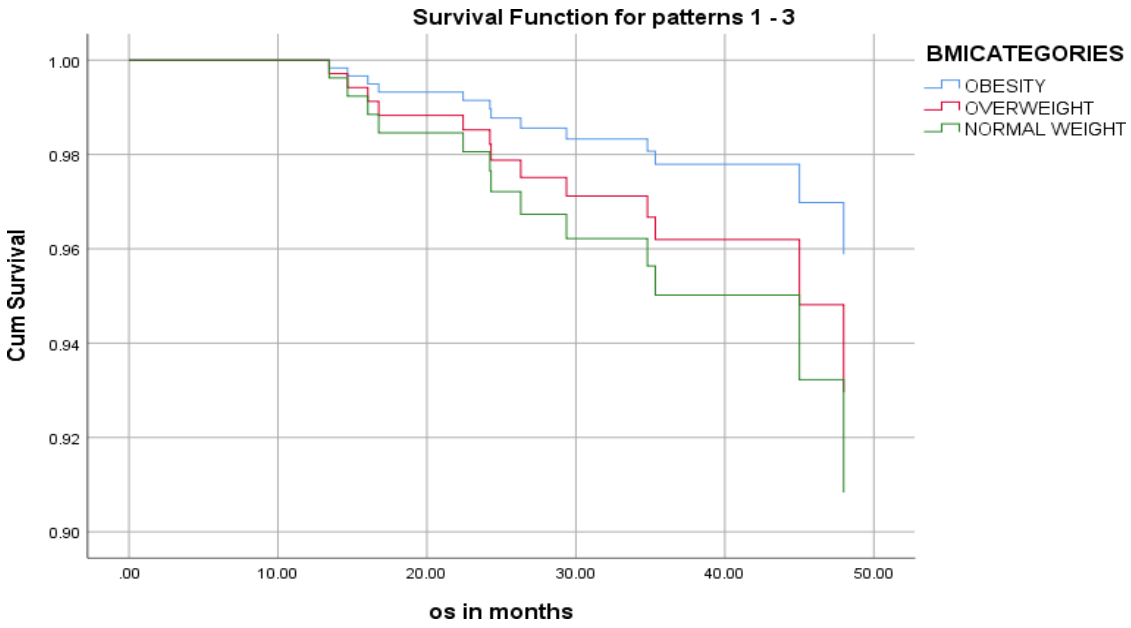
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
BMICATEGORIES	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
OBESE	78.165	3.300	71.697	84.633	.	.	.	.
OVERWEIGHT	50.848	3.638	43.717	57.980	.	.	.	.
NORMAL WEIGHT	46.040	2.594	40.955	51.124	.	.	.	.
Overall	75.547	2.893	69.876	81.217	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	2.213	1	.137

The vector of trend weights is -1, 0, 1. This is the default.



EFFECT OF LATERALITY ON OVERALL SURVIVAL:

Means and Medians for Survival Time

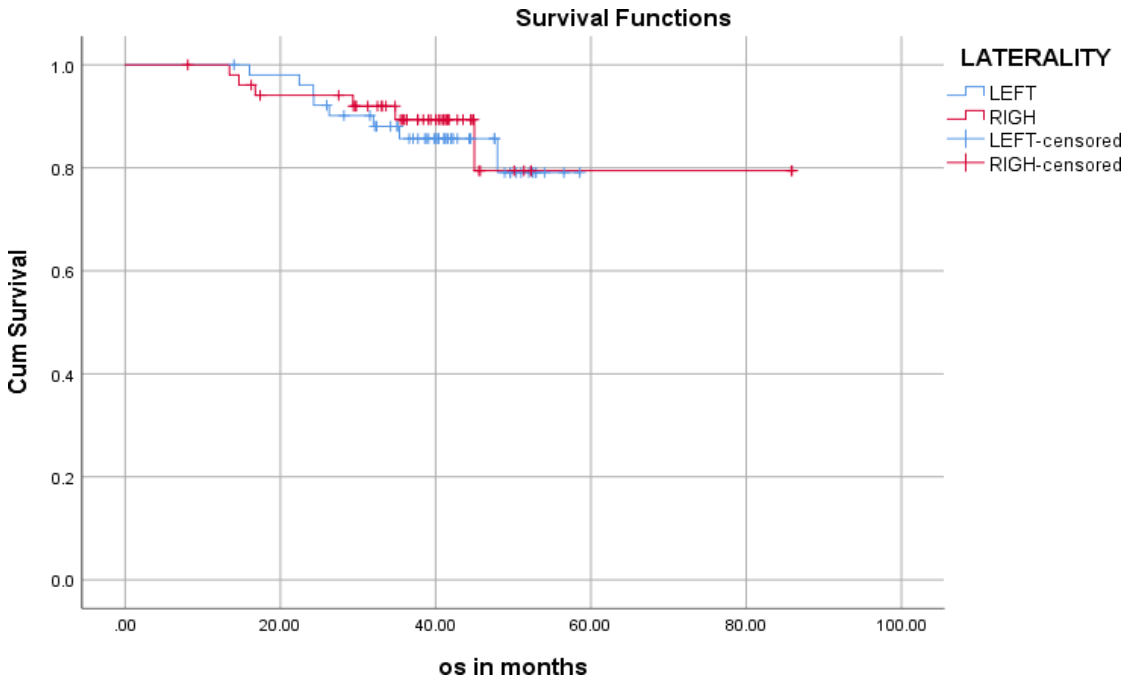
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
LATERALITY	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
LEFT	53.224	1.740	49.813	56.635	.	.	.	.
RIGHT	75.113	4.659	65.981	84.245	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.089	1	.766

The vector of trend weights is -1, 1. This is the default.



EFFECT OF MENSTRUAL STATUS ON OVERALL SURVIVAL:

Means and Medians for Survival Time

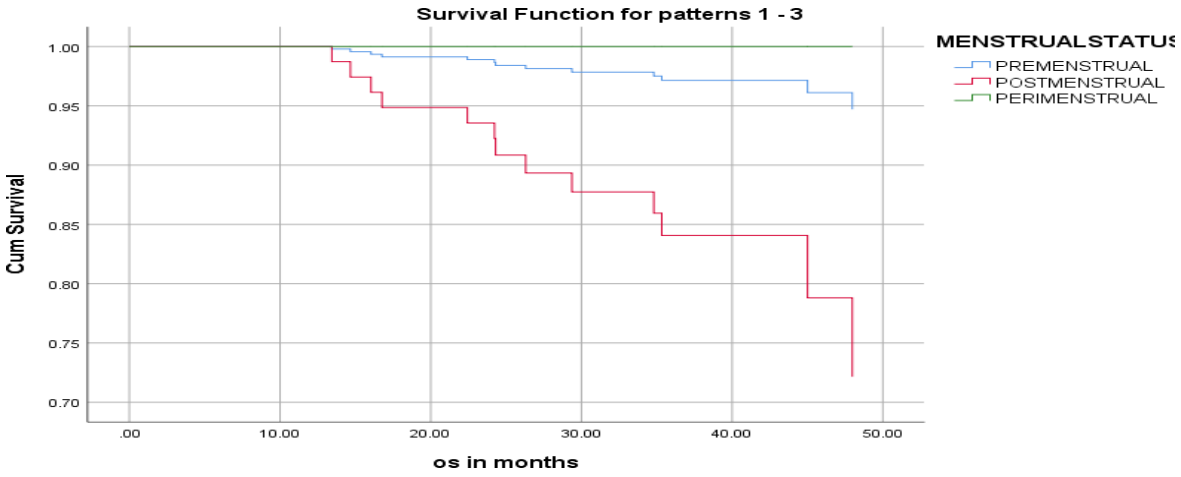
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
MENSTRUALSTATUS	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
PREMENSTRUAL	51.447	2.135	47.264	55.631	.	.	.	.
POST MENSTRUAL	73.093	4.387	64.495	81.691	.	.	.	.
PERI MENSTRUAL	51.830	2.090	47.733	55.927	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.130	1	.718

The vector of trend weights is -1, 0, 1. This is the default.



76. PROGRESSION FREE SURVIVAL/RECURRENCE FREE SURVIVAL-DEMOGRAPHIC VARIBALES

KAPLAN MEIER ANALYSIS:

a. AGE</>50

Means and Medians for Survival Time

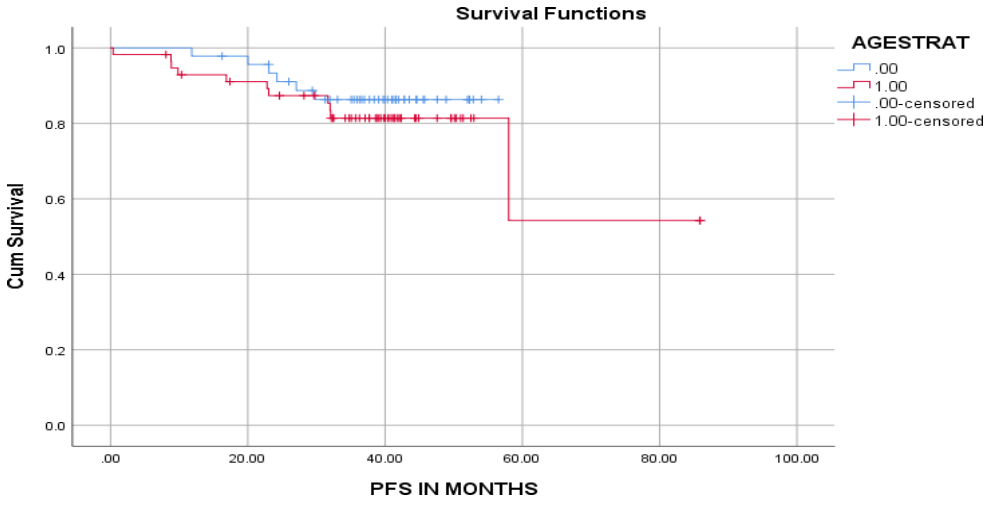
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
AGESTRAT	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
AGE<50	51.925	1.770	48.456	55.394	.	.	.	.
AGE>50	65.904	6.914	52.352	79.456	.	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

a.Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.467	1	.494

The vector of trend weights is -1, 1. This is the default.



b) EFFECT OF BMI ON PFS/RFS

Means and Medians for Survival Time

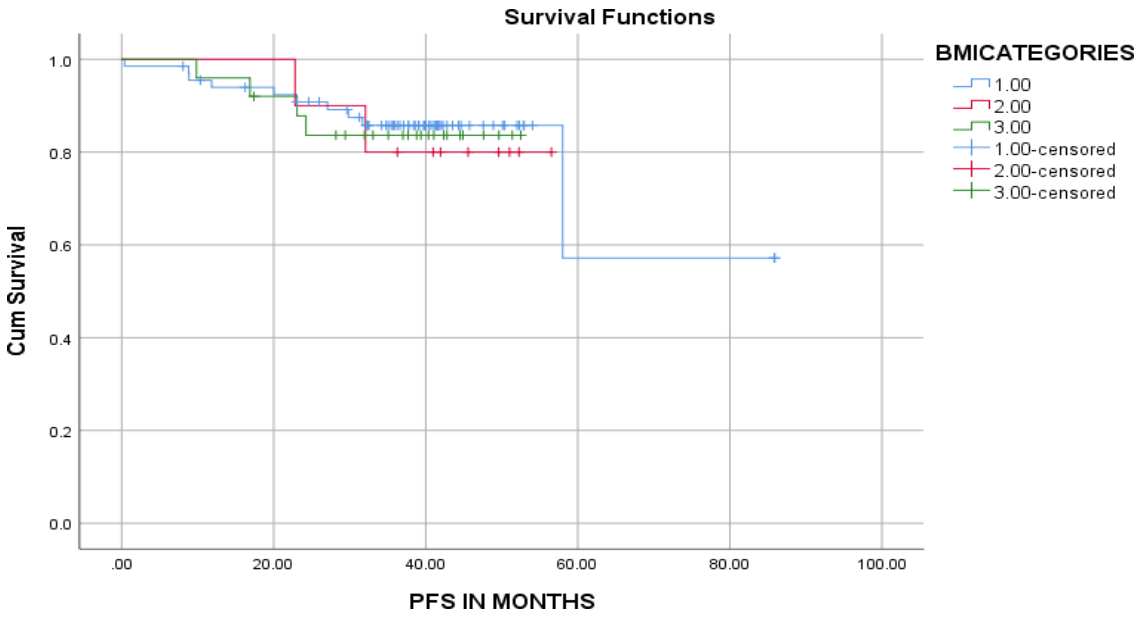
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
BMICATEGORIES	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
OBESITY	68.311	7.008	54.575	82.048	.	.	.	.
OVERWEIGHT	50.713	3.739	43.385	58.041	.	.	.	.
NORMAL WEIGHT	46.955	2.572	41.914	51.996	.	.	.	.
Overall	67.788	6.757	54.545	81.031	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.116	1	.733

The vector of trend weights is -1, 0, 1. This is the default.



c) EFFECT OF RELIGION ON PFS/RFS

Means and Medians for Survival Time

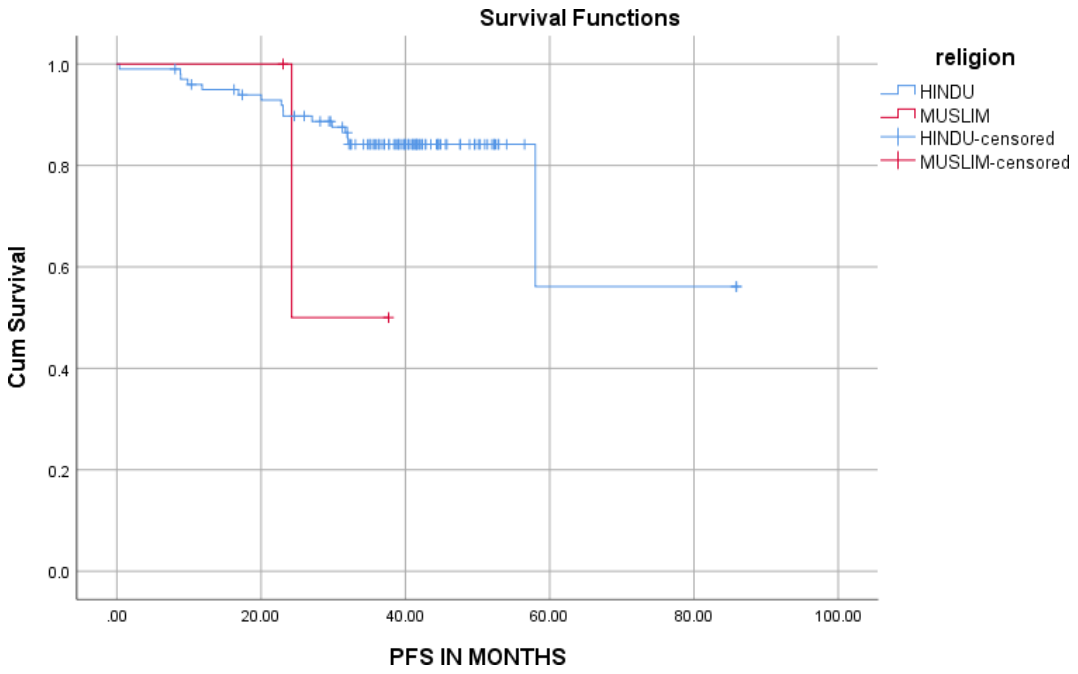
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
religion	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
HINDU	67.681	6.740	54.471	80.891	.	.	.	.
MUSLIM	30.950	4.749	21.641	40.259	24.233	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.995	1	.319

The vector of trend weights is -1, 1. This is the default.



d) EFFECT OF PRESENCE OF COMORIDITIES ON PFS/RFS

Means and Medians for Survival Time

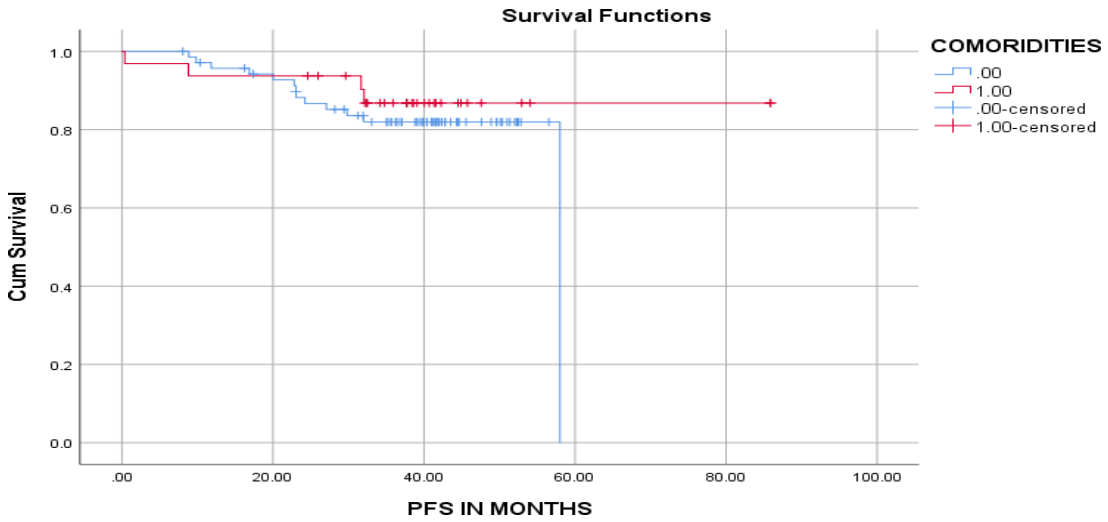
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
COMORIDITIES	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
WITH	51.332	1.847	47.713	54.952	58.000	.000	.	.
WITHOUT	77.065	4.183	68.867	85.264	.	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.922	1	.337

The vector of trend weights is -1, 1. This is the default.



e) EFFECT OF MENSTRUAL STATUS ON PFS/RFS

Means and Medians for Survival Time

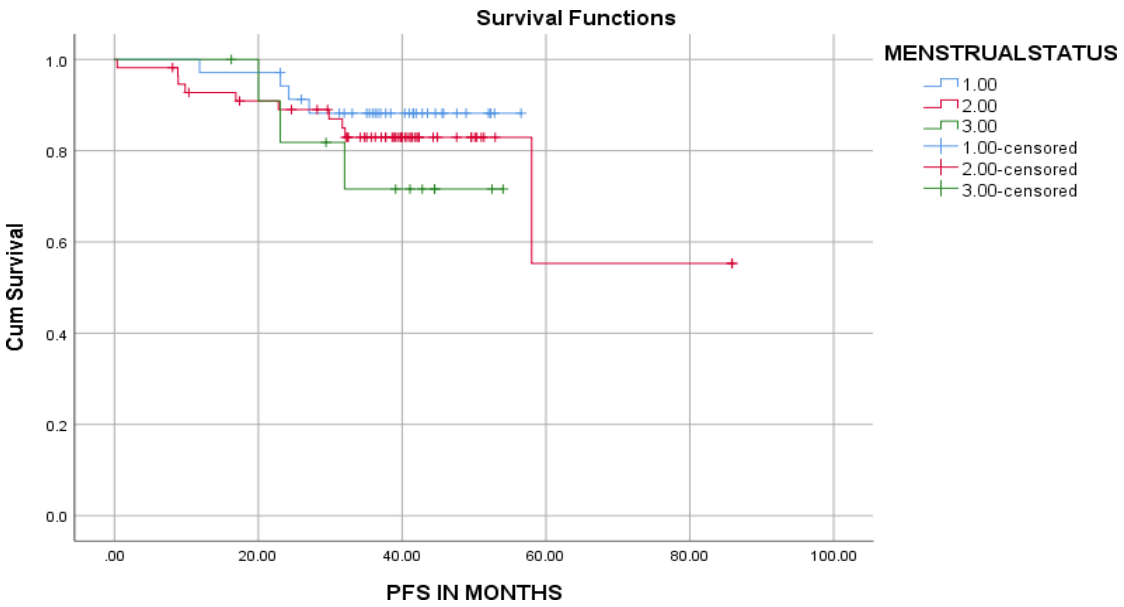
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
MENSTRUALSTATUS	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
PRE MENSTRUAL	52.424	1.954	48.594	56.254	.	.	.	.
POST MENSTRUAL	66.676	7.001	52.954	80.399	.	.	.	.
PERI MENSTRUAL	45.871	4.055	37.922	53.819	.	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.353	1	.245

The vector of trend weights is -1, 0, 1. This is the default.



f) EFECT OF LATERALITY ON PFS/RFS

Means and Medians for Survival Time

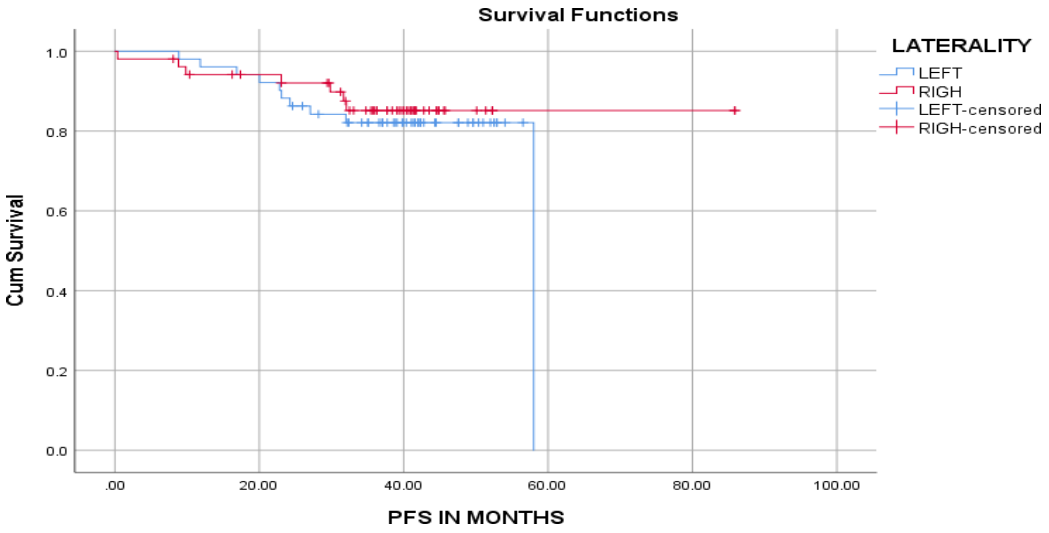
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
LATERALITY	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
LEFT	51.360	2.153	47.140	55.581	58.000	.000	.	.
RIGHT	76.154	3.435	69.422	82.886	.	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.557	1	.456

The vector of trend weights is -1, 1. This is the default.



77. EFFECT OF DEMOGRAPHIC VARIABLES ON DFS- A KAPLAN MEIER SURVIVAL ANALYSIS.

a. EFFECT OF AGE WISE STRATIFICATION ON DFS:

Means and Medians for Survival Time

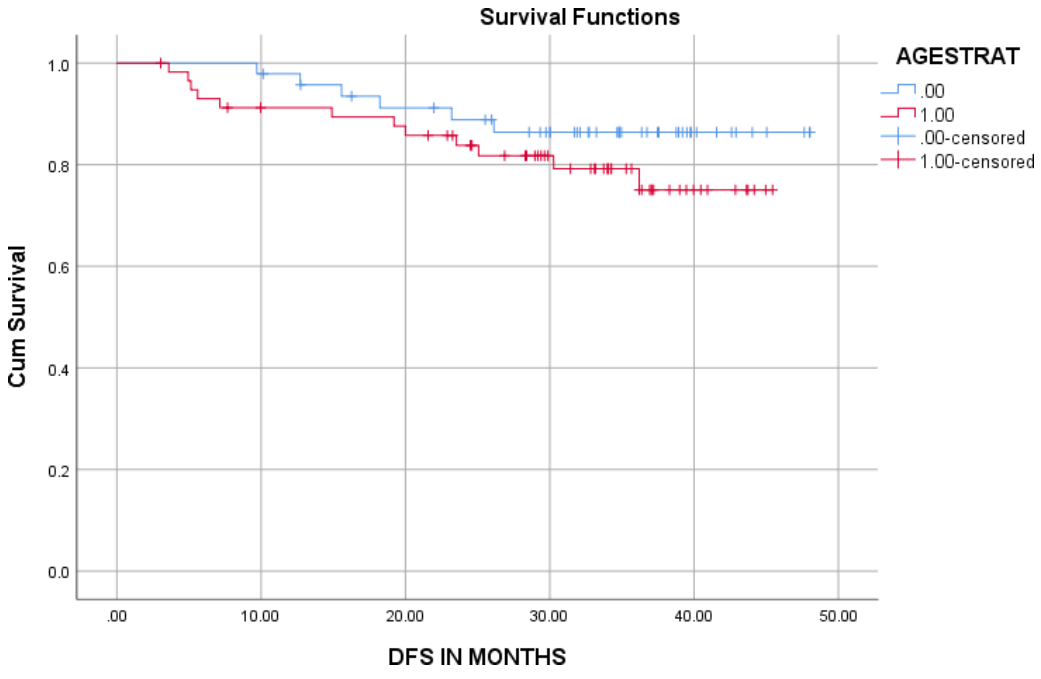
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
AGESTRAT	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
AGE<=50	43.926	1.581	40.828	47.024	.	.	.	.
AGE>50	38.796	1.760	35.345	42.246	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.300	1	.254

The vector of trend weights is -1, 1. This is the default.0



b. EFFECT OF BMI ON DFS

Means and Medians for Survival Time

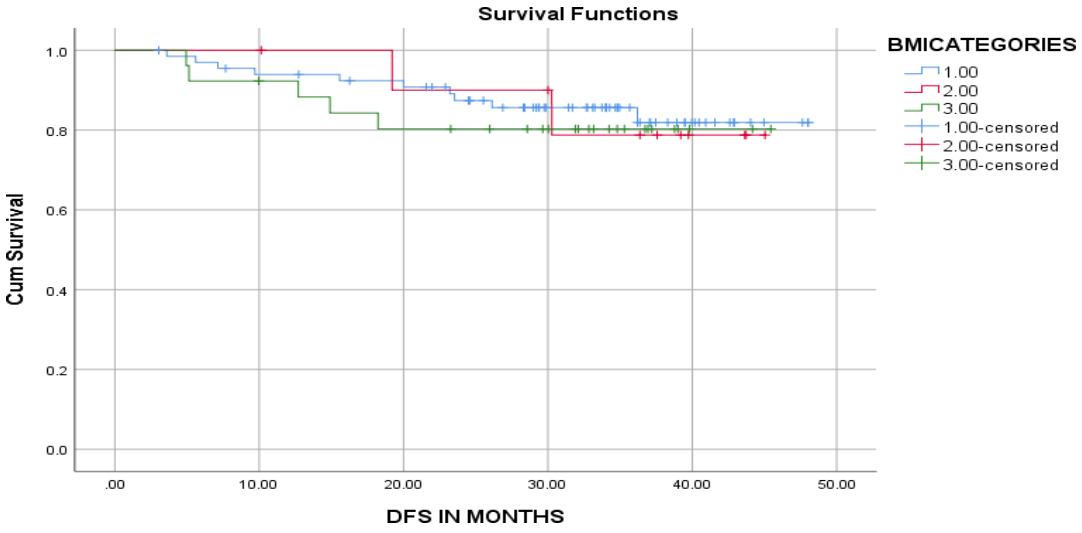
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
BMICATEGORIES	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
OBESITY	42.893	1.527	39.899	45.886	.	.	.	.
OVERWEIGHT	40.789	2.756	35.388	46.190	.	.	.	.
NORMAL WEIGHT	38.695	2.735	33.335	44.055	.	.	.	.
Overall	42.399	1.274	39.902	44.896	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.302	1	.582

The vector of trend weights is -1, 0, 1. This is the default.



c. EFFECT OF RELIGION ON DFS

Means and Medians for Survival Time

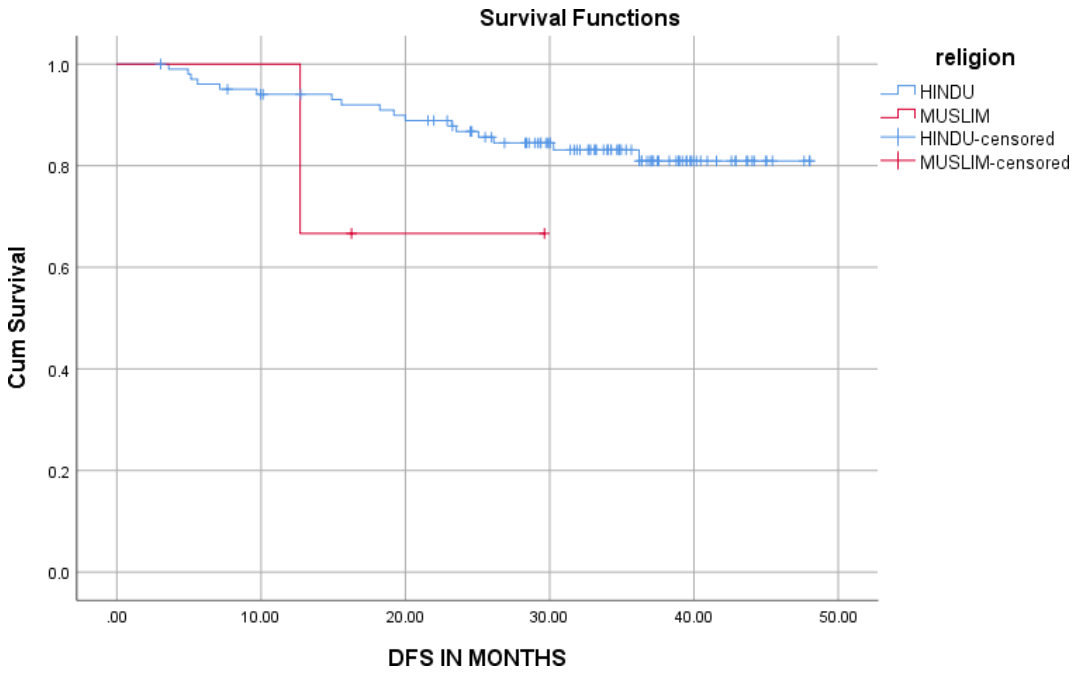
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
religion	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
HINDU	42.422	1.271	39.930	44.913	.	.	.	.
MUSLIM	23.989	4.609	14.956	33.022	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.344	1	.246

The vector of trend weights is -1, 1. This is the default.



d. EFFECT OF COMORBIDITY STATUS ON DFS

Means and Medians for Survival Time

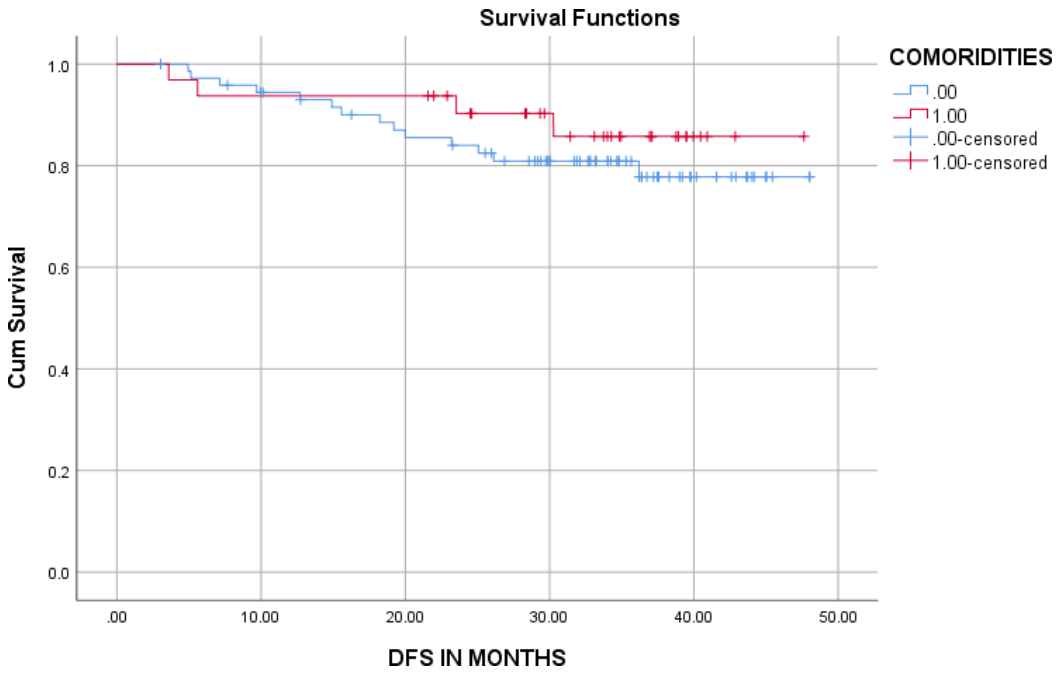
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
COMORIDITIES	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
NO COMORIDITY	41.510	1.590	38.393	44.627	.	.	.	.
COMORBIDITY PRESENT	43.323	2.082	39.242	47.404	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.751	1	.386

The vector of trend weights is -1, 1. This is the default.



e. EFFECT OF MENSTRUAL STATUS ON DFS

Means and Medians for Survival Time

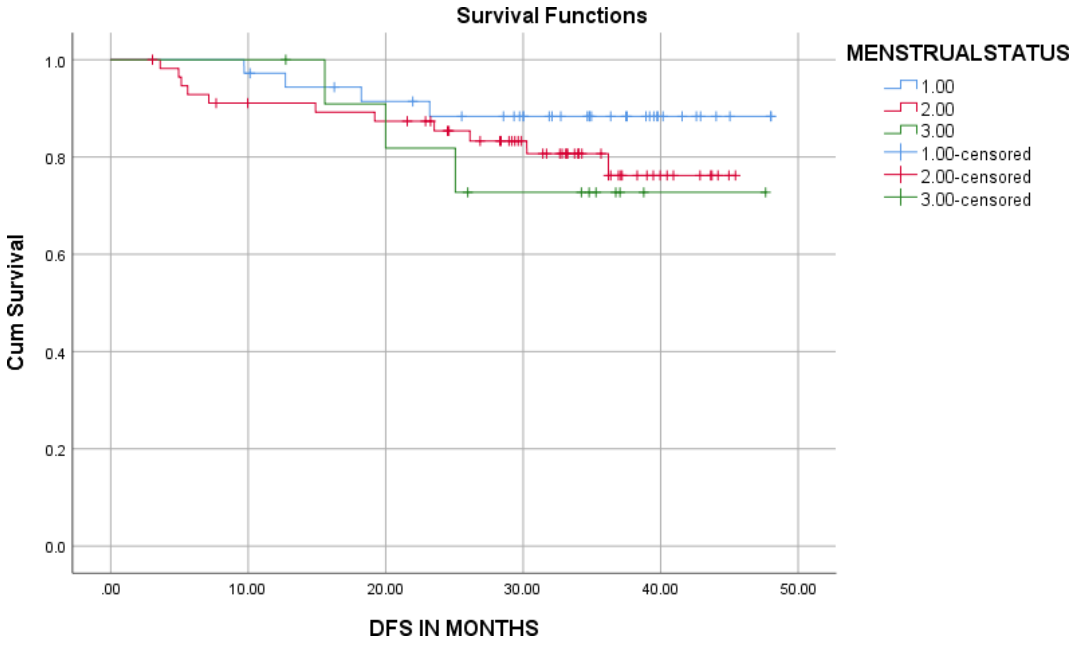
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
MENSTRUALSTATUS	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
PREMENSTRUAL	44.323	1.763	40.867	47.778	.	.	.	.
POSTMENSTRUAL	39.148	1.756	35.705	42.591	.	.	.	.
PERIMENSTRUAL	40.155	3.733	32.839	47.471	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.594	1	.207

The vector of trend weights is -1, 0, 1. This is the default.



f) **EFFECT OF LATERALITY ON DFS**

Means and Medians for Survival Time

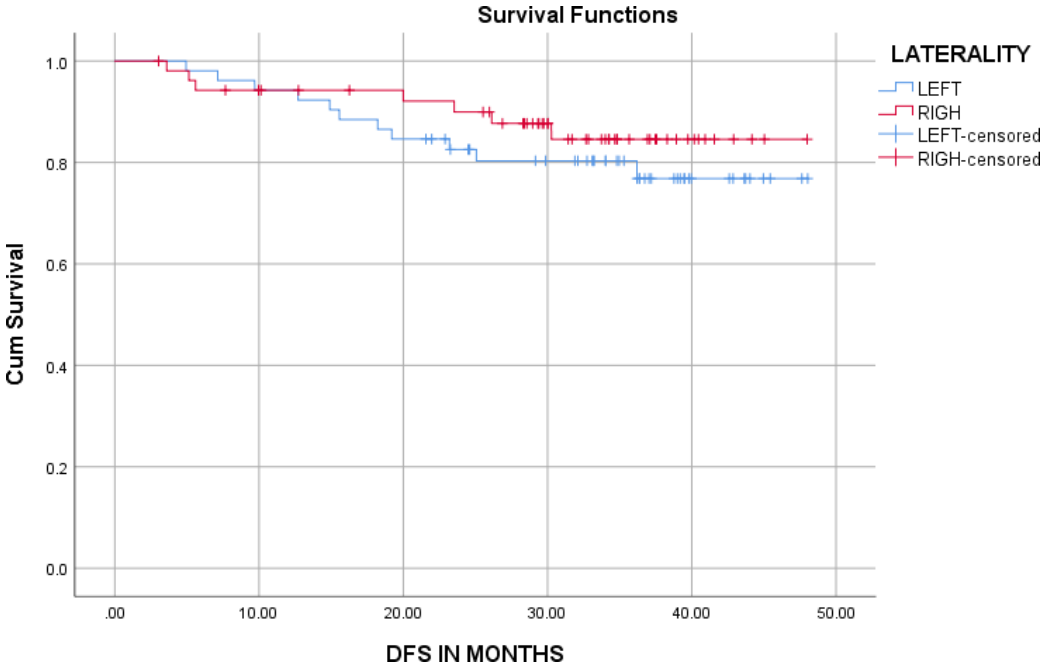
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
LATERALITY	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
LEFT	41.174	1.878	37.494	44.854	.	.	.	.
RIGHT	43.336	1.681	40.042	46.629	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

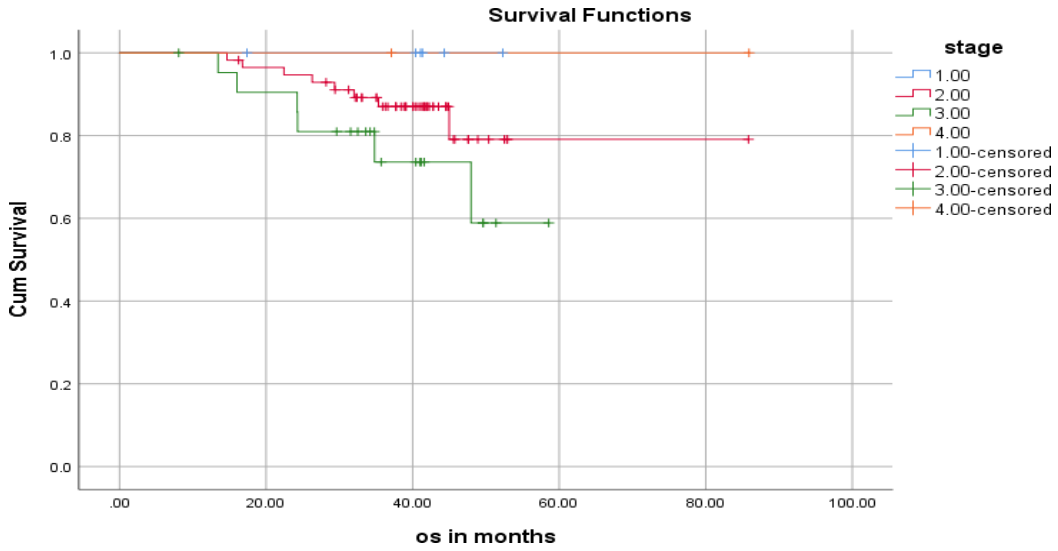
	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.764	1	.382

The vector of trend weights is -1, 1. This is the default.



78. PRESURGICAL CONSIDERATIONS ON OVERALL SURVIVAL:

a. PRE SURGICAL STAGING :



Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.420	1	.233

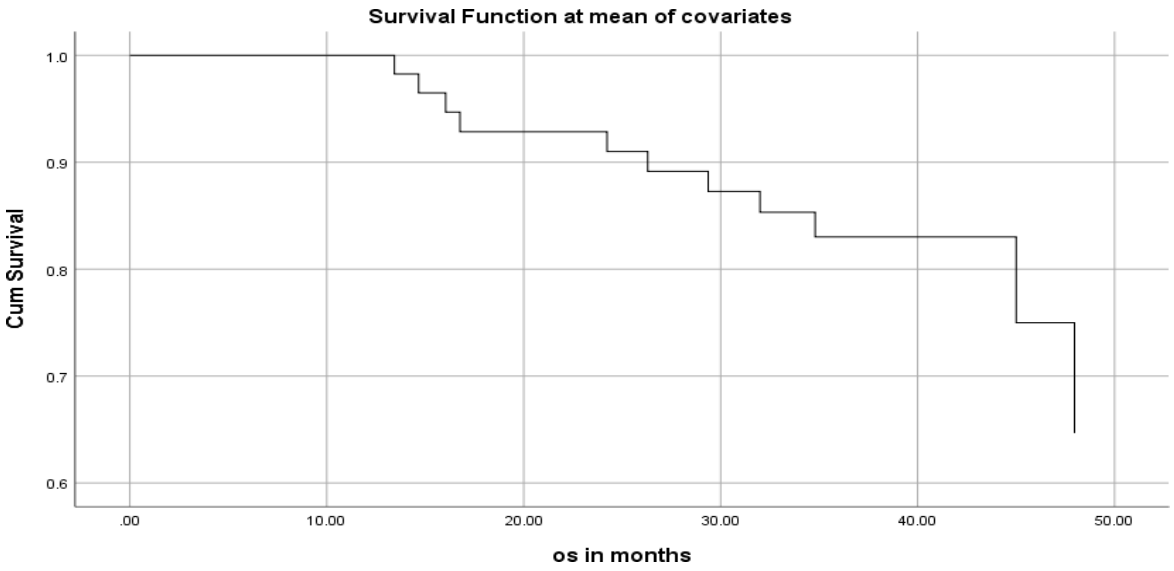
The vector of trend weights is -3, -1, 1, 3. This is the default.

Mean overall survival could not be calculated due to censored events.

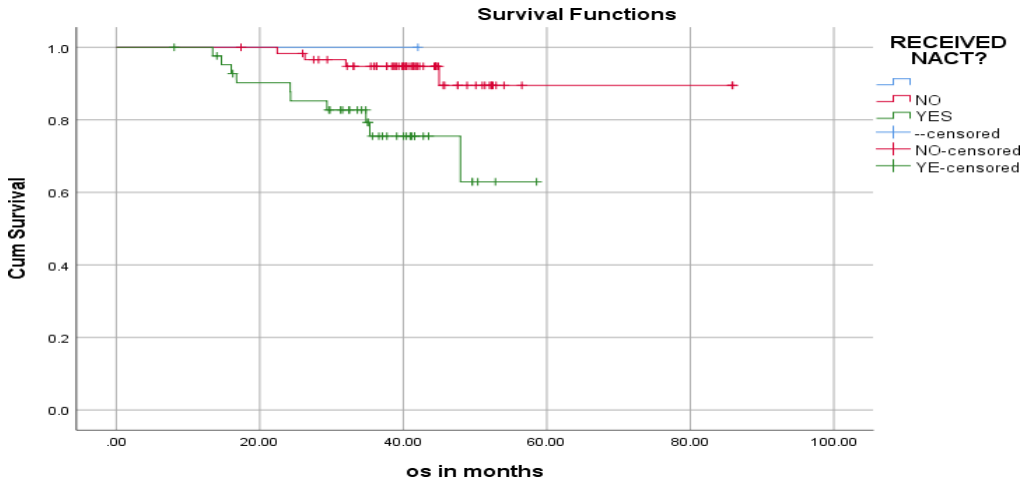
b. EFFECT OF LONG AXIS DIAMETER OF TUMOUR AND SHORT AXIS NODAL DIAMETER ON OVERALL SURVIVAL BY COX REGRESSION ANALYSIS.

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
LAD	.048	.114	.173	1	.677	1.049	.838	1.312
SAD	.515	.368	1.958	1	.162	1.674	.814	3.443



c. EFFECT OF NEOADJUVANT CHEMOTHERAPY STATUS ON OVERALL SURVIVAL



Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	7.767	1	.005

The vector of trend weights is -1, 0, 1. This is the default.

79. PRESURGICAL CONSIDERATIONS: ON PROGRESSION FREE SURVIVAL/RECURRENCE FREE SURVIVAL

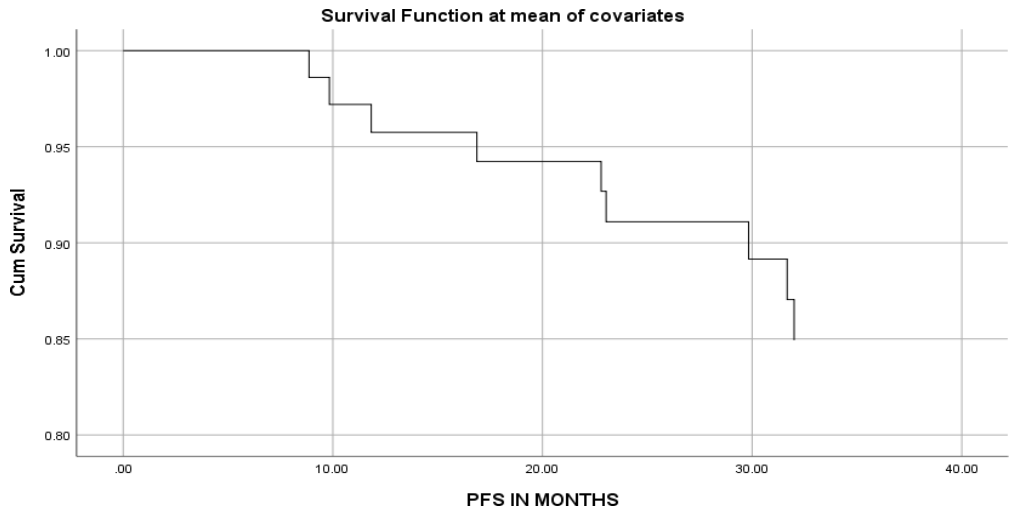
a. EFFECT OF LONG AXIS DIAMETER OF TUMOUR AND SHORT AXIS NODAL DIAMETER ON PFS /RFS BY COX REGRESSION ANALYSIS.

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
LAD	.208	.096	4.667	1	.031	1.231	1.019	1.486
SAD	.767	.403	3.613	1	.057	2.153	.976	4.748

Covariate Means

	Mean
LAD	4.052
SAD	1.409

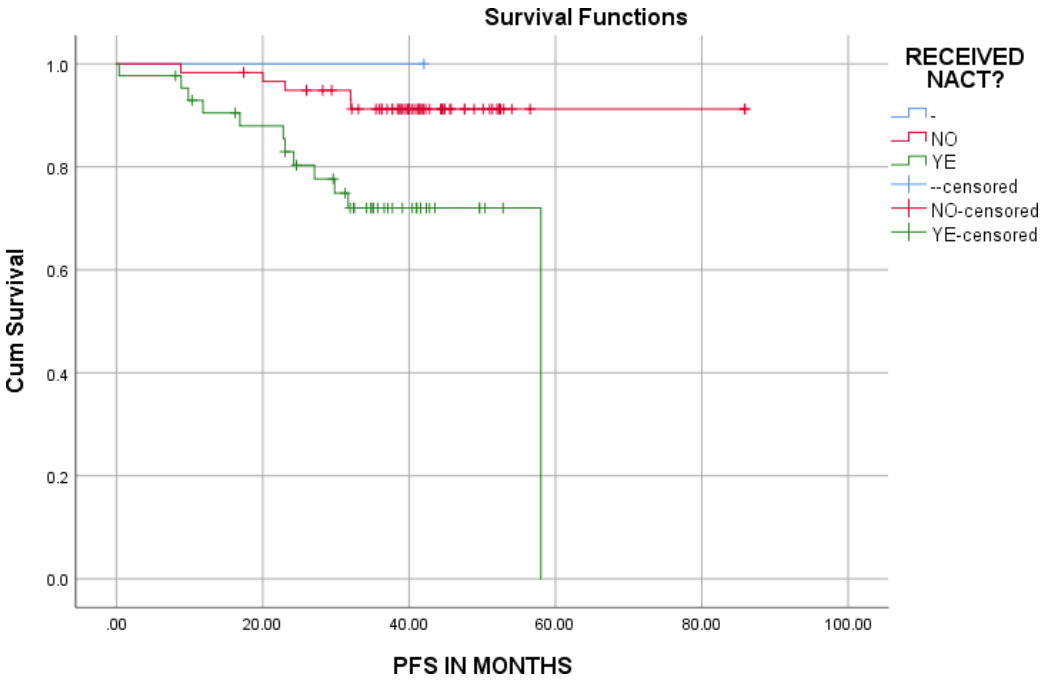


b. EFFECT OF NEOADJUVANT CHEMOTHERAPY STATUS ON PFS/RFS

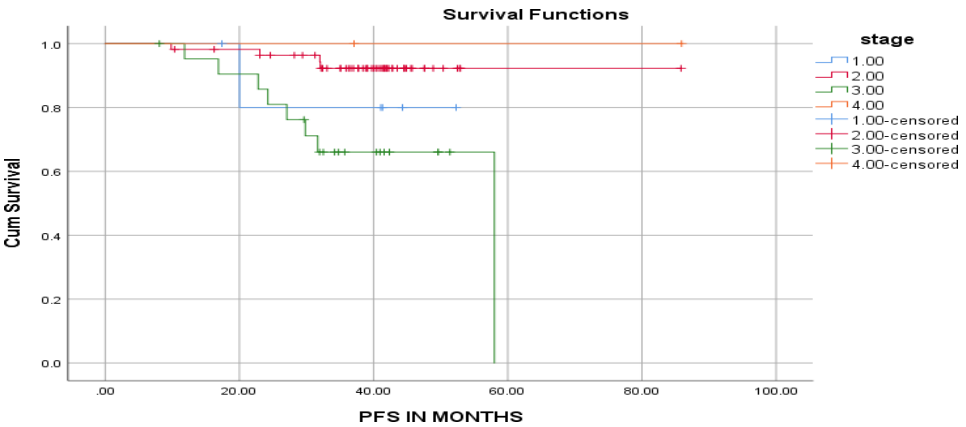
Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	8.284	1	.004

The vector of trend weights is -1, 0, 1. This is the default.



c. EFFECT OF PRESURGICAL STAGE ON PFS/RFS



Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	2.315	1	.128

The vector of trend weights is -3, -1, 1, 3. This is the default.

80. EFFECT OF PRESURGICAL CONSIDERATIONS ON DFS

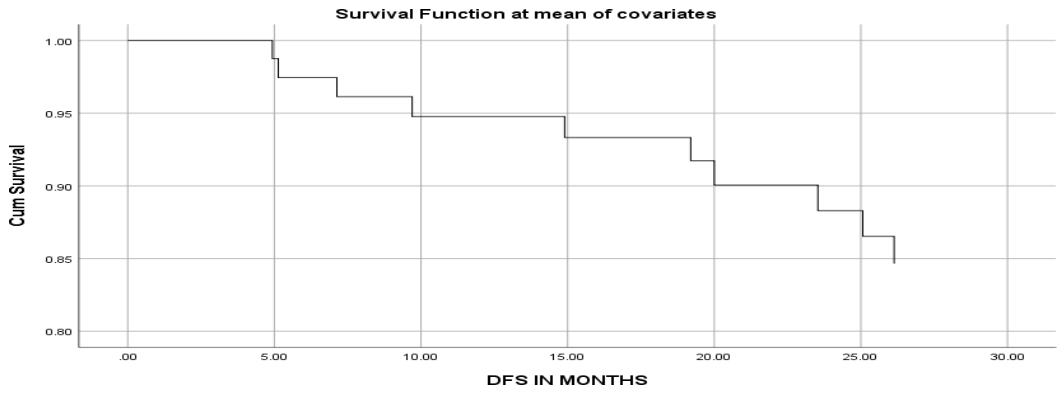
a. EFFECT OF LONG AXIS DIAMETER OF PRIMARY TUMOUR AND SHORT AXIS NODAL DIAMETER ON DFS BY COX REGRESSION ANALYSIS

Variables in the Equation

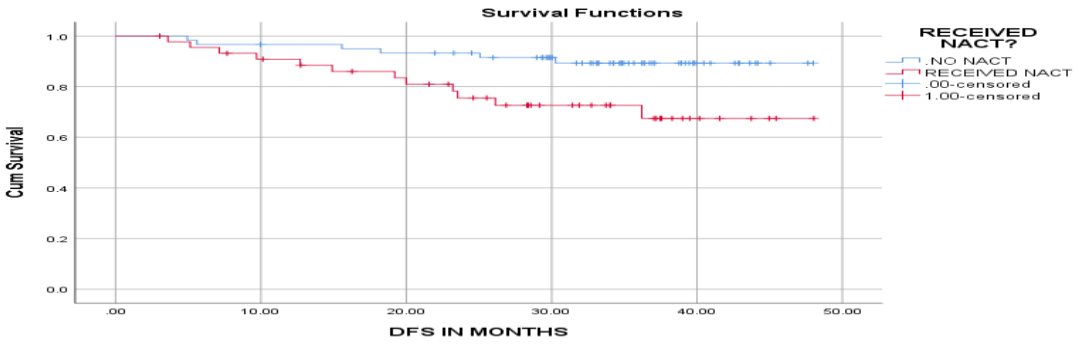
	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
LAD	.178	.091	3.799	1	.05	1.195	.999	1.429
SAD	.983	.350	7.891	1	.005	2.673	1.346	5.307

Covariate Means

	Mean
LAD	4.006
SAD	1.449



b) EFFECT OF NEOADJUVANT CHEMOTHERAPY STATUS ON DFS



Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
RECEIVED NACT?	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
NO NACT	44.723	1.307	42.161	47.285	.	.	.	.
RECEIVED NACT	38.547	2.357	33.927	43.167	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	6.153	1	.013

The vector of trend weights is -1, 1. This is the default.

c) EFFECT OF PRESURGICAL STAGE ON DFS

Means and Medians for Survival Time

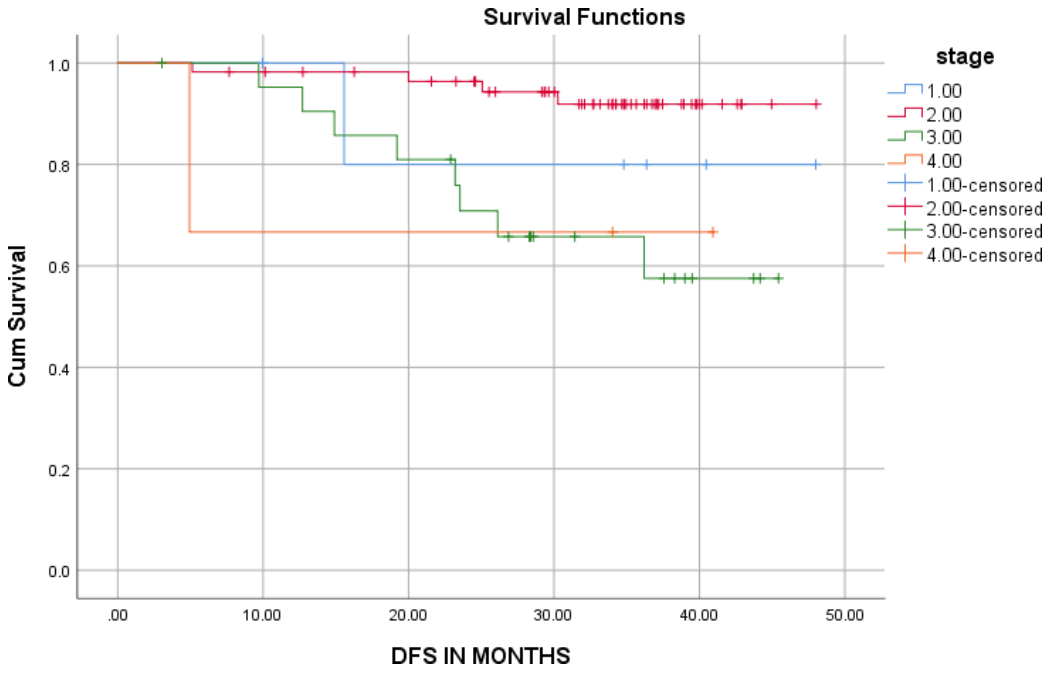
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
stage	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
1.00	41.513	5.802	30.142	52.885	.	.	.	.
2.00	45.851	1.079	43.735	47.966	.	.	.	.
3.00	35.501	2.870	29.875	41.127	.	.	.	.
4.00	28.933	9.798	9.729	48.137	.	.	.	.
Overall	42.888	1.282	40.374	45.401	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	7.026	1	.008

The vector of trend weihts is -3, -1, 1, 3. This is the default.



81. SURGICAL FACTORS AFFECTING OVERALL SURVIVAL

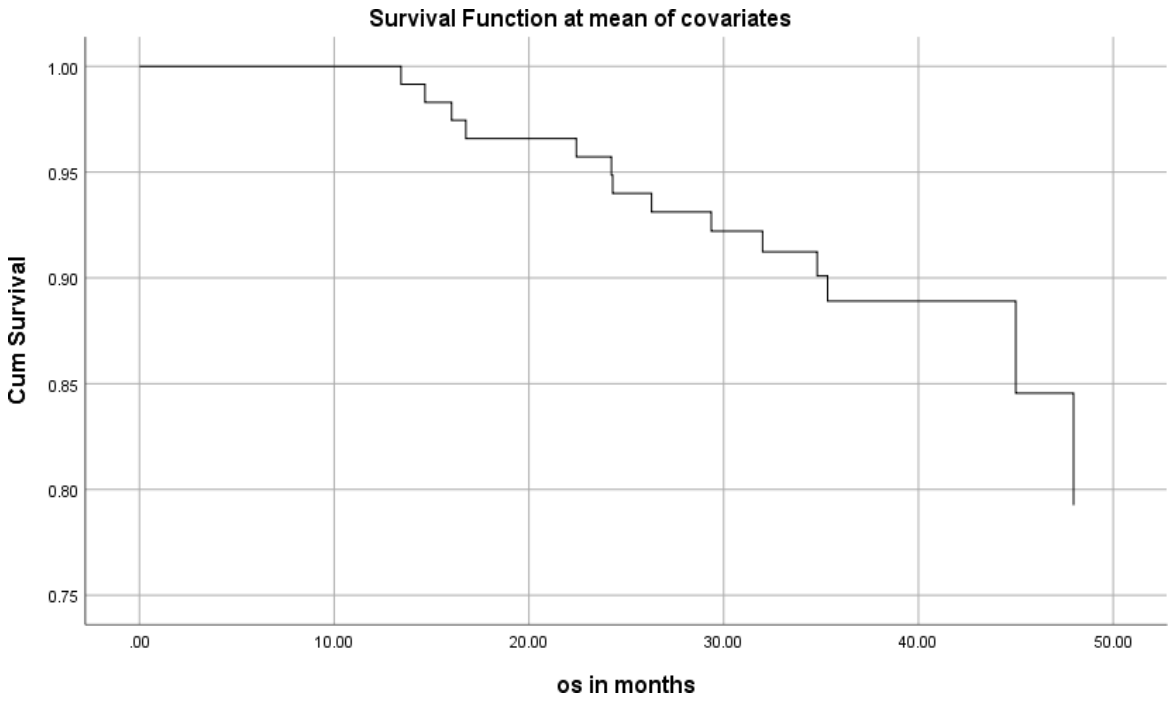
a. EFFECT OF NUMBER OF DISSECTED NODES AND NUMBER OF POSITIVE NODES ON OVERALL SURVIVAL BY COX REGRESSION ANALYSIS

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
NODES DISSECTED	.024	.014	2.708	1	.100	1.024	.995	1.053
NODES POSITIVE	.071	.037	3.607	1	.058	1.073	.998	1.154

Covariate Means

	Mean
NODES DISSECTED	18.327
NODES POSITIVE	3.010



b. EFFECT OF ADEQUACY OF NODAL DISSECTION ON OVERALL SURVIVAL

Means and Medians for Survival Time

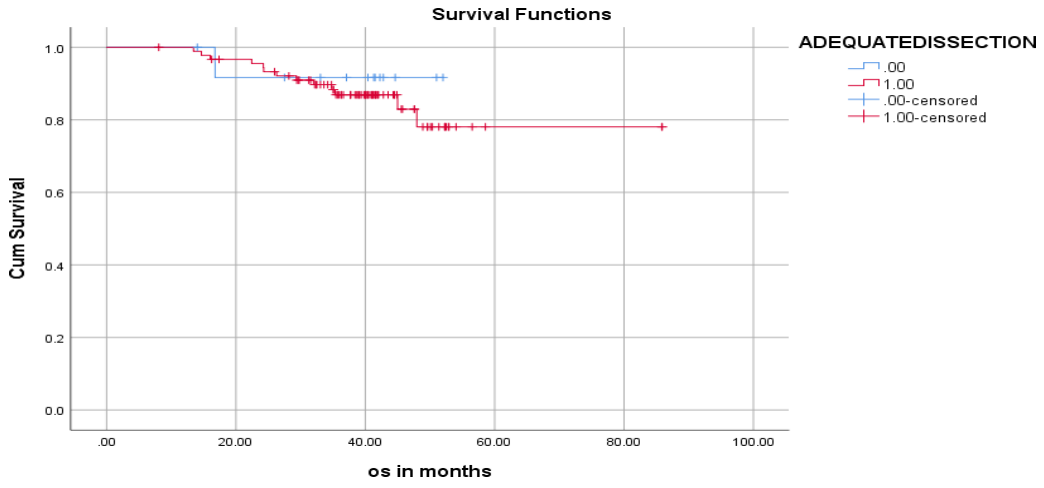
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
ADEQUATEDISSECTION	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
INADEQUATE DISSECTION	49.064	2.811	43.554	54.574	.	.	.	.
ADEQUATE DISSECTION	74.495	3.138	68.345	80.646	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

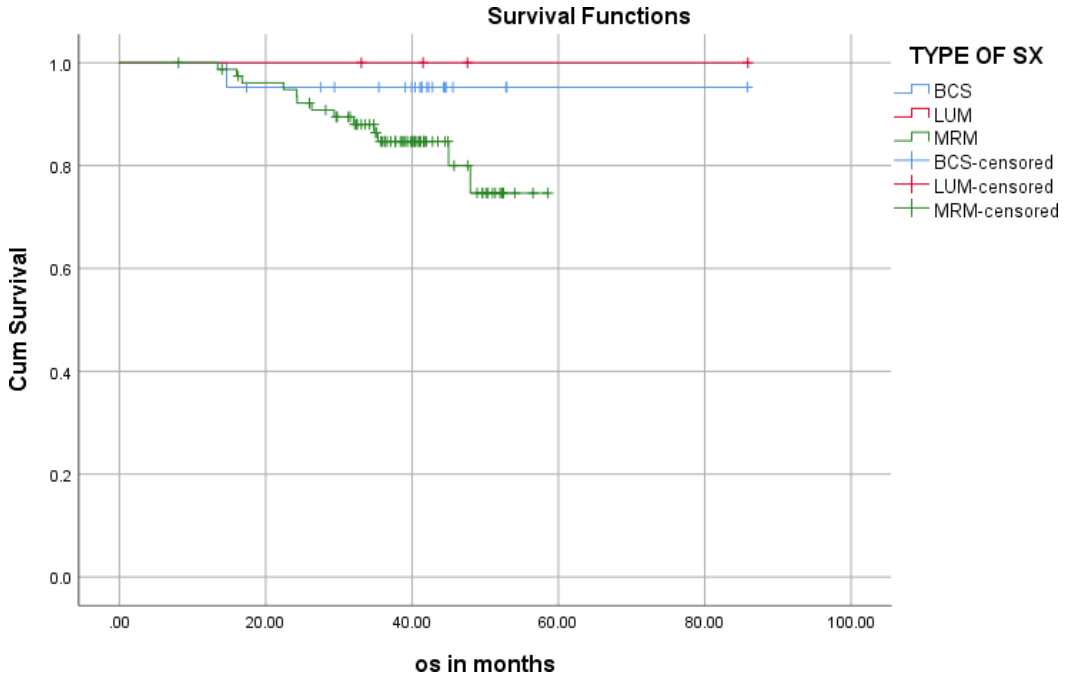
Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.272	1	.602

The vector of trend weights is -1, 1. This is the default.



c. EFFECT OF TYPE OF SURGERY ON OVERALL SURVIVAL



Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	2.021	1	.155

The vector of trend weights is -1, 0, 1. This is the default.

82. SURGICAL FACTORS AFFECTING PFS/RFS

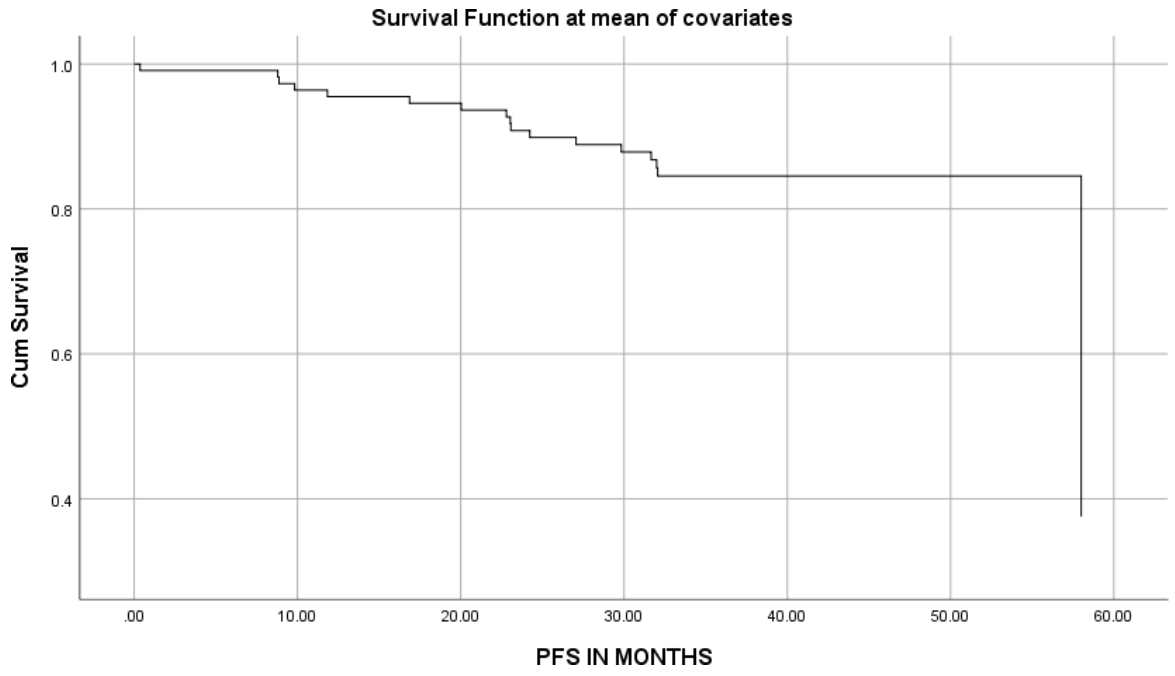
a. EFFECT OF NUMBER OF DISSECTED NODES AND NUMER OF POSITIVE NODES ON PFS/RFS BY COX REGRESSION ANALYSIS

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
NODES DISSECTED	.021	.014	2.129	1	.145	1.021	.993	1.049
NODES POSITIVE	.056	.036	2.478	1	.115	1.057	.986	1.134

Covariate Means

	Mean
NODES DISSECTED	18.327
NODES POSITIVE	2.851



b) EFFECT OF ADEQUACY OF NODAL DISSECTION ON PFS/RFS

Kaplan-Meier

Means and Medians for Survival Time

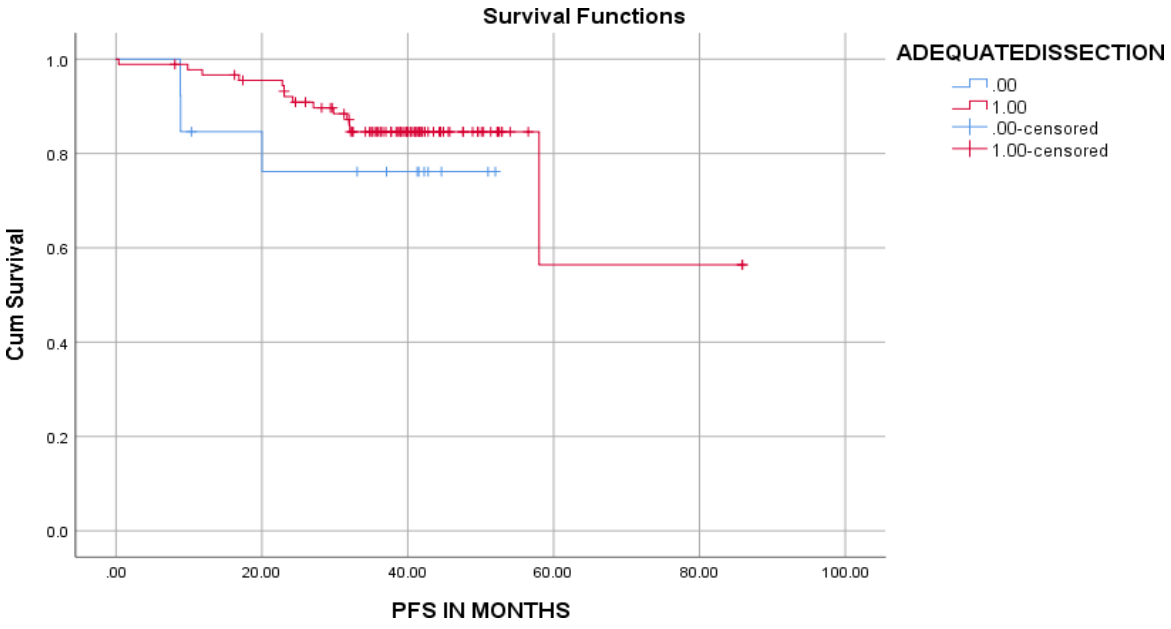
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
ADEQUATEDISSECTION	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
INADEQUATE	42.654	4.752	33.340	51.968	.	.	.	.
ADEQUATE	68.242	6.777	54.958	81.525	.	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

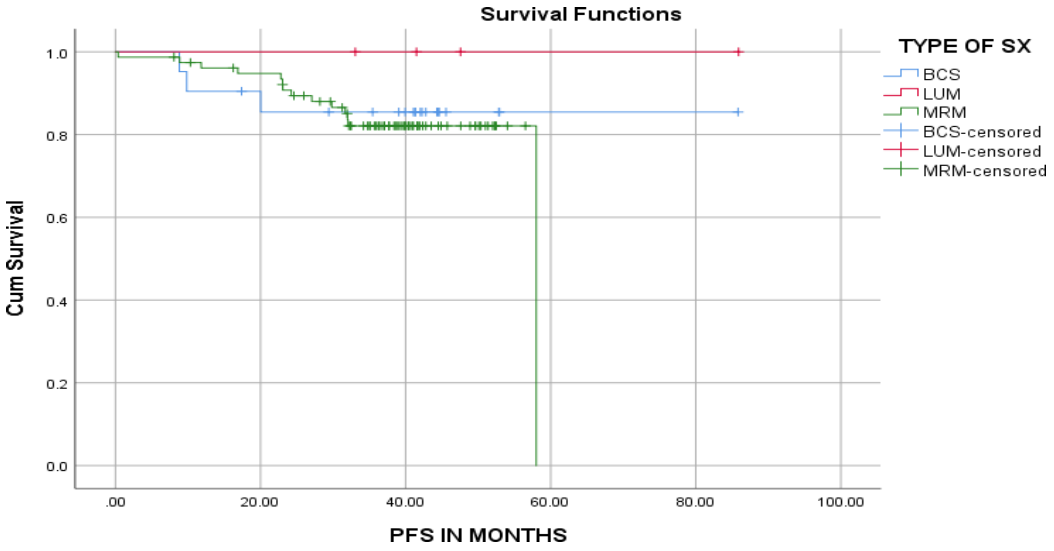
Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.965	1	.326

The vector of trend weights is -1, 1. This is the default.



c. EFFECT OF TYPE OF SURGERY ON PFS/RFS



Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.391	1	.532

The vector of trend weights is -1, 0, 1. This is the default.

83. SURGICAL FACTORS AFFECTING DFS

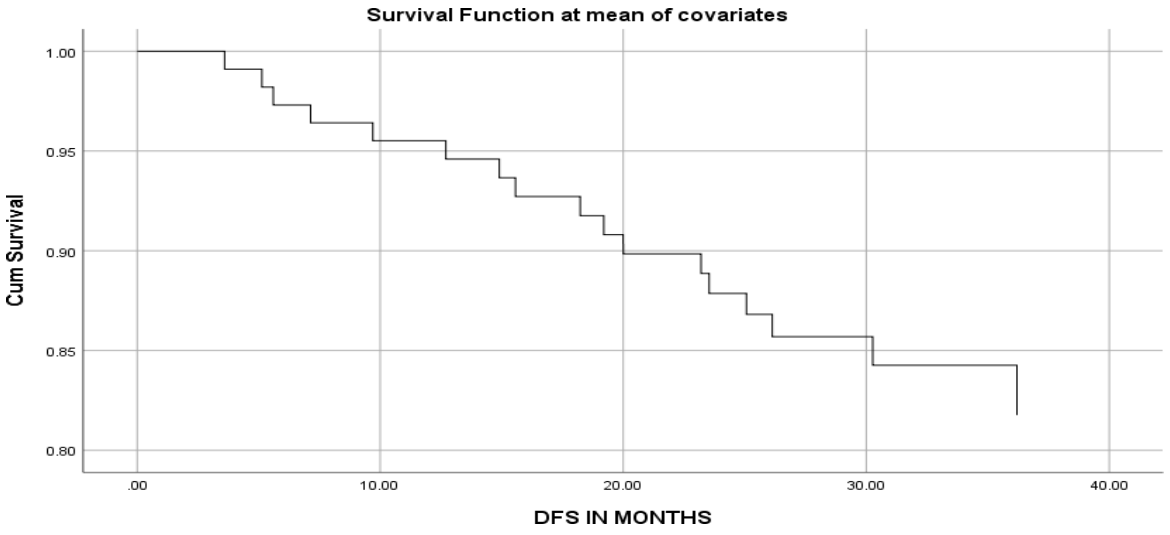
a. EFFECT OF NUMBER OF DISSECTED NODES AND NUMBER OF POSITIVE NODES ON DFS BY COX REGRESSION ANALYSIS

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
NODES DISSECTED	.018	.014	1.725	1	.189	1.019	.991	1.047
NODES POSITIVE	.060	.036	2.831	1	.092	1.062	.990	1.139

Covariate Means

	Mean
NODES DISSECTED	18.228
NODES POSITIVE	2.871



b. EFFECT OF ADEQUACY OF NODAL DISSECTION ON DFS

Kaplan Meier

Means and Medians for Survival Time

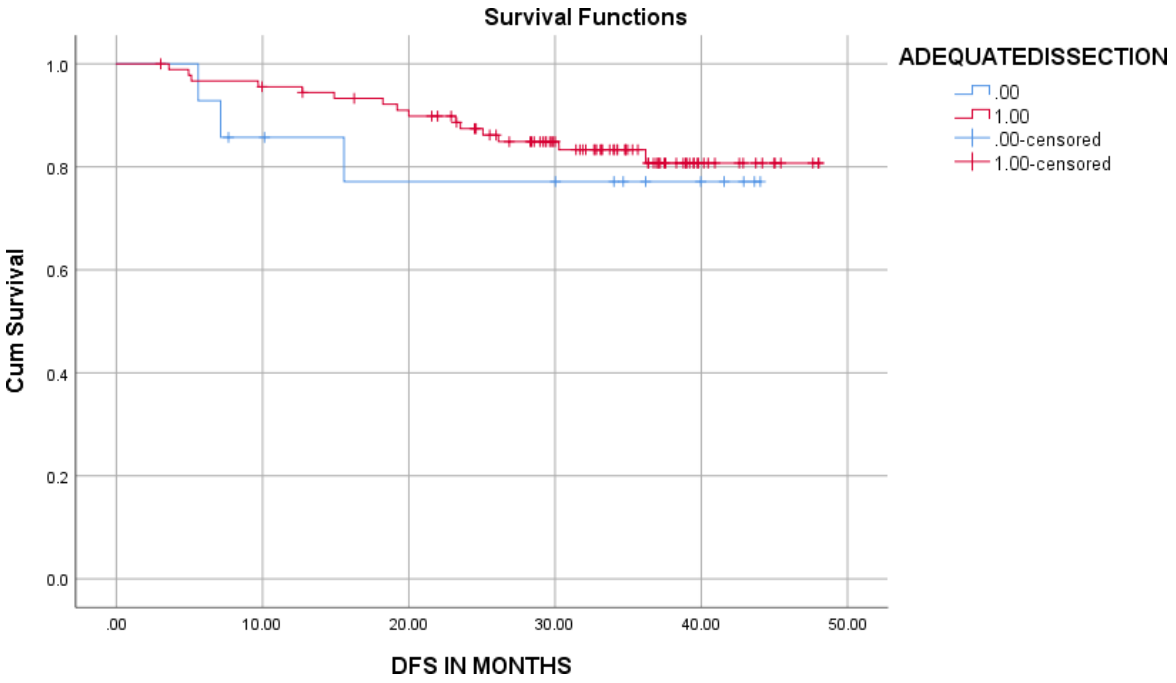
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
ADEQUATEDISSECTION	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
INADEQUATE	36.212	3.996	28.380	44.045	.	.	.	.
ADEQUATE	42.635	1.301	40.085	45.185	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.383	1	.536

The vector of trend weights is -1, 1. This is the default.

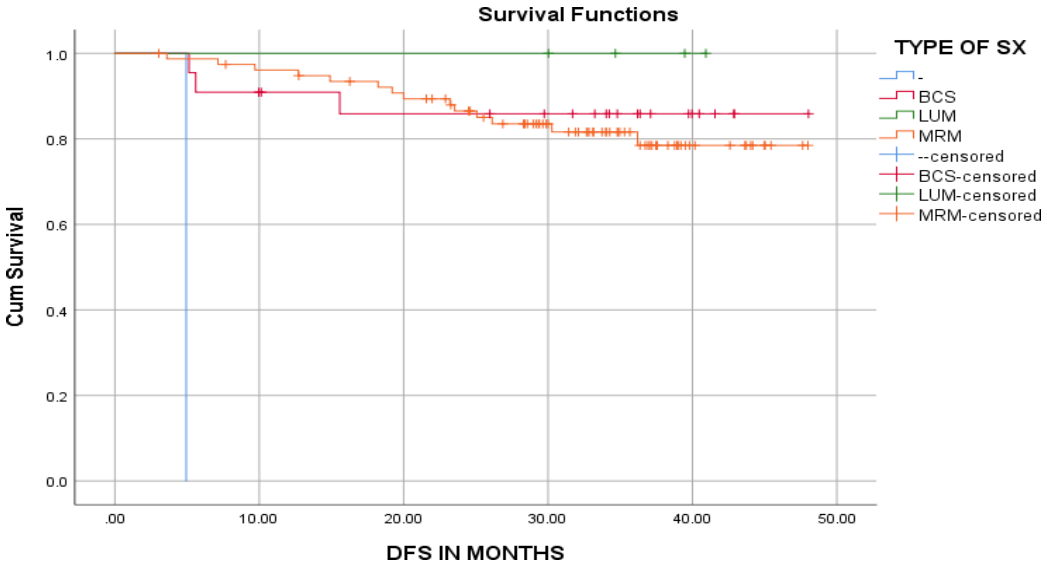


c. EFFECT OF TYPE OF SURGERY ON DFS

Overall Comparisons

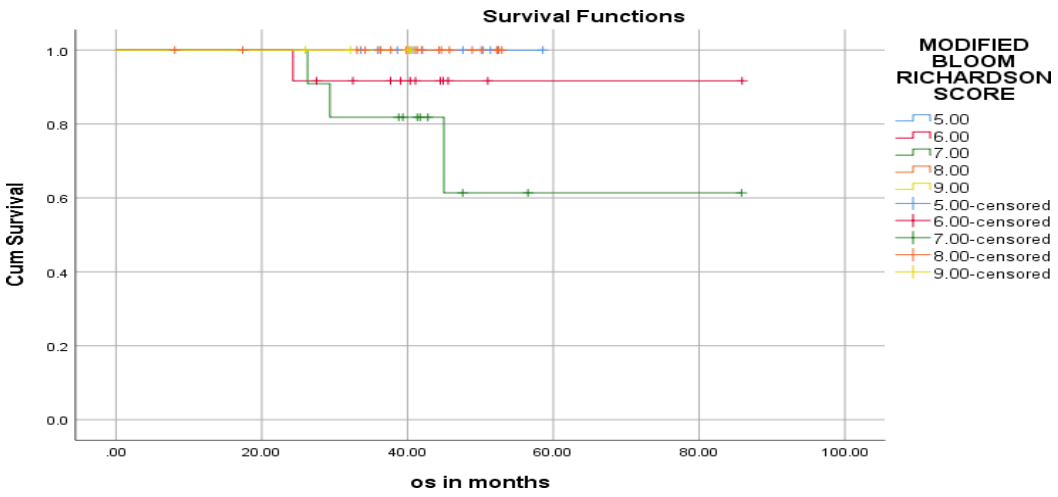
	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.035	1	.851

The vector of trend weights is -3, -1, 1, 3. This is the default.



84. EFFECT OF HISTOPATHOLOGICAL VARIABLES ON OVERALL SURVIVAL

a. EFFECT OF MODIFIED BLOOM RICHARDSON SCORE ON OS

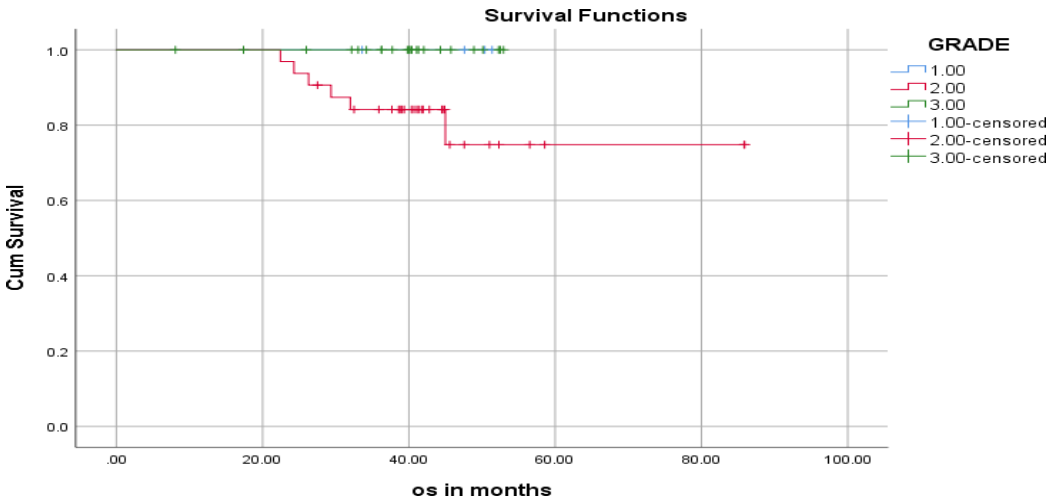


Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.010	1	.918

The vector of trend weights is -2, -1, 0, 1, 2. This is the default.

b. EFFECT OF GRADE OF TUMOUR ON OS



Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.252	1	.263

The vector of trend weights is -1, 0, 1. This is the default.

c. EFFECT OF MARGIN STATUS ON OS

Means and Medians for Survival Time

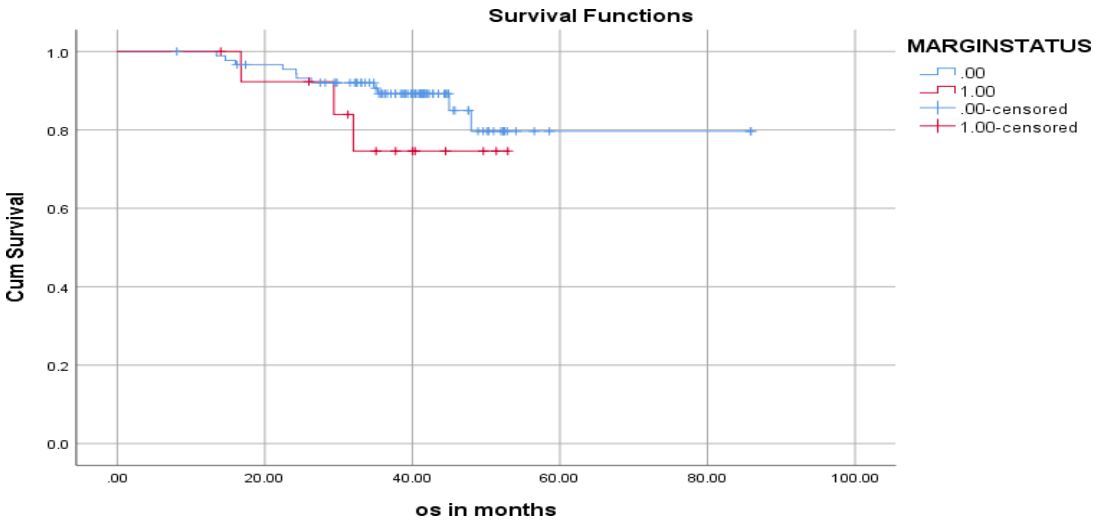
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
MARGINSTATUS	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
UNINVOLVED	75.486	3.196	69.221	81.751	.	.	.	.
INVOLVED	46.222	3.440	39.479	52.965	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

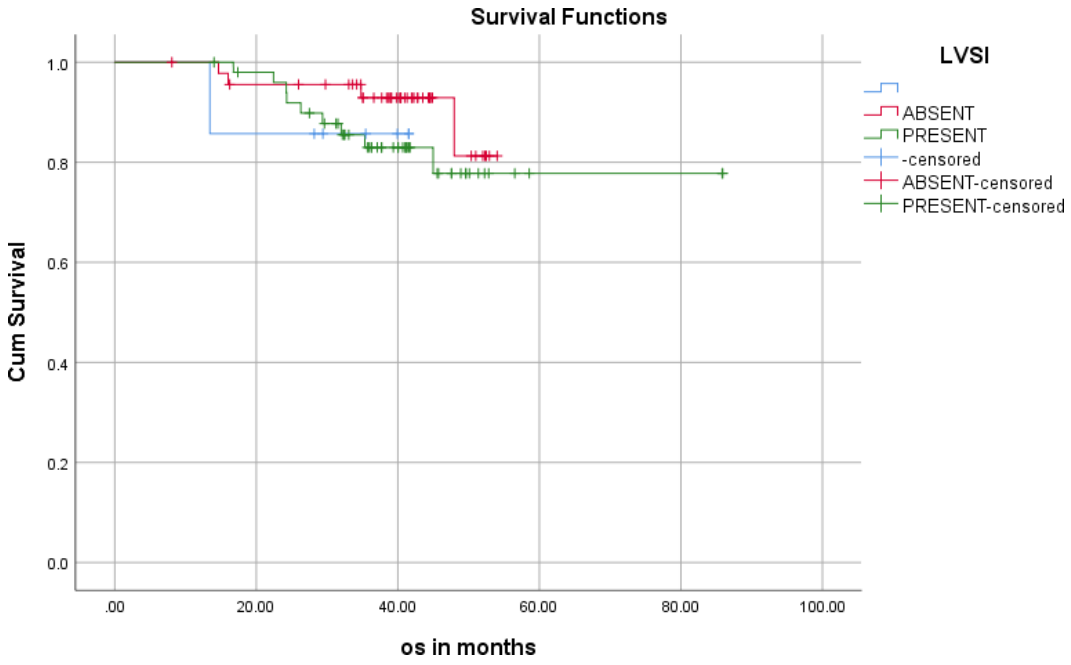
Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.028	1	.311

The vector of trend weights is -1, 1. This is the default.



d. EFFECT OF LYMPHOVASCULAR STROMAL INVASION STATUS ON OS



Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
LVSI	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
ABSENT	51.099	1.410	48.335	53.864	.	.	.	.
PRESENT	73.702	3.736	66.379	81.024	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.534	1	.465

The vector of trend weights is -1, 0, 1. This is the default.

e. <u>EFFECT OF PERINEURAL INFILTRATION STATUS ON OS</u>

Means and Medians for Survival Time

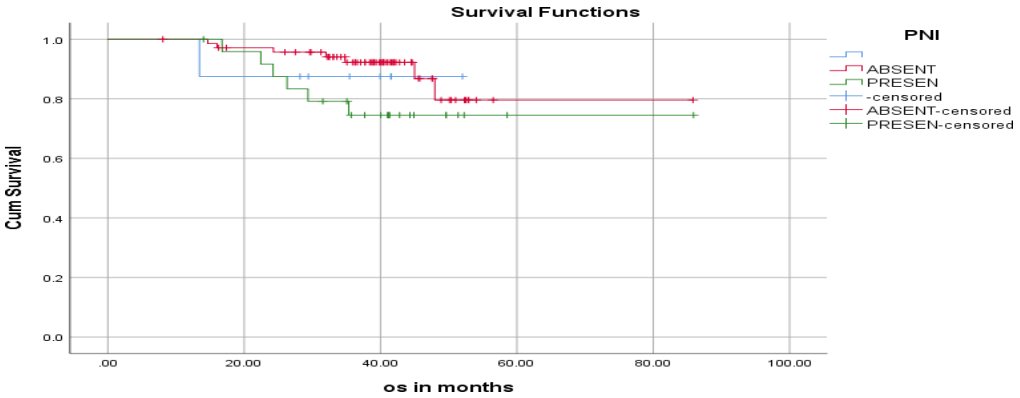
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
PNI	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
ABSENT	76.159	3.776	68.758	83.561	.	.	.	.
PRESENT	70.612	5.420	59.988	81.236	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.695	1	.193

The vector of trend weights is -1, 0, 1. This is the default.



f. **EFFECT OF EXTRANODAL EXTENSION STATUS ON OS**

Means and Medians for Survival Time

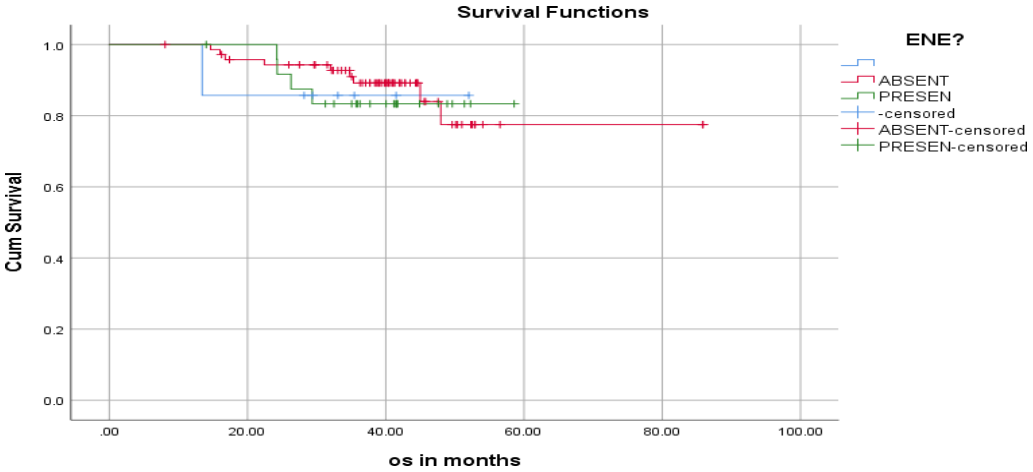
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
ENE?	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
ABSENT	74.765	3.727	67.459	82.071	.	.	.	.
PRESEN	53.147	2.480	48.287	58.008	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.037	1	.847

The vector of trend weights is -1, 0, 1. This is the default.



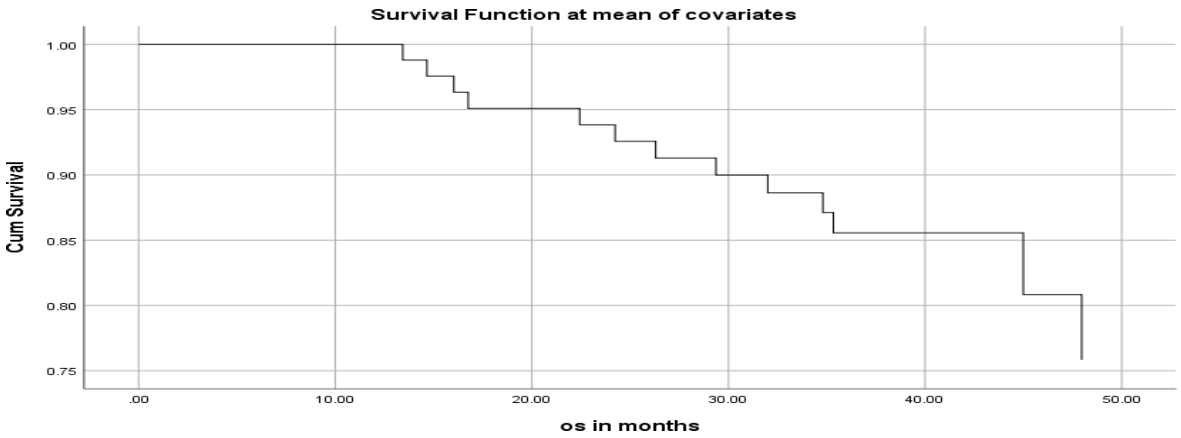
g. <u>EFFECT OF POST OPERATIVE TUMOR LONG AXIS DIAMETER ON OS BY COX REGRESSION ANALYSIS</u>

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
LAD	.112	.088	1.617	1	.204	1.119	.941	1.331

Covariate Means

	Mean
LAD	3.621



h. EFFECT OF PRESENCE OR ABSENCE OF DCIS/LCIS ON OS

Means and Medians for Survival Time

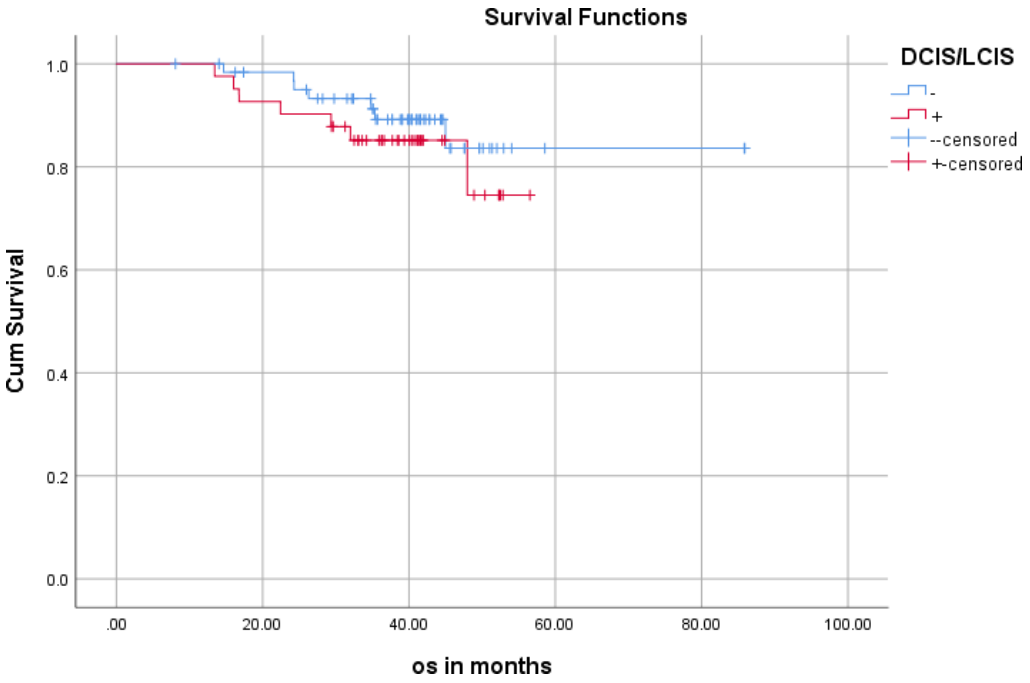
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
DCIS/LCIS	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
ABSENT	77.270	3.225	70.948	83.592	.	.	.	.
PRESENT	50.466	2.104	46.341	54.590	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.688	1	.407

T vector of trend weights is -1, 1. This is the default.



i. EFFECT OF MOLECULAR SUBTYPE OF BREAST CANCER ON OS

Means and Medians for Survival Time

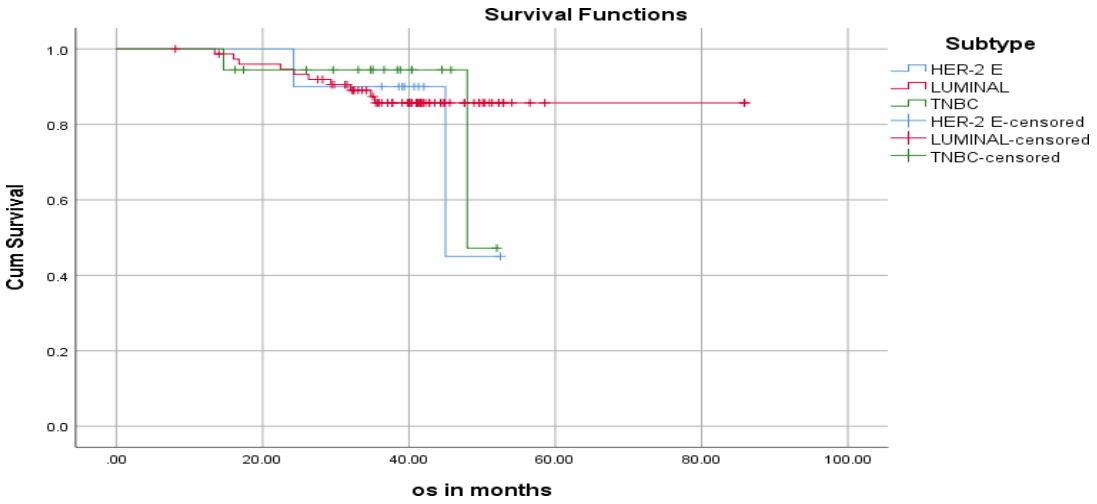
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
Subtype	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
HER-2 E	46.298	3.332	39.767	52.830	45.000	14.847	15.901	74.099
LUMINAL	77.280	2.540	72.302	82.257	.	.	.	.
TNBC	48.021	2.334	43.446	52.597	47.967	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

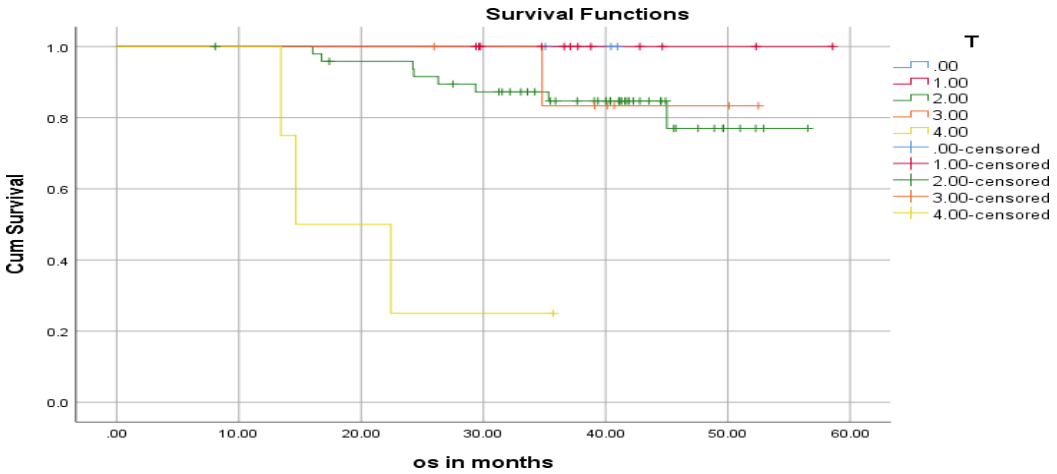
Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.161	1	.688

The vector of trend weights is -1, 0, 1. This is the default.



j. EFFECT OF POST OPERATIVE T STAGE ON OS



Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	10.882	1	.001

The vector of trend weights is -2, -1, 0, 1, 2. This is the default.

k. EFFECT OF POST OPERATIVE N STAGE ON OS

Means and Medians for Survival Time

N	Mean[a]	Median

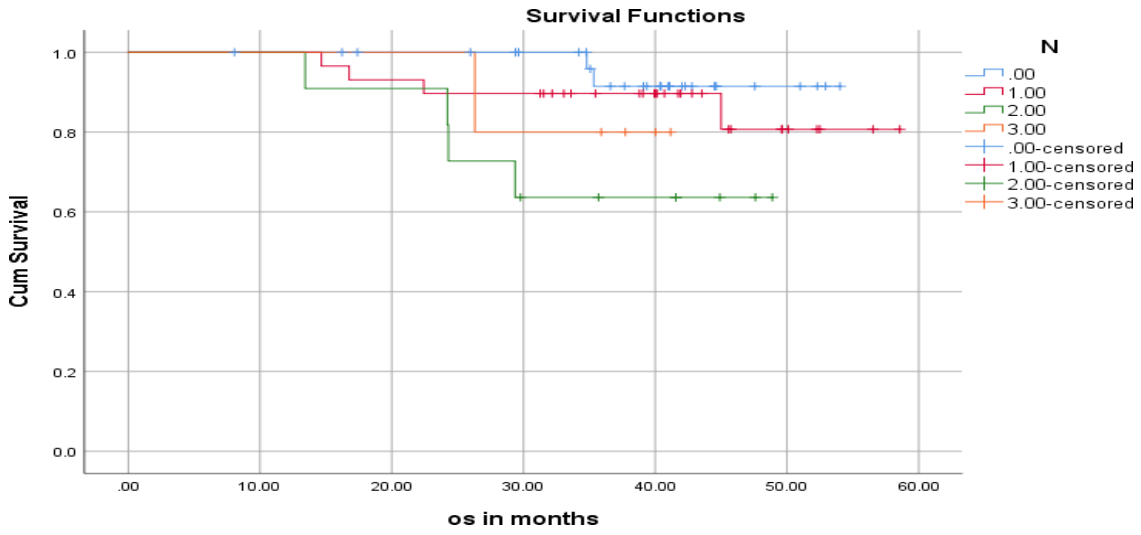
			95% Confidence Interval				95% Confidence Interval	
	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
.00	52.417	1.093	50.274	54.561	.	.	.	.
1.00	53.149	2.510	48.230	58.068	.	.	.	.
2.00	39.421	3.926	31.727	47.116	.	.	.	.
3.00	38.193	2.659	32.981	43.406	.	.	.	.
Overall	53.122	1.539	50.106	56.138	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3.802	1	.051

The vector of trend weights is -3, -1, 1, 3. This is the default.



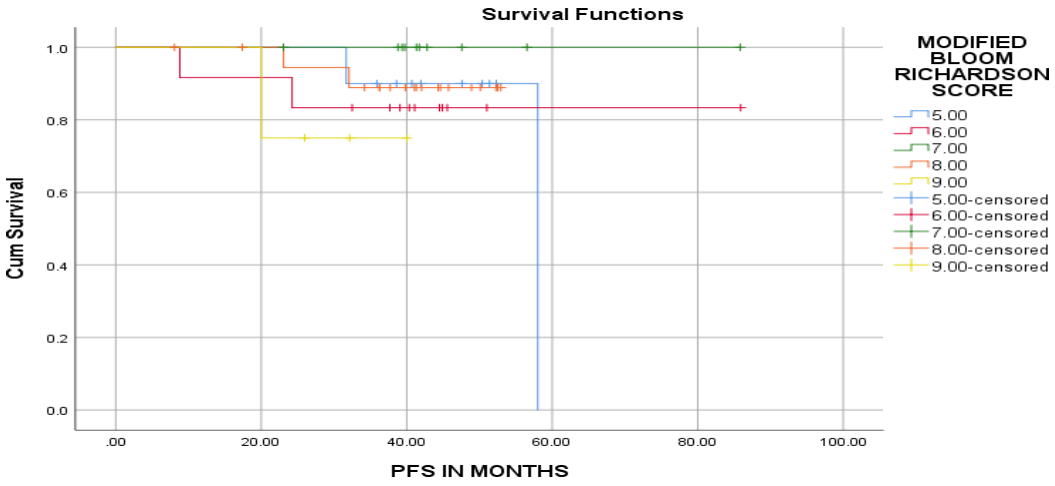
85. EFFECT OF HISTOPATHOLOGICAL VARIABLES ON PFS/RFS

a. EFFECT OF MODIFIED BLOOM RICHARDSON SCORE ON PFS/RFS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.003	1	.954

The vector of trend weights is -2, -1, 0, 1, 2. This is the default.



b. EFFECT OF GRADE OF TUMOUR ON PFS/RFS

Means and Medians for Survival Time

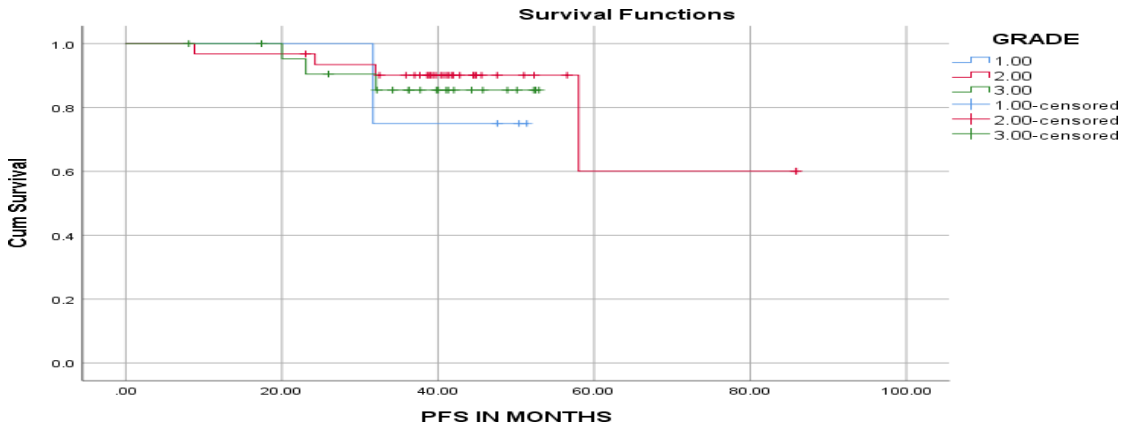
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
GRADE	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
1.00	46.442	4.265	38.082	54.801	.	.	.	.
2.00	71.177	7.477	56.523	85.831	.	.	.	.
3.00	48.896	2.190	44.602	53.189	.	.	.	.
Overall	69.984	7.033	56.199	83.769	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.005	1	.942

The vector of trend weights is -1, 0, 1. This is the default.



c. EFFECT OF MARGIN STATUS ON PFS/RFS

Means and Medians for Survival Time

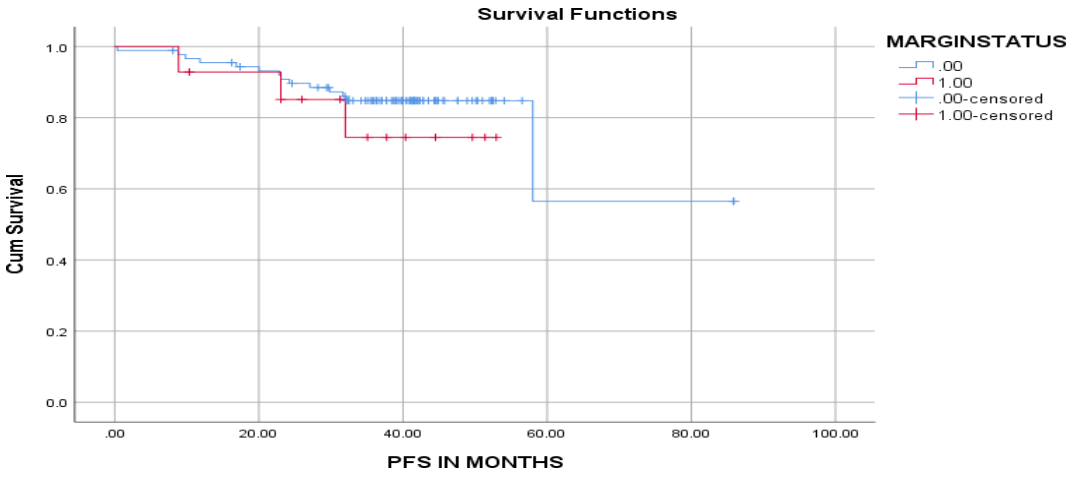
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
MARGINSTATUS	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
.00	68.006	6.810	54.658	81.354	.	.	.	.
1.00	45.245	3.962	37.479	53.010	.	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.680	1	.410

The vector of trend weights is -1, 1. This is the default.

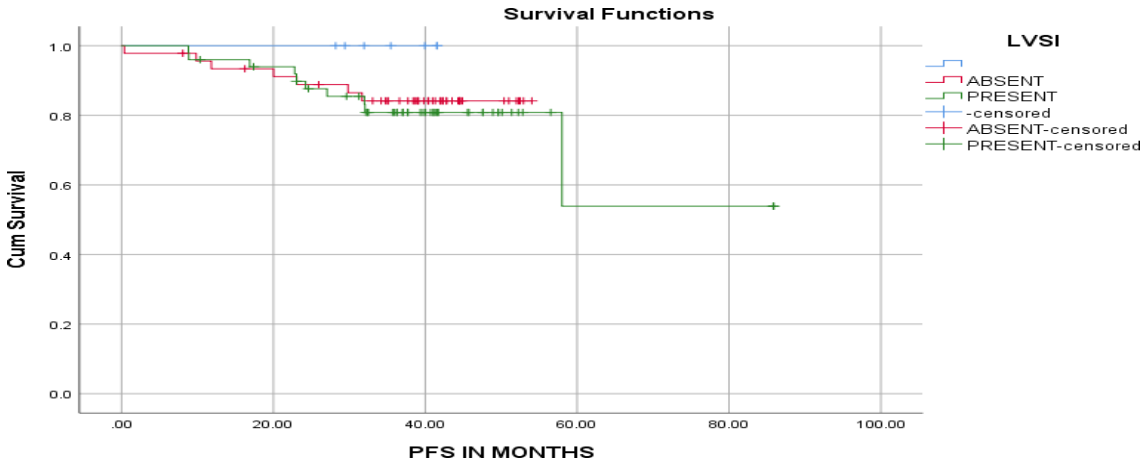


d. EFFECT OF LYMPHOVASCULAR STROMAL INVASION STATUS ON PFS/RFS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.957	1	.328

The vector of trend weights is -1, 0, 1. This is the default.

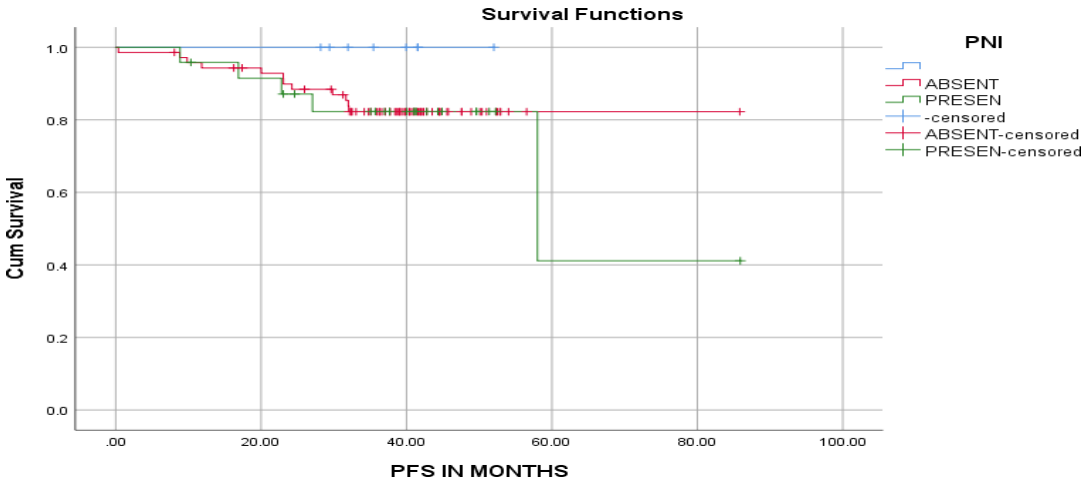


e. EFFECT OF PERINEURAL INFILTRATION STATUS ON PFS/RFS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.878	1	.349

The vector of trend weights is -1, 0, 1. This is the default.

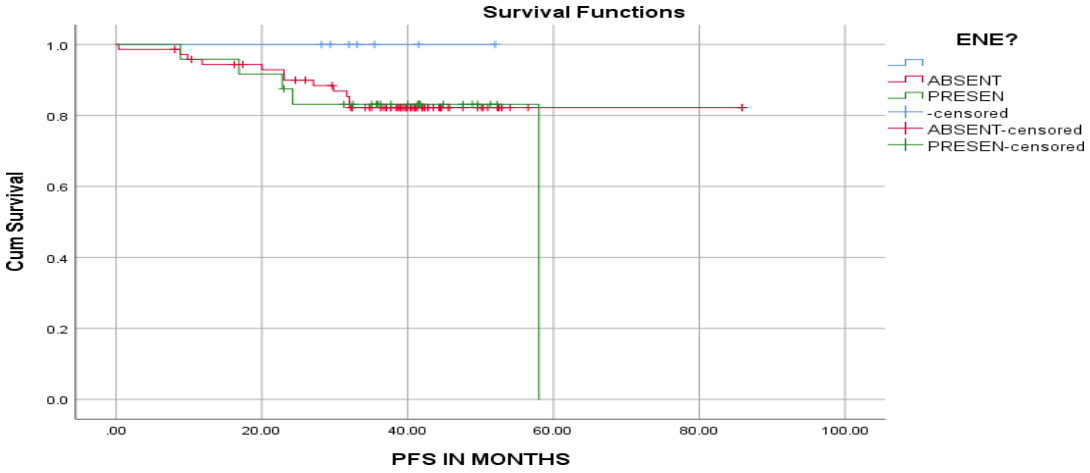


f. EFFECT OF EXTRANODAL EXTENSION STATUS ON PFS/RFS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.905	1	.341

The vector of trend weights is -1, 0, 1. This is the default.



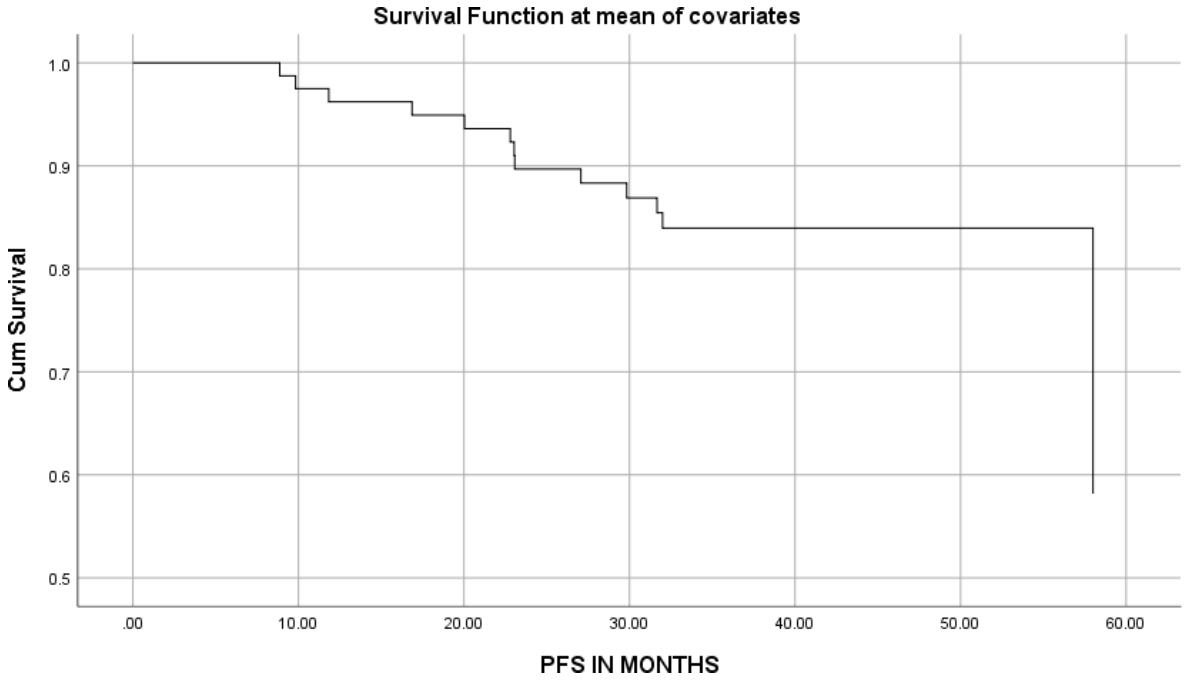
g. EFFECT OF POST OPERATIVE TUMOR LONG AXIS DIAMETER ON PFS/RFS BY COX REGRESSION ANALYSIS

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
LAD	.051	.099	.264	1	.608	1.052	.866	1.279

Covariate Means

	Mean
LAD	3.629



EFECT OF PRESENCE OR ABSENCE OF DCIS/LCIS ON PFS/RFS

Means and Medians for Survival Time

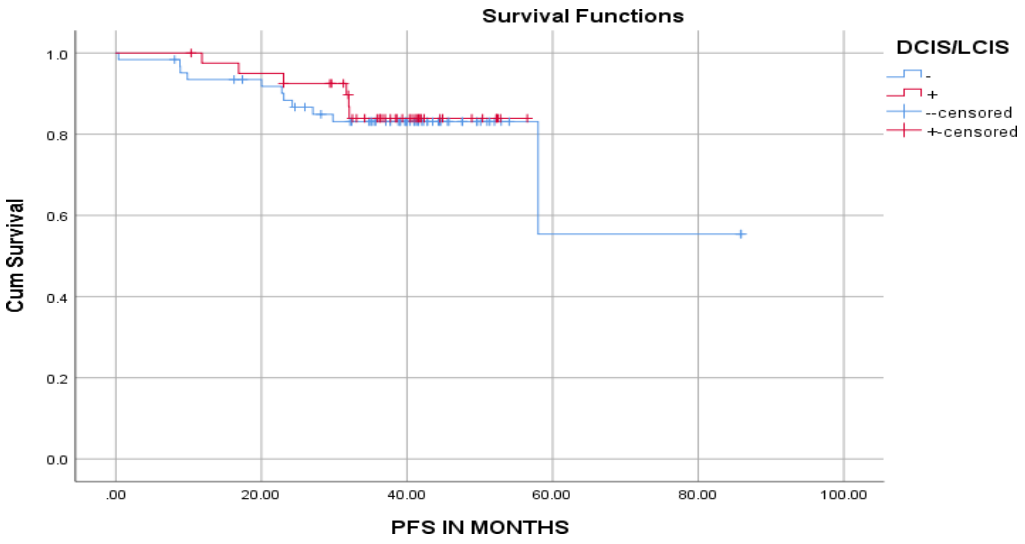
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
DCIS/LCIS	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
-	66.657	6.944	53.047	80.267	.	.	.	.
+	51.472	1.941	47.668	55.276	.	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.082	1	.775

The vector of trend weights is -1, 1. This is the default.



h. **EFFECT OF MOLECULAR SUBTYPE OF BREAST CANCER ON PFS/RFS**

Means and Medians for Survival Time

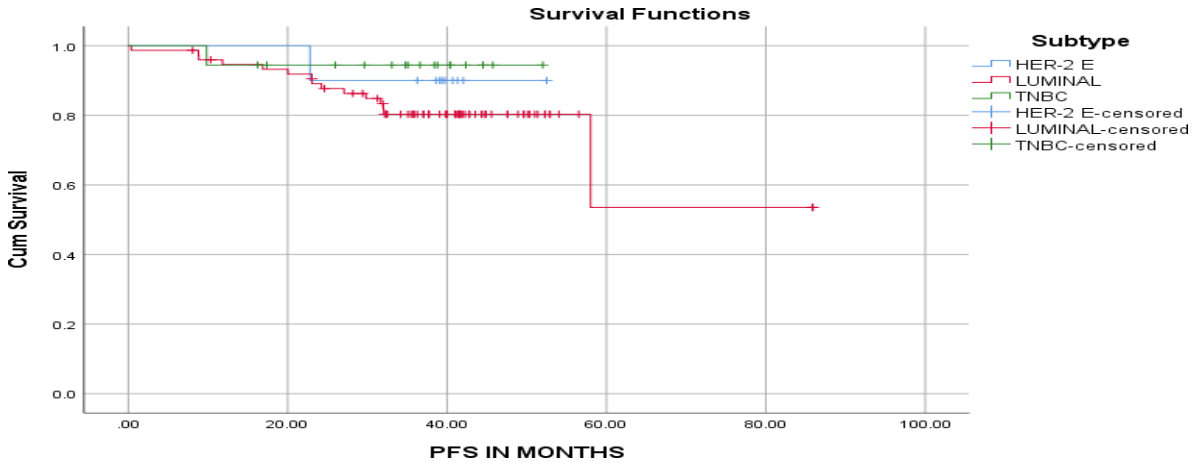
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
Subtype	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
HER-2 E	49.530	2.818	44.008	55.052	.	.	.	.
LUMINAL	65.657	6.652	52.619	78.696	.	.	.	.
TNBC	49.657	2.277	45.195	54.120	.	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.243	1	.622

The vector of trend weights is -1, 0, 1. This is the default.

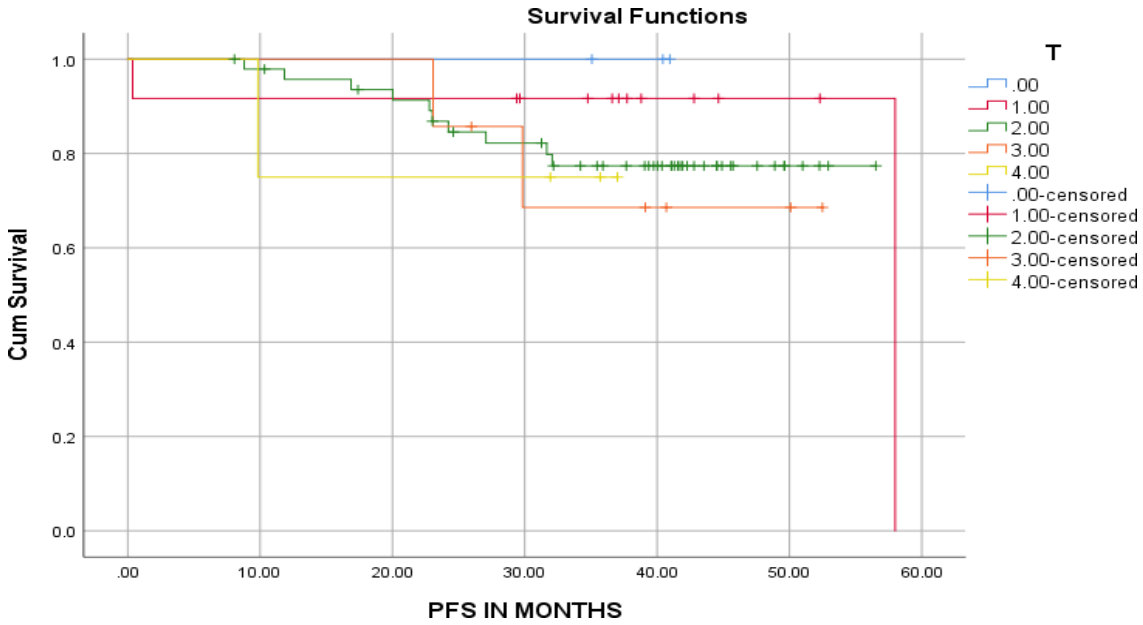


i. EFFECT OF POST OPERATIVE T STAGE ON PFS/RFS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.719	1	.190

The vector of trnd weights is -2, -1, 0, 1, 2. This is the default.



j. EFFECT OF POST OPERATIVE N STAGE ON PFS/RFS

Means and Medians for Survival Time

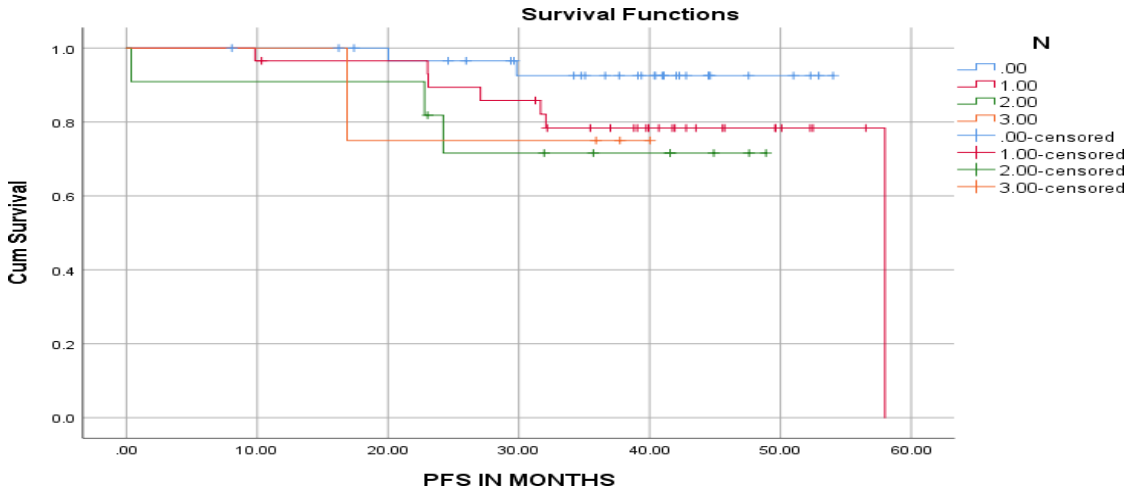
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
N	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
.00	51.887	1.469	49.008	54.767	.	.	.	.
1.00	50.783	2.891	45.116	56.450	58.000	.000	.	.
2.00	39.592	4.847	30.092	49.093	.	.	.	.
3.00	34.242	5.016	24.411	44.072	.	.	.	.
Overall	51.874	1.719	48.504	55.244	58.000	.000	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3.268	1	.071

The vector of trend weights is -3, -1, 1, 3. This is the default.



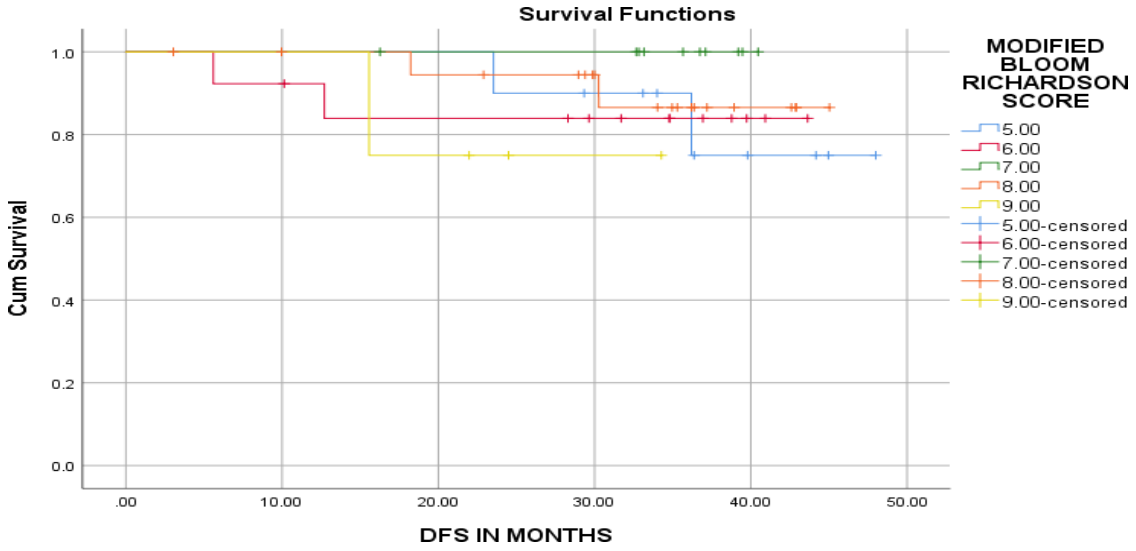
86. EFFECT OF HISTOPATHOLOGICAL VARIABLES ON DFS

a. EFFECT OF MODIFIED BLOOM RICHARDSON SCORE ON DFS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.053	1	.818

The vector of trend weights is -2, -1, 0, 1, 2. This is the default.



b. EFFECT OF GRADE OF TUMOUR ON DFS

Means and Medians for Survival Time

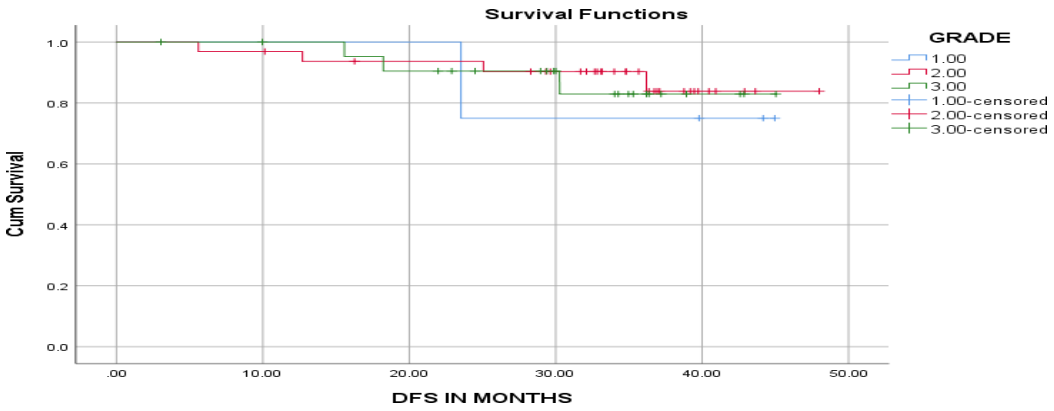
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
GRADE	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
1.00	39.608	4.640	30.513	48.704	.	.	.	.
2.00	44.007	1.922	40.240	47.774	.	.	.	.
3.00	41.241	2.028	37.265	45.216	.	.	.	.
Overall	43.777	1.412	41.009	46.545	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.012	1	.914

The vector of trend weights is -1, 0, 1. This is the default.



c. **EFFECT OF MARGIN STATUS ON DFS**

Means and Medians for Survival Time

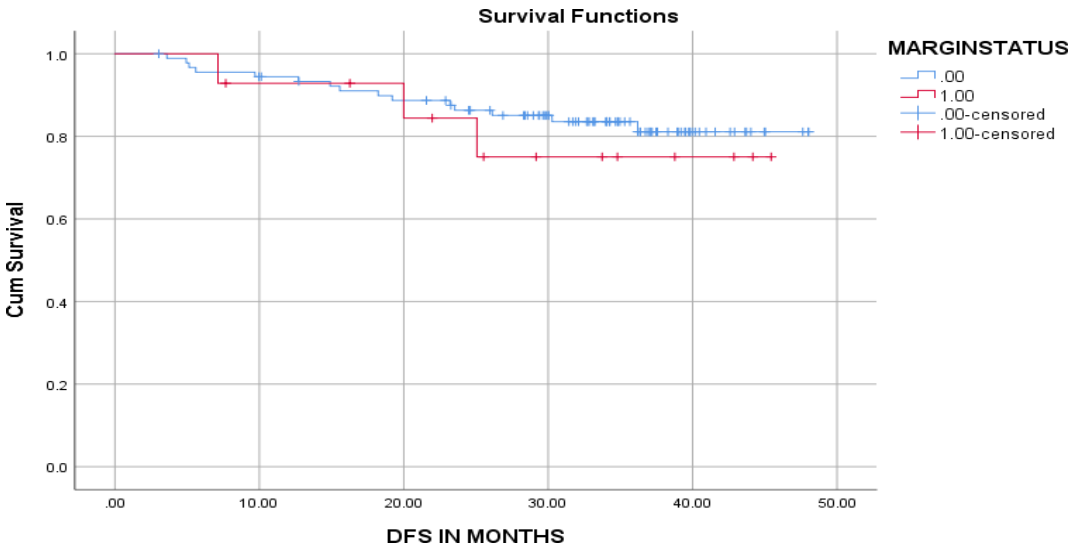
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
MARGINSTATUS	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
FREE	42.431	1.352	39.781	45.082	.	.	.	.
INVOLVED	38.640	3.489	31.801	45.480	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.341	1	.559

The vector of trend weights is -1, 1. This is the default.



d. EFFECT OF LYMPHOVASCULAR STROMAL INVASION STATUS ON DFS

Means and Medians for Survival Time

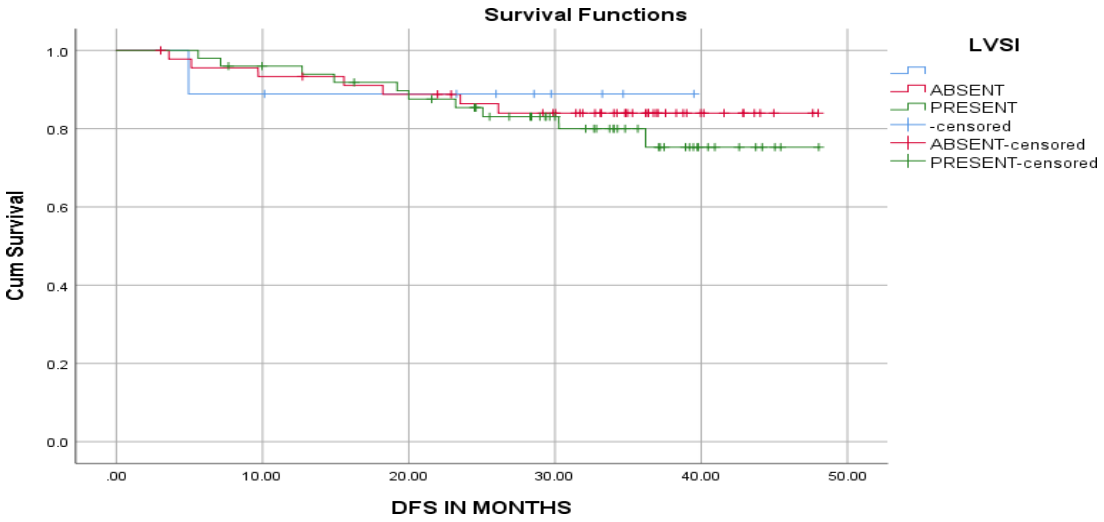
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
LVSI	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
ABSENT	42.682	1.896	38.965	46.399	.	.	.	.
PRESENT	41.547	1.855	37.911	45.182	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.443	1	.506

The vector of trend weights is -1, 0, 1. This is the default.



e. EFECT OF PERINEURAL INFILTRATION STATUS ON DFS

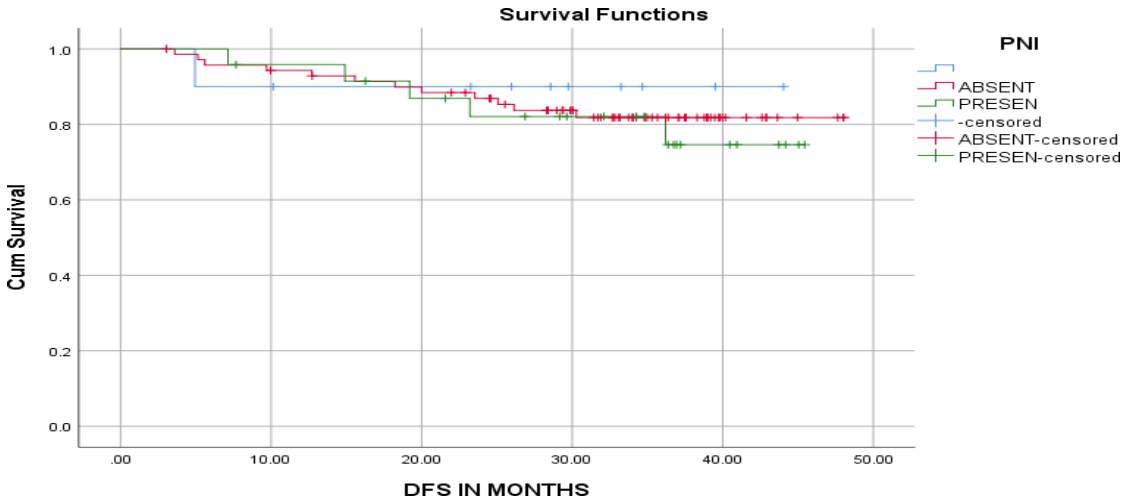
Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
PNI	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
ABSENT	42.362	1.531	39.361	45.363	.	.	.	.
PRESEN	39.545	2.420	34.802	44.288	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.375	1	.541

The vector of trend weights is -1, 0, 1. This is the default.



f. EFFECT OF EXTRANODAL EXTENSION STATUS ON DFS

Means and Medians for Survival Time

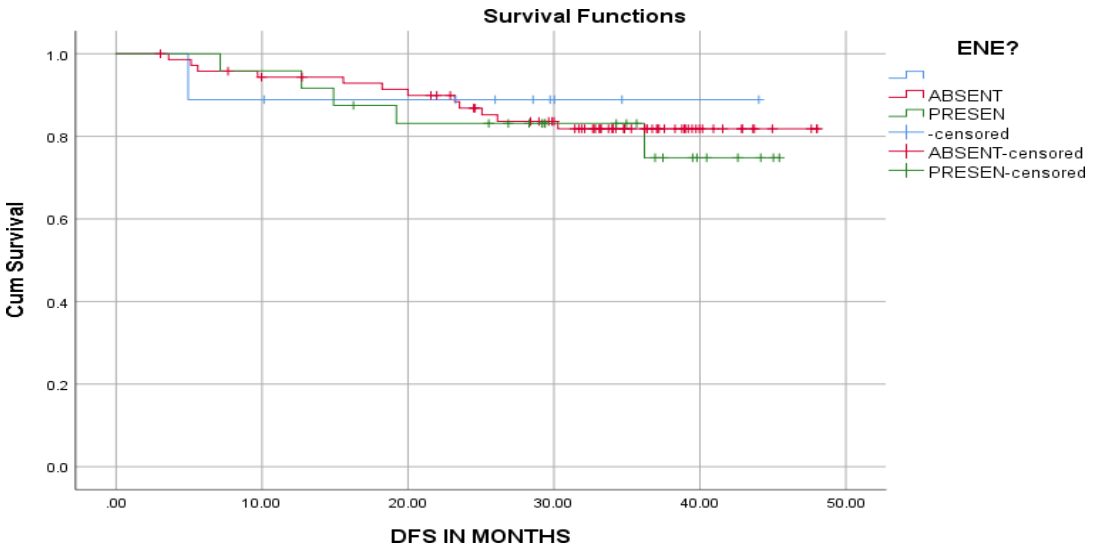
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
ENE?	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
	39.689	4.096	31.661	47.717	.	.	.	.
ABSENT	42.524	1.490	39.603	45.445	.	.	.	.
PRESEN	39.286	2.514	34.359	44.214	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.250	1	.617

The vector of trend weights is -1, 0, 1. This is the default.



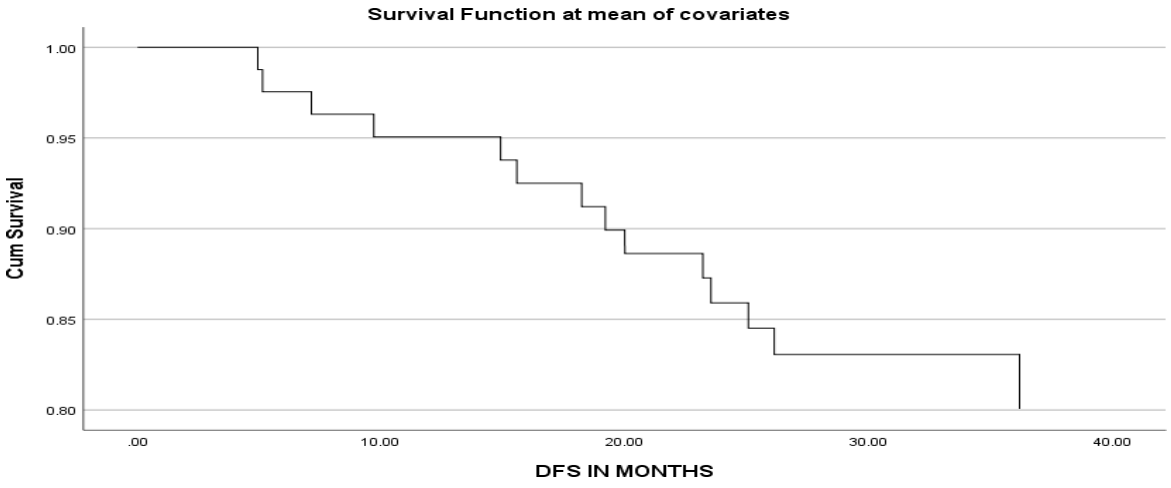
g. EFFECT OF POST OPERATIVE TUMOR LONG AXIS DIAMETER ON DFS BY COX REGRESSION ANALYSIS

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
LAD	.073	.088	.688	1	.407	1.076	.905	1.279

Covariate Means

	Mean
LAD	3.646



h. EFFECT OF PRESENCE OR ABSENCE OF DCIS/LCIS ON DFS

Means and Medians for Survival Time

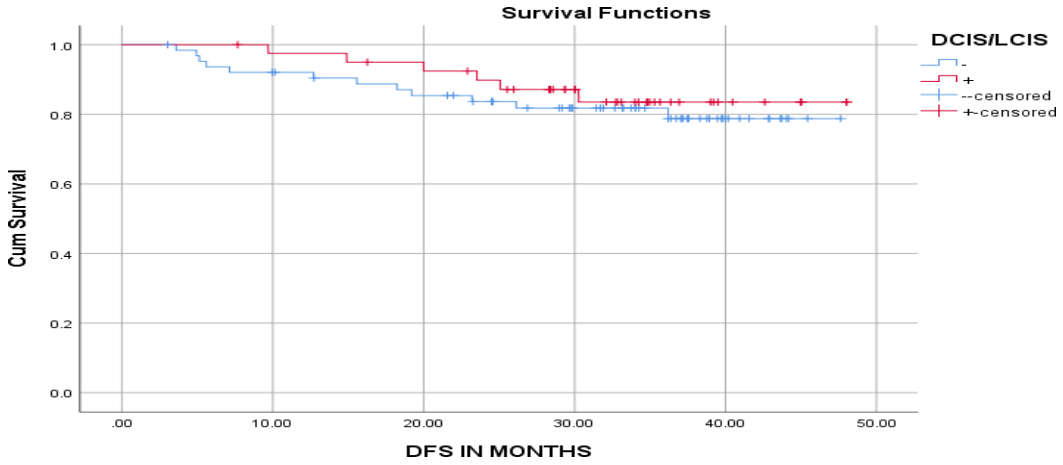
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
DCIS/LCIS	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
ABSENT	41.020	1.762	37.568	44.473	.	.	.	.
PRESENT	43.628	1.682	40.332	46.924	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.372	1	.542

The vector of trend weights is -1, 1. This is the default.



i. **EFFECT OF MOLECULAR SUBTYPE OF BREAST CANCER ON DFS**

Means and Medians for Survival Time

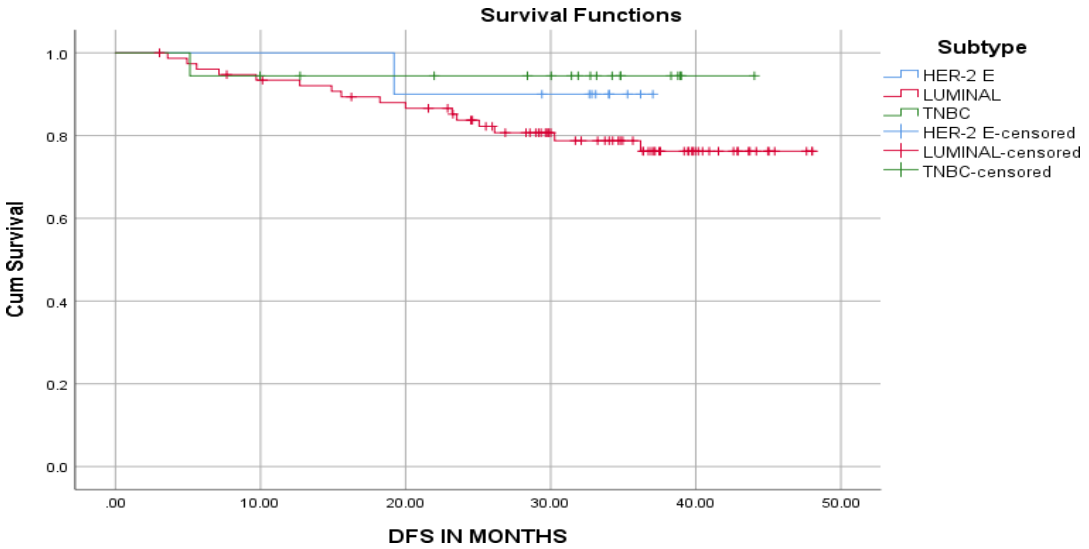
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
Subtype	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
HER-2 E	35.250	1.692	31.934	38.566	.	.	.	.
LUMINAL	41.081	1.582	37.981	44.181	.	.	.	.
TNBC	41.872	2.100	37.756	45.989	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.291	1	.590

The vector of trend weights is -1, 0, 1. This is the default.

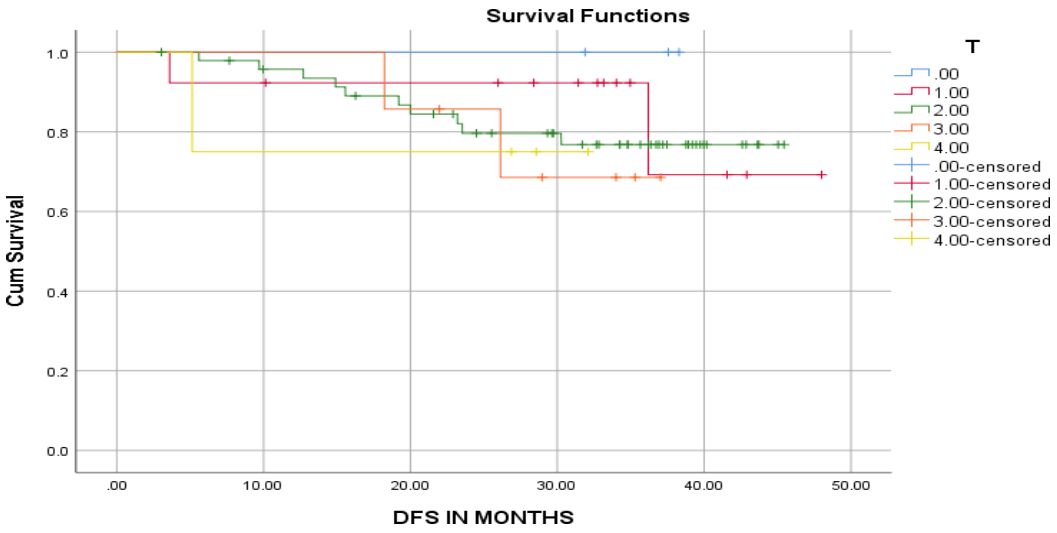


j. **EFFECT OF POST OPERATIVE T STAGE ON DFS**

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.250	1	.264

The vector of trend weights is -2, -1, 0, 1, 2. This is the default.



k. EFFECT OF POST OPERATIVE N STAGE ON DFS

Means and Medians for Survival Time

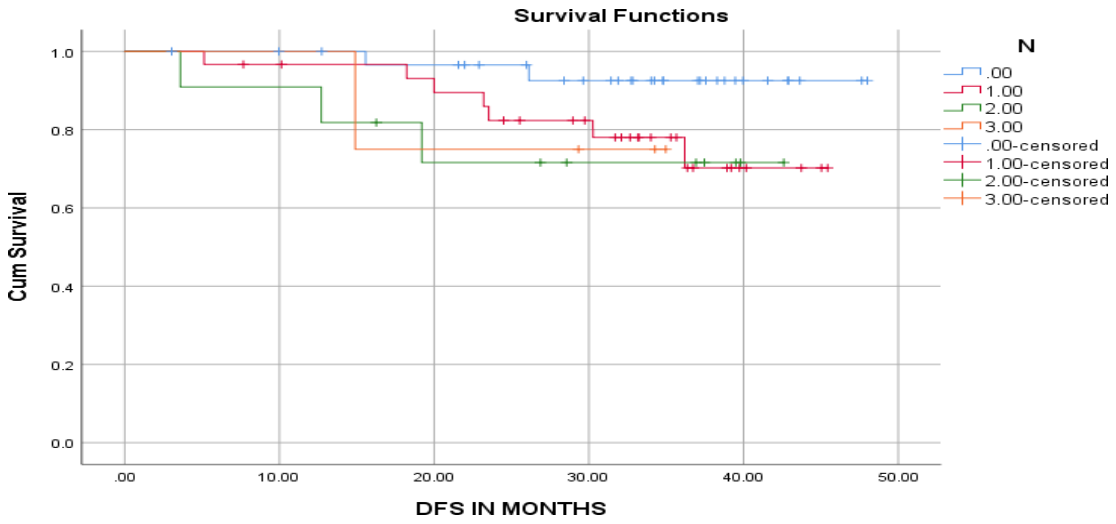
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
N	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
.00	46.002	1.372	43.313	48.691	.	.	.	.
1.00	39.248	2.099	35.134	43.362	.	.	.	.
2.00	33.943	4.335	25.446	42.440	.	.	.	.
3.00	29.950	4.345	21.435	38.465	.	.	.	.
Overall	42.494	1.412	39.726	45.261	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3.559	1	.059

The vector of trend weights is -3, -1, 1, 3. This is the default.



87. <u>EFFECT OF ADJUVANT THERAPY VARIABLES ON OVERALL SURVIVAL:</u>

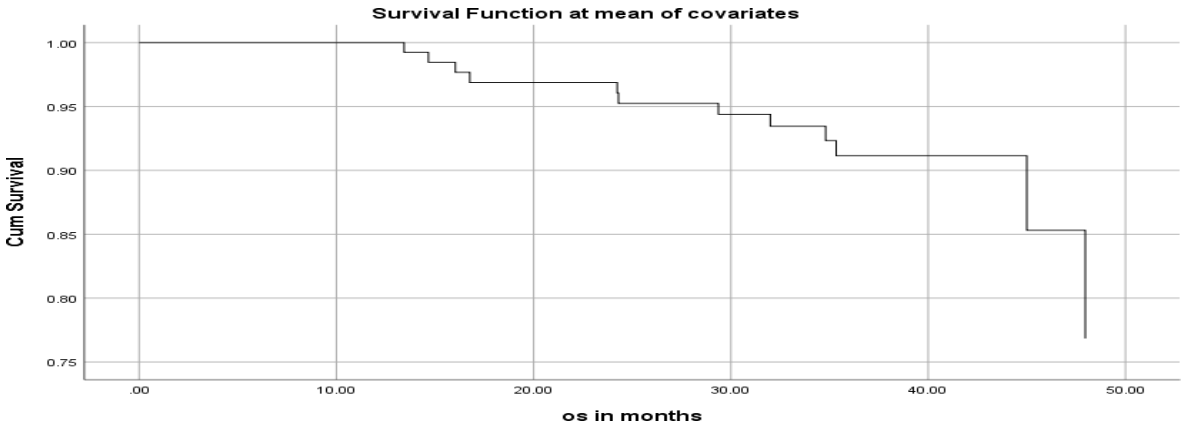
a. <u>EFFECT OF TIME FROM DATE OF SURGERY TO START OF RT AND DURATION OF RADIOTHERAPY ON OVERALL SURVIVAL BY CO X REGRESSION ANALYSIS.</u>

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
DURATION OF RT WITHOUT BOOST	-.029	.061	.218	1	.641	.972	.862	1.096
DURATION FROM SURGERY TO START OF RT	-.006	.004	2.229	1	.135	.994	.987	1.002
TIME TO POST RADIOTHERAPY FOLLOW UP	.000	.001	.079	1	.779	1.000	.998	1.002

Covariate Means

	Mean
DURATION OF RT WITHOUT BOOST	25.421
DURATION FROM SURGERY TO START OF RT	201.642
TIME TO POST RADIOTHERAPY FOLLOW UP	390.568

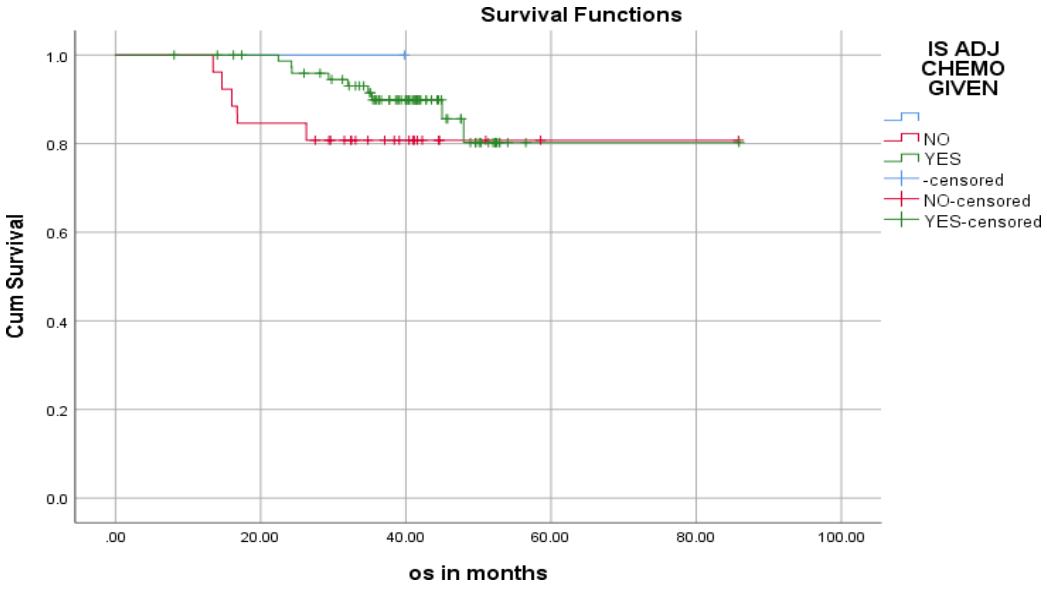


b. EFFECT OF ADJUVANT CHEMOTHERAPY RECEIPT ON OS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.125	1	.289

The vector of trend weights is -1, 0, 1. This is the default.

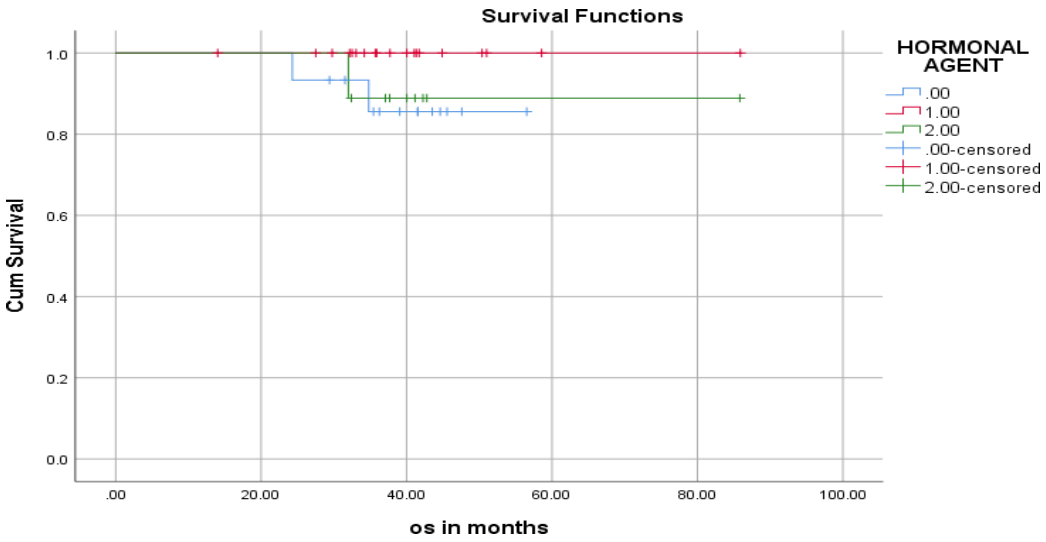


c. EFFECT OF HORMONAL THERAPY AGENT ON OS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.222	1	.637

The vector of trend weights is -1, 0, 1. This is the default.



d. EFFECT OF RADIOTHERAPY TECHNIQUE ON OS

Means and Medians for Survival Time

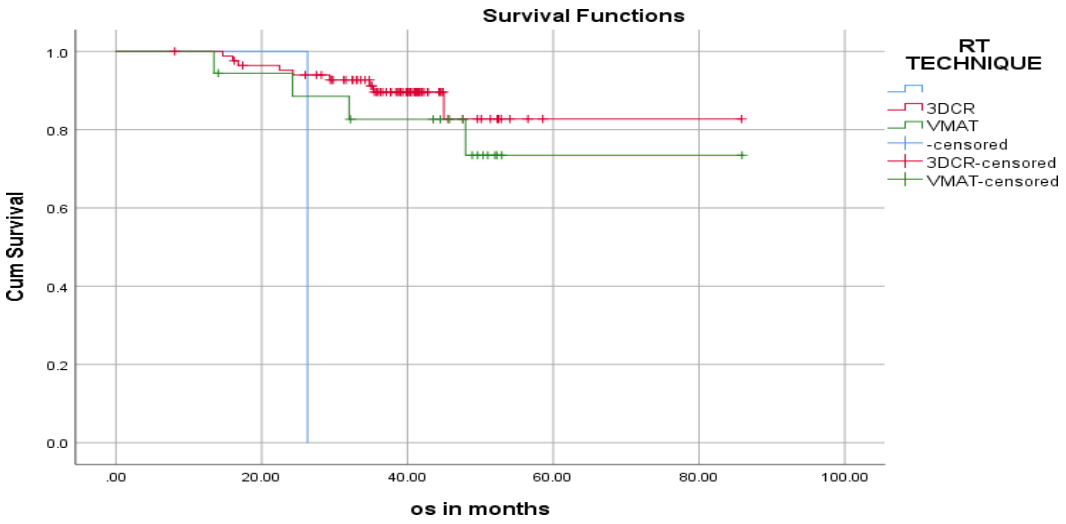
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
RT TECHNIQUE	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
	26.300	.000	26.300	26.300	26.300	.	.	.
3DCR	76.697	3.373	70.085	83.309	.	.	.	.
VMAT	71.569	6.279	59.262	83.877	.	.	.	.
Overall	75.063	2.902	69.375	80.752	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.007	1	.933

The vector of trend weights is -1, 0, 1. This is the default.

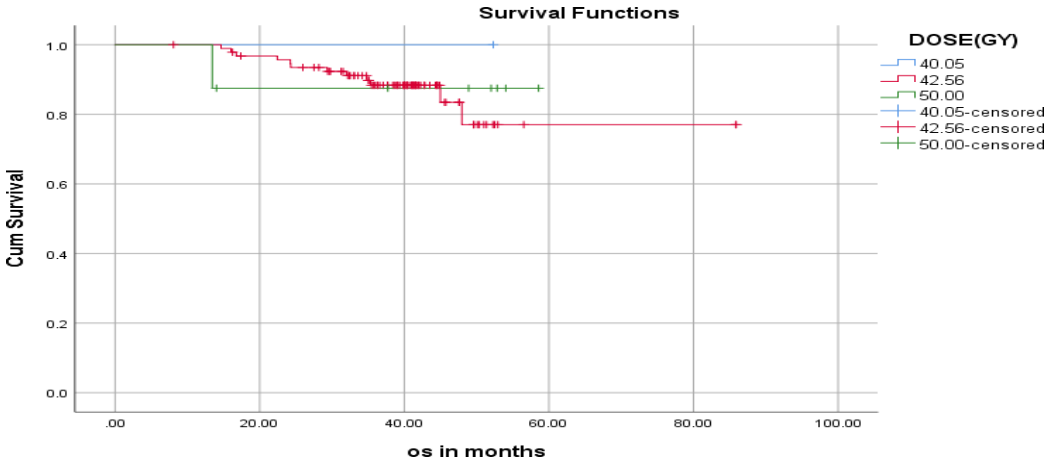


e. **EFFECT OF RADIOTHERAPY DOSE REGIMENS ON OS**

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.000	1	.992

The vector of trend weights is -1, 0, 1. This is the default.



88. EFFECT OF ADJUVANT THERAPY VARIABLES ON PROGRESSION FREE SURVIVAL/RECURRENCE FREE SURVIVAL:

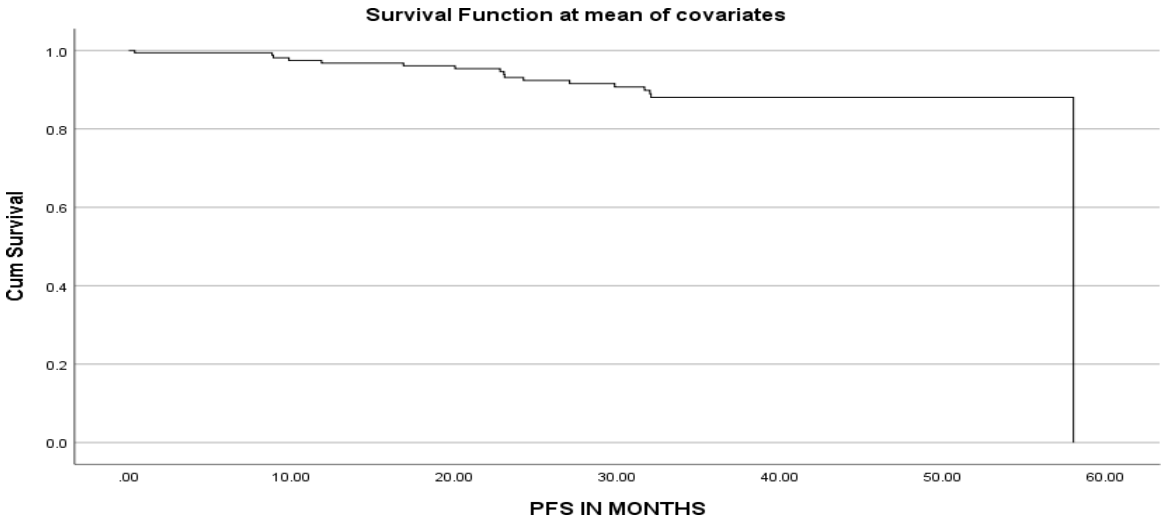
a. EFFECT OF TIME FROM CT SIMULATION TO START OF RADIOTHERAPY, FROM DATE OF SURGERY TO START OF RT AND DURATION OF RADIOTHERAPY ON PFS/RFS BY COX REGRESSION ANALYSIS.

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
DURATION OF RT WITHOUT BOOST	.009	.037	.060	1	.807	1.009	.939	1.084
DURATION FROM SURGERY TO START OF RT	-.008	.003	4.768	1	.029	.992	.986	.999

Covariate Means

	Mean
DURATION OF RT WITHOUT BOOST	25.354
DURATION FROM SURGERY TO START OF RT	201.115

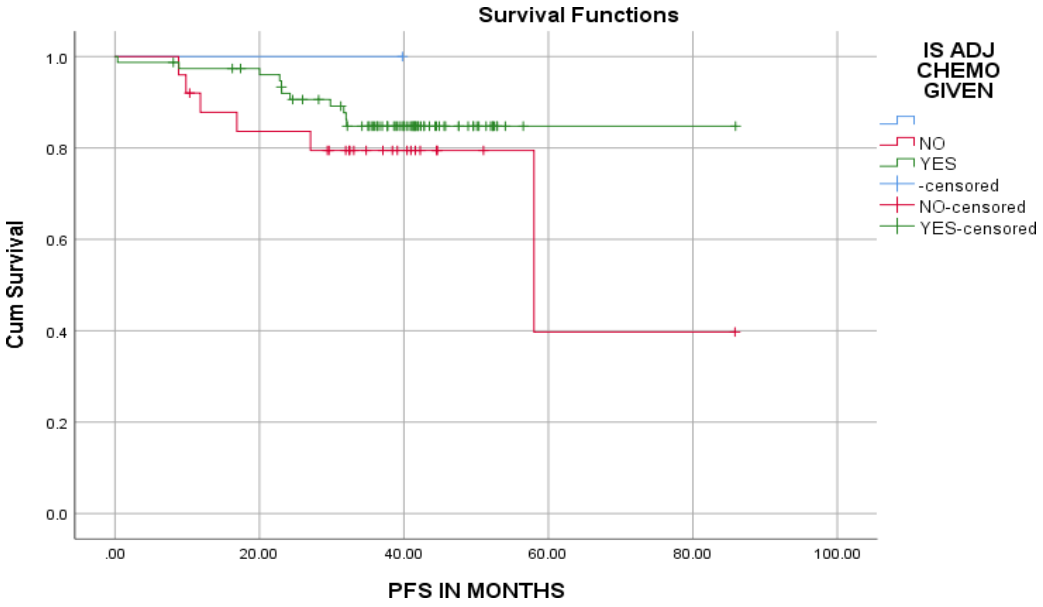


b. EFFECT OF ADJUVANT CHEMOTHERAPY RECEIPT ON PFS/RFS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.530	1	.467

The vector of trend weights is -1, 0, 1. This is the default.



c. EFFECT OF HORMONAL THERAPY AGENT ON PFS/RFS

Means and Medians for Survival Time

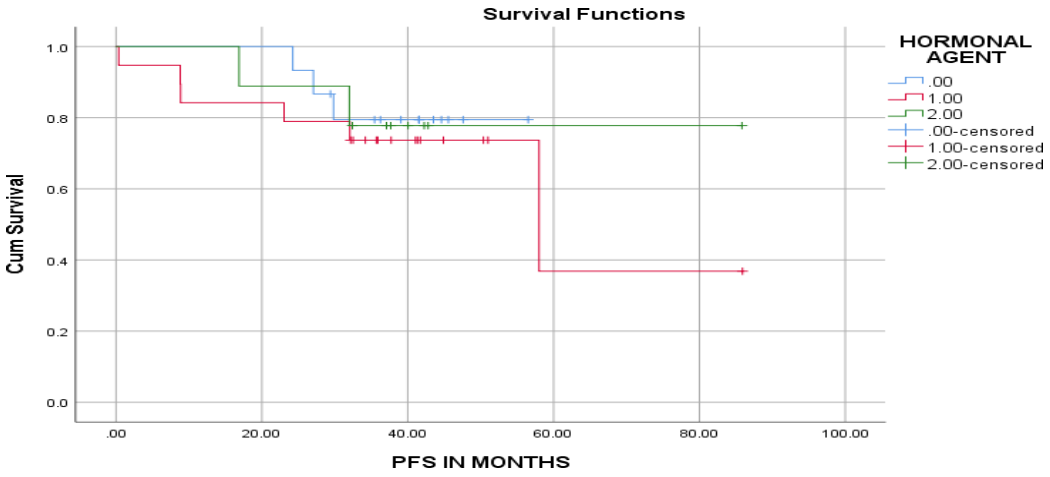
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
HORMONAL AGENT	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
.00	50.487	3.123	44.366	56.608	.	.	.	.
1.00	56.865	9.389	38.463	75.267	58.000	18.679	21.389	94.611
2.00	72.189	8.591	55.350	89.028	.	.	.	.
Overall	63.420	6.904	49.888	76.951	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.002	1	.969

The vector of trend weights is -1, 0, 1. This is the default.



d. EFFECT OF RADIOTHERAPY TECHNIQUE ON PFS/RFS

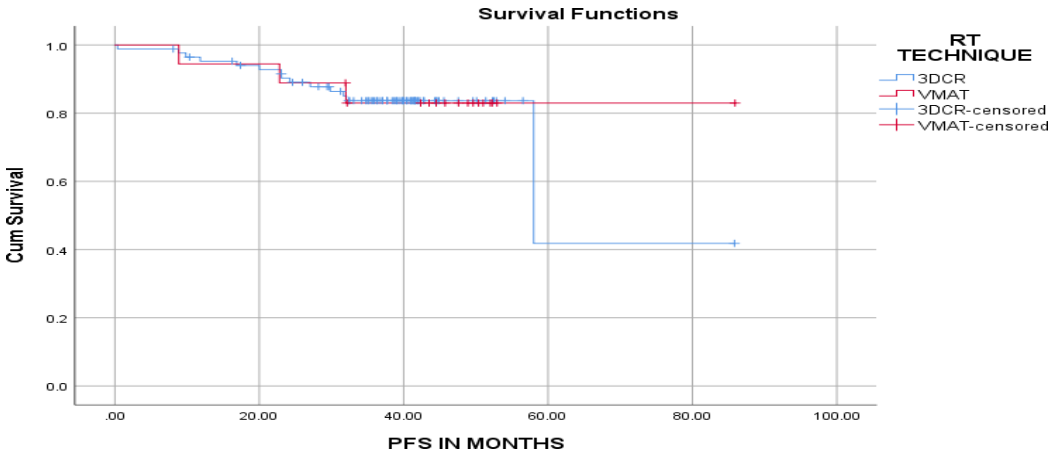
Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
RT TECHNIQUE	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
3DCR	63.485	8.513	46.801	80.170	58.000	18.383	21.969	94.031
VMAT	74.921	5.837	63.481	86.361	.	.	.	.
Overall	67.381	6.693	54.262	80.500	.	.	.	.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.027	1	.870

The vector of trend weights is -1, 1. This is the default.

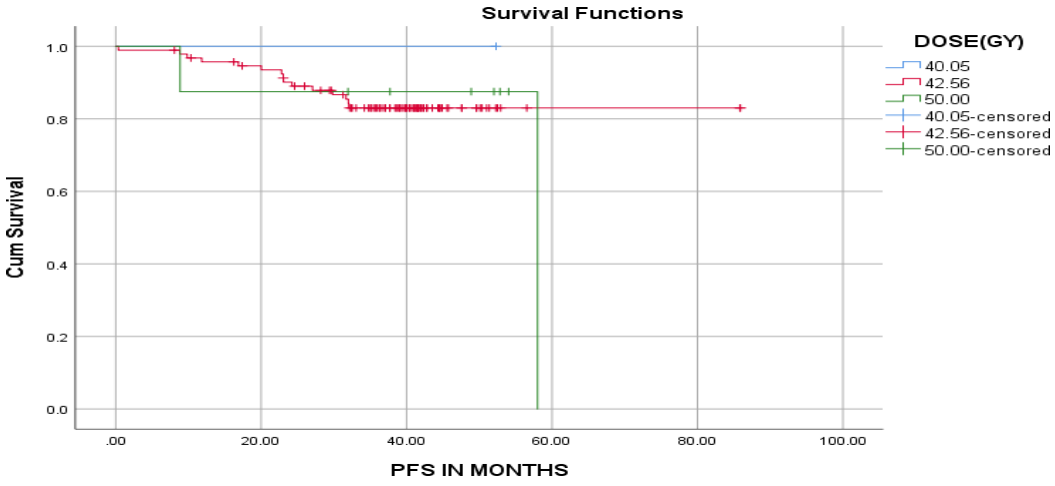


e. **EFFECT OF RADIOTHERAPY DOSE REGIMENS ON PFS/RFS**

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.221	1	.638

The vector of trend weights is -1, 0, 1. This is the default.



89. EFFECT OF ADJUVANT THERAPY VARIABLES ON DISEASE FREE SURVIVAL:

a. EFFECT OF TIME FROM FROM DATE OF SURGERY TO START OF RT AND DURATION OF RADIOTHERAPY ON DFS BY COX REGRESSION ANALYSIS.

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B) Lower	Upper
DURATION OF RT WITHOUT BOOST	.016	.031	.291	1	.590	1.017	.958	1.079
DURATION FROM SURGERY TO START OF RT	-.003	.002	1.265	1	.261	.997	.993	1.002

Covariate Means

	Mean
DURATION OF RT WITHOUT BOOST	25.421
DURATION FROM SURGERY TO START OF RT	201.642

b. EFFECT OF ADJUVANT CHEMOTHERAPY RECEIPT ON DFS

Means and Medians for Survival Time

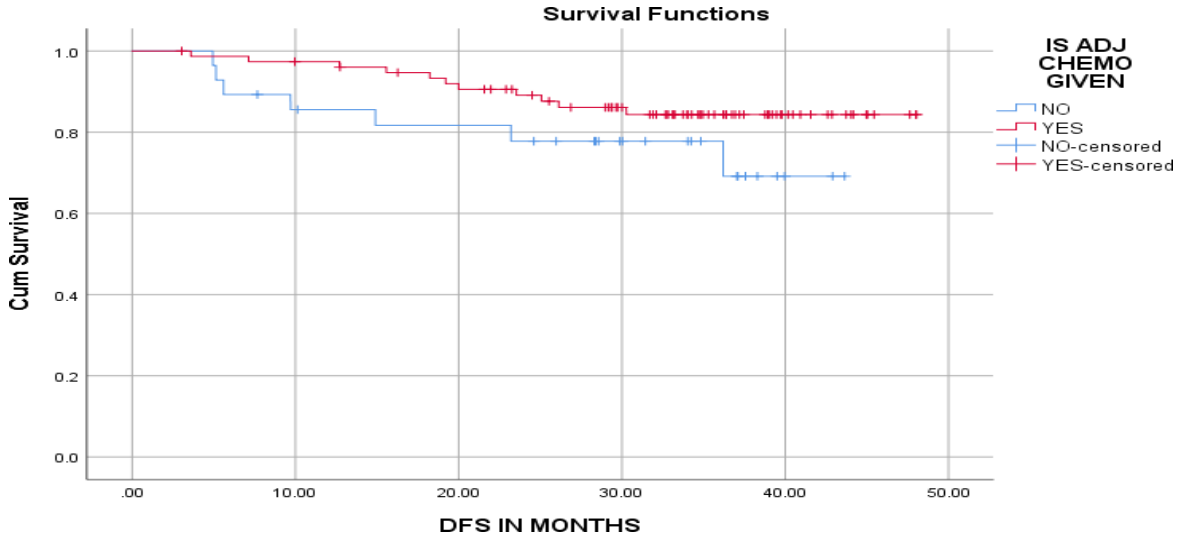
IS ADJ CHEMO GIVEN	Mean[a] Estimate	Mean[a] Std. Error	Mean[a] 95% Confidence Interval Lower Bound	Mean[a] 95% Confidence Interval Upper Bound	Median Estimate	Median Std. Error	Median 95% Confidence Interval Lower Bound	Median 95% Confidence Interval Upper Bound
NO	35.701	2.688	30.433	40.968	.	.	.	.
YES	43.469	1.299	40.923	46.015	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	2.073	1	.150

The vector of trend weights is -1, 1. This is the default.



c. EFFECT OF HORMONAL THERAPY AGENT ON DFS

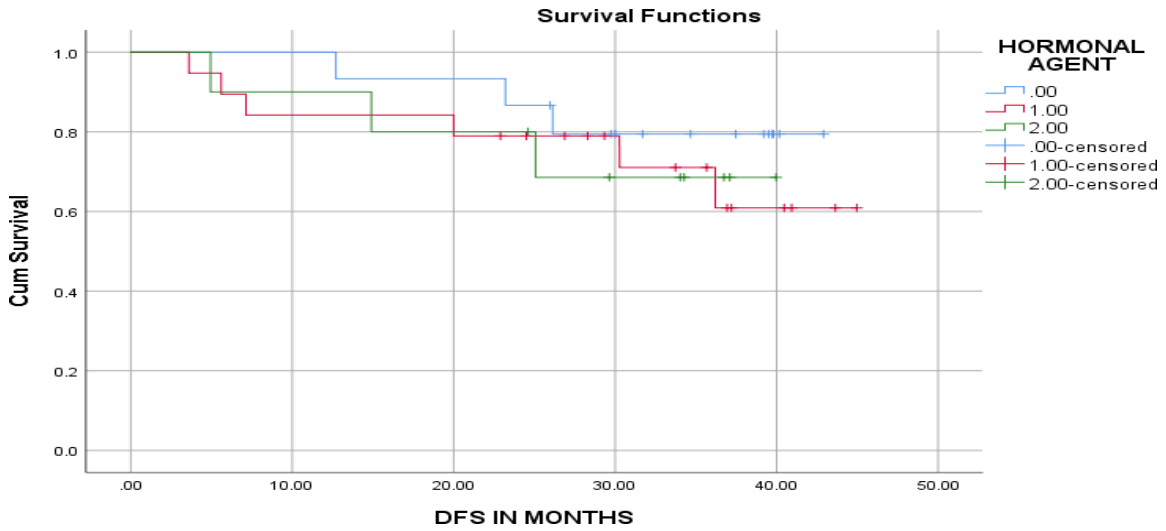
Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
HORMONAL AGENT	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
.00	38.362	2.421	33.617	43.108	.	.	.	.
1.00	35.362	3.441	28.617	42.107	.	.	.	.
2.00	32.254	3.931	24.548	39.959	.	.	.	.
Overall	37.046	2.057	33.014	41.077	.	.	.	.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.536	1	.464

The vector of trend weights is -1, 0, 1. This is the default.



d. EFFECT OF RADIOTHERAPY TECHNIQUE ON DFS

Means and Medians for Survival Time

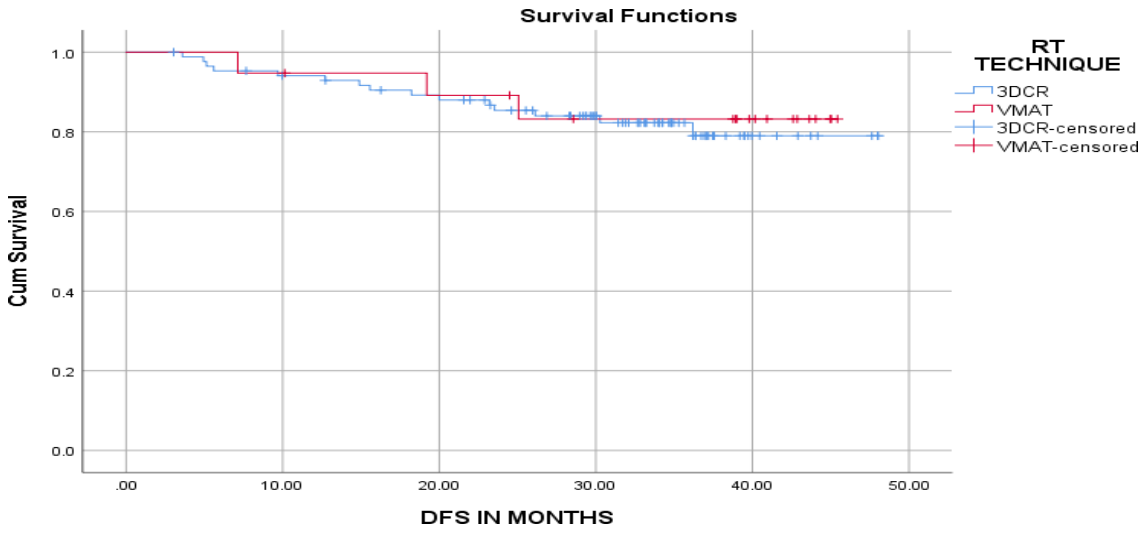
	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
RT TECHNIQUE	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
3DCR	41.960	1.448	39.122	44.797	.	.	.	.
VMAT	40.745	2.546	35.756	45.734	.	.	.	.
Overall	42.206	1.276	39.705	44.706	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.102	1	.750

The vector of trend weights is -1, 1. This is the default.

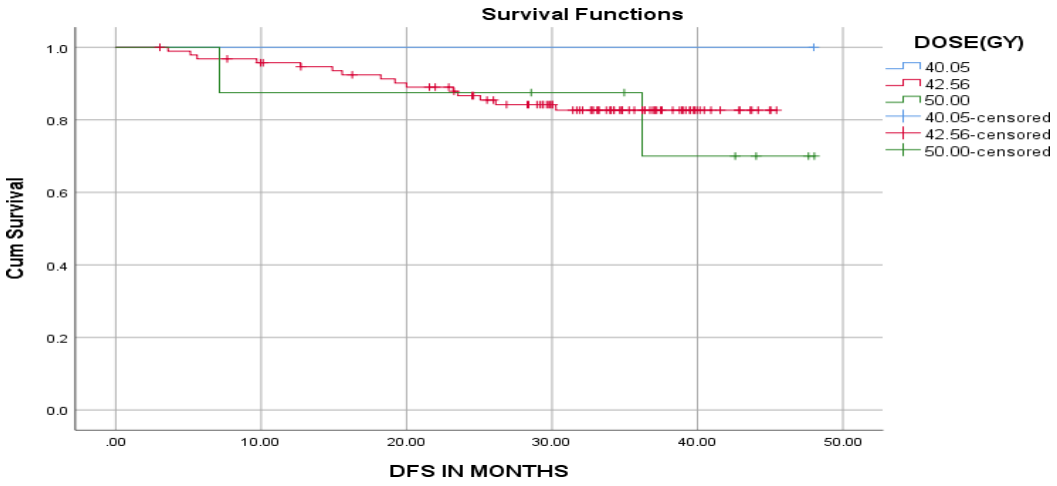


e. EFFECT OF RADIOTHERAPY DOSE REGIMENS ON DFS

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.396	1	.529

The vector of trend weights is -1, 0, 1. This is the default.



90. CORRELATION BETWEEN RADIATION DOSES TO HEART,LEFT CORONARY ARTERY, LEFT CIRCUMFLEX ARTERY , LEFT ANTERIOR DESCENDING ARTERY WITH MARKERS OF SUBCLINICAL CARDIOTOXICITY-MPI, LVEF, TWPTE, NT-PROBNP

Correlations

			LAD MEAN DOSE(cGY)	NTPROBNP	EJECTION FRACTION	MPI	TWPTE(ms)	HEART Mean dose	LCA MEAN DOSE(cGY)	LCX MEAN DOSE(cGY)	LADV25	LADV45
Spearman's rho	LAD MEAN DOSE(cGY)	Correlation Coefficient	1.000	.203	-.166	-.125	.233	.785**	.858**	.839**	.902**	.274
		Sig. (2-tailed)	.	.292	.373	.494	.243	.000	.000	.000	.000	.123
		N	33	29	31	32	27	33	33	33	33	33
	NTPROBNP	Correlation Coefficient	.203	1.000	-.132	-.028	.300	.267	.035	.026	.327	.264
		Sig. (2-tailed)	.292	.	.502	.884	.137	.162	.857	.894	.084	.167
		N	29	30	28	29	26	29	29	29	29	29
	EJECTION FRACTION	Correlation Coefficient	-.166	-.132	1.000	-.307	-.330	-.062	-.212	-.121	-.200	.045

		Sig. (2-tailed)	.373	.502	.	.088	.093	.742	.253	.516	.281	.811
		N	31	28	32	32	27	31	31	31	31	31
	MPI	Correlation Coefficient	-.125	-.028	-.307	1.000	.174	-.243	-.120	-.145	-.132	-.260
		Sig. (2-tailed)	.494	.884	.088	.	.375	.180	.514	.428	.473	.151
		N	32	29	32	33	28	32	32	32	32	32
	TWPTE(ms)	Correlation Coefficient	.233	.300	-.330	.174	1.000	.201	.289	.264	.230	.180
		Sig. (2-tailed)	.243	.137	.093	.375	.	.316	.144	.184	.248	.368
		N	27	26	27	28	28	27	27	27	27	27
	HEART Mean dose	Correlation Coefficient	.785**	.267	-.062	-.243	.201	1.000	.789**	.785**	.730**	.294
		Sig. (2-tailed)	.000	.162	.742	.180	.316	.	.000	.000	.000	.097
		N	33	29	31	32	27	33	33	33	33	33
	LCA MEAN DOSE(cGY)	Correlation Coefficient	.858**	.035	-.212	-.120	.289	.789**	1.000	.940**	.737**	.168

		Sig. (2-tailed)	.000	.857	.253	.514	.144	.000	.	.000	.000	.351
		N	33	29	31	32	27	33	33	33	33	33
	LCX MEAN DOSE(cGY)	Correlation Coefficient	.839**	.026	-.121	-.145	.264	.785**	.940**	1.000	.708**	.190
		Sig. (2-tailed)	.000	.894	.516	.428	.184	.000	.000	.	.000	.289
		N	33	29	31	32	27	33	33	33	33	33
	LAD V25	Correlation Coefficient	.902**	.327	-.200	-.132	.230	.730**	.737**	.708**	1.000	.288
		Sig. (2-tailed)	.000	.084	.281	.473	.248	.000	.000	.000	.	.104
		N	33	29	31	32	27	33	33	33	33	33
	LAD V45	Correlation Coefficient	.274	.264	.045	-.260	.180	.294	.168	.190	.288	1.000
		Sig. (2-tailed)	.123	.167	.811	.151	.368	.097	.351	.289	.104	.
		N	33	29	31	32	27	33	33	33	33	33

**. Correlation is significant at the 0.01 level (2-tailed).

91. QUALITATIVE ANALYSIS OF THE CAUSES AND FACTORS RESPONSIBLE FOR DEATH

SERIAL	REPORTED CAUSE OF DEATH	PROBABLE REASON FOR EARLY DEATH
1	Died due to recurrence/metastasis	Left sided cancer (Luminal) with positive margins and nodes positive (20) with no pCR and presence of DCIS.
2	Non cancer related	Left sided cancer, Advanced stage(3B), poorly differentiated histology, TNBC, Absent pCR, Presence of DCIS
3	Died due to brain metastasis	Left sided cancer, Obese, Advanced Stage (3B), Node positivity (4), No pCR,
4	Died due to metastasis	Left sided cancer, Advanced stage(T4B), Did not follow up for long time. Did not receive Herceptin nor get treatment for metastasis.
5	Died due to lung metastasis	TNBC, Advanced stage ypT4bN1, No pCR
6	Non cancer related	Young age (35), pre-menopausal, History of Ca BM (received Sx +RT in 2016), Stage 3B(pT4bN2), No pCR, DCIS present.
7	Died due to lung / liver metastasis	Age <50, Left sided, Obese, pre-menopausal, Advanced Stage(cT4bN1), No pCR, DCIS present.
8	Died due to pleural metastasis	Age<50, Obese, Advanced Stage (3A), Metaplastic carcinoma, Both local and distant recurrence.
9	Non cancer related	Advanced Age (68 years), Obese, Smoker, Node positive (1), Margin positive, DCIS positive, No pCR.
10	Died due to liver metastasis	Age<50 (42 years), Left sided, Premenopausal, Stage 3(ypT2N2B), No pCR
11	Non cancer related	Age<50 (42 years), Left sided, Pre-menopausal, Advanced stage(pT4bN1), DCIS positive.
12	Non cancer related	Advanced age (83), Left sided, Node positive (16), Advanced stage(pT2N2a)

13	Non cancer related	Age<50 (45), Obesity, Pre-menopausal, Node positive. Margin involved, DCIS present.
14	Non cancer related	Age<50(48), Obesity, Node positivity
15	Non cancer related	Advanced age (72 years), Obesity, Left sided, Comorbidity-CAD, DM.

DISCUSSION

I. EPIDEMIOLOGICAL FACTORS

1. AGE-WISE DISTRIBUTION

The results of our trial revealed that the mean age of our Breast cancer population was 52 years with a majority of 62% patients between 40-60 years which is similar to that seen in Indian and International data.(3)[40-50 years in Indian data and 60-70 years being the international mean age]. Thus, our study also confirms that breast cancers in Indian women happens a decade earlier and thus screening for them from the age of 30 years may be required, in an age group when dense breasts pose difficulty to use mammograms.

2. GENDER-WISE DISTRIBUTION

Our study revealed that 0.9% were male and 99.1% were female which was similar to the distribution seen in Indian (1.03%) and western data(0.91%)(21,22). This is a low incidence and sporadic and hence has no screening implications.

3. GEOGRAPHIC DISTRIBUTION

Most of our patients hailed from Jodhpur as expected (77%) with a majority of others from the neighboring districts of Jalore, Nagore and Pali among others. The Institute has been created to cater to these areas where there are no other multispecialty health services available.

4. RELIGION WISE DISTRIBUTION

2.7% of our patients were Muslims and 97.3% of our patients were Hindus which was a ratio lower than seen in previous Indian studies which reported around 7.7% incidence in the Muslim population.(23)

5. ANTHROPROMETRIC PARAMETERS

The mean height of the patients enrolled in our study was 155 cm which was similar to that reported in other Indian studies which show the distribution of maximum number of cases between 150-155cm. The mean weight of patients in our study was 65 kg with maximum distribution between 60-6 kg which was higher compared to previous studies which showed maximum distribution between 50-60kg. BMI of 111 patients were studied, ranging from a minimum of 15.04 kg/m2 to a maximum of 45.61 kg/m2 with a mean and median BMI of

27.05 kg/m2 and 26.7 kg/m2 respectively out of which 61.8% Patients were Obese, 12.73% were overweight which was higher compared to the previous studies which showed a lesser overweight population ranging from 18-23 kg/m2 (46.1%) which might be attributed to change in geographical regions or temporal development of a more obese population with time.(32)

6. LATERALITY

Our study showed that Out of the 111 patients studied, 55(49.5%) had left sided malignancy and 56(50.5%) had right sided malignancy which is almost similar to data from other north Indian studies showing a tendency for right sided breast cancers (53.5%>45.9%)(24)

7. DE NOVO VS RECURRENT CASES

Out of 111 patients, 3(2.7%) were recurrences and 108(97.3%) were new cases

8. INITIAL CLINICAL PRESENTATION

93.69% of our patients presented with the complaint of breast lump followed by 2.7% patients who presented with ulceration in breast or axilla. Around 9 patients reported secondary complaints which included Bleeding from nipple, Discharge, Nipple retraction, Pain in axilla, Supraclavian lymph node ,Skin changes, Breast Ulceration, Ulcero-proliferative growth in axilla. Out of the 84 patients assessed for pain at presentation, 66 patients(78.5%) reported presence of painful lump and 18(21.5%) reported presence of painless lump which was in contrast with other Indian trials in North India which showed 77%,17% and 3% patients with painless lump, painful lump and nipple discharge respectively as the presenting complaints(96). Only 1 patient was found with incident lump on screening.

9. PARITY

Out of 111 patients, 44 patients had answered about parity. A majority of 40.91% patients had 2 children which was higher than that of other reported populations(30%).(31)Out of 110 patients who gave their menstrual information during the study, 56.4% were post menopausal, 34.26% of patients were pre-menopausal and 9.26% were peri-menopausal. Which was also similar to other studies which showed a predilection for breast cancer in post menopausal females over pre menopausal ones.(32)

10. ADDICTION HISTORY AND COMORBIDITY HISTORY

Only 1.94% patients gave a history of tobacco chewing and <1% were smokers and none gave history of alcohol use which is in contrast to the data from Global burden of disease which showed alcohol as a major risk factor. The most common comorbidity associated with our patients were Hypertension(18.2%) followed by Diabetes mellitus(12.6%) , then hypothyroidism(5.5%) and Bronchial asthma(2.3%). Another similar trial from North west India by Ankit Rai et al reported Hypertension(21.8%) as the most common comorbidity associated with Breast cancer in India followed by Chronic Obstructive Pulmonary disease(19.9%) and then Diabetes mellitus(16.7%). Presentation Delay (Months) was shown with a mean of 7.98 ± 8.68 and median of 5.00 (4.00-8.00). (96) There is a hypothesis linking metabolic disease as diabetes and obesity with cancers.

PRE-SURGICAL TREATMENT CONSIDERATIONS

11. STAGE ADJUSTED INCIDENCE OF BREAST CANCER

Out of the 91 patients, a majority of 32.97% patients were Stage 2B followed by 31.87% from stage 2A and the minimum from stage 3C (1.10%). Considering only stages, stage 2 had the highest representation with nearly 64% cases followed by stage 3 with nearly 42%. Other Indian data show a higher representation from Stage 3(42%) followed by those in Stage 2(32.7%).(20)

12. NEOADJUVANT CHEMOTHERAPY

Out of the 111 patients, 64 did not receive NACT. 46 patients(41%) received NACT which is similar to data from other high volume centres in India(41.7%).(20)Most common regimen received was TEC(22.52%) followed by AC regimen(4.5%). Only 34% patients received complete Neoadjuvant chemotherapy. No direct comparison of TEC/FEC with AC-T in a randomised setting were found. The use of triple regimen TEC was a part of the Institute protocol which gradually shifted to AC followed by Taxol based protocol for most patients.

13. TYPE OF SURGERY DONE

Out of the 110 patients whose records about type of surgery were available, a majority of 75.45% underwent Modified Radical Mastectomy followed by 20% who underwent breast Conservation Surgery. Other Indian trials show a higher percentage of patients who have undergone BCS with around 28.2% of cases.(20)

14. ADEQUACY OF NODAL DISSECTION

With many studies showing that removal of greater than 10 axillary LN's resulted in a more favorable survival profile, we studied for adequacy of nodal dissection among our patients.(51) Out of the 108 patients, 85.19% patients had underwent adequate dissection while 14.81% patient had inadequate dissection which was similar to other prospective trials which show around 81.3% patients who had adequate axillary dissection done(97). The node positivity data of 108 patients were collected, out of which maximum and minimum node positivity were 75 and 0 respectively with a mean of 3.56 nodes positive.

II. HISTOPATHOLOGICAL FACTORS

15. POST OPERATIVE HISTOPATHOLOGY

As per our study invasive ductal carcinoma was the most common subtype noted, covering 39.64% cases followed by 36.04% cases represented by just Invasive breast cancer, NOS. Other similar studies from AIIMS Delhi, report a higher Invasive ductal carcinoma incidence of 96%. We also have minimal number of other histology reported such as IBC, Ductal + Lobar histology, Colloid Carcinoma, IBC with apocrine differentiation, IBC with sebaceous differentiation, IBC with signet cell carcinoma, Metaplastic carcinoma, Invasive Papillary carcinoma, Mucinous carcinoma.(20)

16. MODIFIED BLOOM RICHARDSON GRADE

Out of the 64 patients with reported Modified Bloom Richardson Grade, the majority had a grade of 2(54.69%) followed 39.06% patients with a grade of 3. Only 6.25% patients had a grade of 1.(66) Rangarajan et al in his overview of trend of breast cancer in India showed that socioeconomic trend was a factor deciding grade of tumors presenting at a centre with a majority of 80% patients presenting with Grade 3 disease in large referral centres and an equal distribution between grade 2 and 3 seen in private hospitals.(98)

17. MILLER-PAYNE GRADING

Out of the 19 patients with reported Miller Payne Grading, 31.58% had grade 5 followed by 21.05% had grade 4. The other 3 grades had equal shares among the rest.(67)

18. MARGIN STATUS

Out of the 107 patients with margin status on record, 86.92% had free margins while 13.08% patients had involved margins which was mostly deep margin in MRM and operated outside

the Institute. The involved margin percentage is comparatively higher compared to other studies and meta-analysis which show around 9.4% patients with an involved or inked margin.(52). Only 3 out of these 14 margin positive patients died with 1 dying due to cancer and 2 from non-cancer related causes.

19. LYMPHOVASCULAR SPACE INFILTRATION STATUS(LVSI), PERINEURAL INVASION.

Out of the 102 patients whose LVSI records were available, a majority of 52.94% had LVSI present and 46.08% had absent LVSI and 0.98% had an indeterminate status. Out of the 101 patients whose PNI records were available, a majority of 74.26% had PNI present and the rest had PNI absent. Incidence of PNI alone, LVSI alone, both PNI & LVSI was seen as 1.49%, 11.2%, 3% in another study from India.(99)Another large trial by Emre et al showed 27.3% incidence of LVSI and 7.6% incidence of PNI in breast cancer patients(54). This points towards a higher percentage of patients with positive LVI in our population pointing towards a possibly worse prognosis. The higher rates of LVI and PNI in this part of the country requires tumour biological studies for further interpretation and implementation in practice.

20. SUBTYPE OF BREAST CANCER

Out of the 111 patients assessed, 71.17% of patients were of Luminal subtype, 18.02% patients were of TNBC subtype, 9.01% patients were of Her-2 enriched subtype. Another study from North west India showed 57.5%, 44.1%, and 26.6% of people had tested positive for the ER, PR, and HER2neu receptors, respectively. Luminal A subtype was the most prevalent molecular subtype (41.7%), followed by triple negative subtype (30.8%). There were 15% and 12.5%, respectively, of Luminal B and HER2neu overexpressing kinds. (100)Another similar trial from AIIMS Delhi reported a total of 58% of cases tested positive for ER, PR, or both, while only 30.89% of patients had HER2/neu positive results. In 29.88% of cases, triple negativity was discovered.(20) We also found that our patients with TNBC showed a lower age wise distribution(with mean age of 48.8) as seen in other similar trials which might also be a reason for the poorer prognosis associated with the same. Patients of Luminal subtype showed a peak in the 4th decade while TNBC showed a broader distribution starting the earliest and extending till menopausal age group while Her 2 enriched status showed incidence mainly in the younger age group. Similarily we found that TNBC subtype was associated with a higher rate of pathological CR which indirectly points towards its intrinsic chemosensitivity. 4/5 patients of TNBC treated with NACT in our trial showed pCR

compared to 1/34 in luminal type(57). This also reaffirms the fact that India also apparently has a higher population of TNBC compared to western population(30 % vs 12-15%)(60)

21. PRESENCE OR ABSENCE OF LCIS/DCIS WITH INVASIVE CARCINOMA

Out of the 111 patients whose records were available, 39.64% were positive for DCIS/LCIS which is comparatively higher to other contemporary data, one of which reported 25.4%.(61) Out of the 44 patients whose information on focality was available; 68% had Unifocal DCIS while 32% had multifocal DCIS.

III. ADJUVANT TREATMENT FACTORS

22. ADJUVANT CHEMOTHERAPY

Out of the 109 patients whose data about adjuvant chemotherapy were retrieved, 75.2% had received adjuvant chemotherapy while the rest had received NACT or hormonal therapy which is higher than the rates seen in other similar studies from India(59%)(101). This can be attributed to the fact that there were also many cases which came after initial treatment from other primary centers i.e. inadvertent surgical lump removal or mastectomy without neoadjuvant therapy.

23. ADJUVANT HORMONAL THERAPY

Out of the 76 patients, 84% had received hormonal therapy while records of 16% were not available. (102)Out of the 47 patients whose records of hormonal therapy were available, 45% received Anastrozole, 34% received Tamoxifen and 21% received Letrozole. 3 patients later changed to a different regimen due to intolerance or change of menstrual status. The use of hormonal agents has always been a point of contention with physicians' choice predominating as there has not been any conclusive evidence showing superiority of Anastrozole or letrozole over one another. A study in South India demonstrated 35% prevalence of use of Letrozole followed by 27% patients on Tamoxifen when assessed regardless of Menopausal status.(101)

24. DURATION FROM SURGERY TO START OF RT

The study revealed that the mean time from Surgery to start of Radiation was 28 weeks and ranged from 3.7 weeks to 209 weeks. There were many reasons for the delay in RT including patient being lost to follow up, the impact of the COVID pandemic as well as neglect from

other primary centres where the patient was sent home after surgery without counselling regarding Adjuvant therapy.

25. RADIOTHERAPY TECHNIQUE AND DOSING REGIMENS

82.7% of the 110 patients whose data were accrued had received RT by 3DCRT followed by 17.3 % of patients by VMAT. The lesser rates of VMAT can be attributed to logistical issues.

26. RADIOTHERAPY DOSES TO CARDIAC SUBSTRUCTURES AND HEART IN PATIENTS WHO RECEIVED 42.56 GY/16#.

According to our study, the average doses to the heart and cardiac substructures were 1255.52 cGy, 0.818 cGy, 0.017 cGy, 167.742cGy, 260.58 cGy, and 644.62 cGy for the mean LAD, LAD V25, LAD V45, mean LCX, mean LCA, and mean heart doses, respectively. Left sided cancers received significantly more dose as expected compared to right sided cancers. The DEGRO breast cancer guidelines recommended the following limits, which demonstrated that our cardiac dosages were higher than dose constraints as indicated by other guidelines. Dmean LAD (mean dose left descending artery): 10 Gy; mean heart dose: 2.5 Gy.(88)

27. RATES OF RECURRENCES

Out of the 106 patients whose response assessment details were accrued, 92.4 % were disease free ,7.6% had recurrent disease on follow up. Amongst the 18 patients with documented recurrence, 72% had distant recurrences, 22% had local recurrences and the remaining had both local as well as distant recurrence. This showed a higher rate of recurrences than other similar studies but similar to the 10-year Breast Cancer Recurrence rates which could not be corroborated well as the duration of our follow up was limited (less than 3 years).

28. SITE OF DISTANT METASTASIS?

A majority of 29% patients had Bone metastasis followed by 23% patients with Liver metastasis in our studied which is similar to a SEER meta-analysis which showed that In terms of both single and multiple metastatic locations, bone continued to be the most frequent site of breast cancer metastasis (65.1%), followed by the lung (31.4%), liver (26.0%), and brain (8.8%) metastasis.(62)

NOTE: Most of the survival analysis could not be completed due to lesser number of events(death/relapses). In those cases where survival analysis was not feasible, correlation

with Log rank test was done to find significant correlation with survival trends and qualitative analysis of probable reasons of death was collated..

29. MEDIAN OVERALL SURVIVAL/DISEASE FREE SURVIVAL/ PROGRESSION FREE SURVIVAL/RECURRENCE FREE SURVIVAL

Out of the 111 patients with accrued data, 86% were alive at last follow up and 14% had passed away. The median duration of follow up was 40.7 months(CI=39.6-41.7 months).The mean and median Overall survival were 38.9 and 39. 9 Months respectively. The mean and median progression free survival/recurrence free survival was 37.5 months and 39.1 months respectively and ranging from 85.9 to 0.37 months. the mean and median Disease-free survival was 30.5 months and 33.1 months respectively and ranging from 3.03 to 48.03 months. This shows a wide discrepancy with other national and international data being much lower in comparison mainly due to the lesser duration of follow up.(20,95)

Site wise distribution of OS, DFS and PFS/RFS showed that the lowest and highest OS, PFS/RFS and DFS were for Lower Inner quadrant and Axillary primaries respectively.

IV. PROGNOSTIC FACTORS FOR SURVIVAL OUTCOMES

30. DEMOGRAPHIC VARIABLES:

Cox regression analysis of demographic variables revealed that only religion (in favour of Hindus, Median OS-76 months vs 30 months) showed a significant correlation with Overall survival (HR=0.102, 95% CI=.016-0.638, p=0.015). Age >50, post-menopausal status, right sided breast cancer, Higher BMI, Presence of comorbidities showed a trend towards improved overall survival and progression free survival/recurrence free survival although statistically insignificant. Although significant correlation was found with Religion, this needs to be studied in a prospective setting due to the limited number of Muslim patients involved in this study. Other similar studies on impact of prognostic epidemiological variables on Breast cancer survival has shown a similar trend with Age >40(37). But a study by Tata Memorial Hospital revealed no relation with religion and prognosis. BMI has long shown to be a poor prognostic factor for breast cancer survival which came as reversed in our study which might be due to a larger ratio of censored cases.(42)Other studies also point towards the superior survival with right sided tumors.(43)

Similarily Right sided tumours, Higher BMI, Presence of comorbidities, Hindu religion showed a trend towards improved Disease free survival while Age<50 and Pre menopausal status showed improved DFS which was the reverse of the trends seen with PFS/RFS and OS, although statistically insignificant.

31. PRE SURGICAL STAGING :

There was no significant correlation between Pre surgical staging and OS and PFS/RFS and median overall survival statistics could not be completed due to censored events in our study. This is contrast to other sufficiently powered studies which demonstrate a clear correlation between stage and outcome.(46)There was a significant correlation seen with Staging and DFS.

32. ROLE OF NEOADJUVANT CHEMOTHERAPY

Our study revealed that receipt of NACT resulted in significantly lesser overall survival, DFS and PFS/RFS which might be due to this study being underpowered to test for this.(48)

33. EFFECT OF NUMBER OF DISSECTED NODES, TYPE OF SURGERY AND NUMBER OF POSITIVE NODES

Higher Number of dissected nodes and positive nodes showed a trend of increased overall survival , DFS and PFS/RFS although insignificant which is in the lines of other studies(50,51). Type of surgery also did not have a significant correlation with survival outcomes although there was a trend to worse outcomes with MRM which can be attributed to later stage at presentation or other poor prognostic features pre-empting MRM over BCS

34. BLOOM RICHARDSON GRADING

Our study showed no significant relation between Grading and survival outcomes such as OS, DFS, PFS/RFS although other trials show a significant correlation with survival.(58)

35. MARGIN STATUS,LVSI,PNI, ENE

Presence of positive margins corresponded with an trend towards decreased OS,DFS and PFS/RFS although non significant in our study. Presence of LVSI and PNI also pointed towards a trend towards worser outcomes although insignificant. This is as expected and seen in other similar studies which show Margin positivity, LVSI, PNI as prognostic for poorer outcomes(52,54)

36. PRESENCE OF DCIS/LCIS ALONG WITH INVASIVE CARCINOMA

Our study showed that presence of DCIS/LCIS with invasive carcinoma pointed to a trend to inferior OS and PFS/RFS with superior DFS although insignificant which was in contrast to some other studies showing an increased DFS survival and OS with DCIS(61)

37. POST SURGICAL STAGE

Post surgical T stage showed a significant correlation with overall survival and similar trends with DFS and PFS/RFS although non significant. N stage also showed trends towards improved survival, DFS, PFS/RFS although insignificant.

38. SUBTYPE OF BREAST CANCER

There was no significant correlation between tumour subtype and survival outcomes but there was a trend towards improved OS and PFS/RFS with Luminal subtype compared to TNBC and Her 2 neu enriched subtypes although non-significant. But other sufficiently powered studies have shown a significant correlation between the two with Luminal subtypes having superior survival and TNBC having the worst.(59)

39. ADJUVANT THERAPY

On Cox regression analysis, Duration from Surgery to start of RT showed a significant correlation with PFS/RFS while duration of radiotherapy did not. Adjuvant chemotherapy and choice of hormonal agent did not reveal any significant correlation with OS, PFS/RFS and DFS, although recent update of the TEXT/SOFT trials reveal a DFS and OS benefit in high-risk premenopausal patients. This subgroup analysis could not be done due to limitations of our study.

While some studies show that delay in start of RT after surgery more than 8 weeks had a detrimental impact on OS but later studies showed that sequencing of chemotherapy before RT resulting in a delay in RT did not result in worse survival outcomes.(71–73)

Choice of Radiotherapy technique or regimen did not reveal any significant correlation with survival outcomes although patients treated with 3DCRT showed a trend towards superior OS, DFS though non- significant which can also be attributed to lower number of patients in the VMAT arm.

40. CARDIAC PARAMETERS FOR PATIENTS WHO RECEIVED 42.56GY/16#

Assessment of correlation between subclinical cardiac toxicity assessment parameters and Dose to Left Anterior descending artery, Left circumflex artery, Left Coronary artery was done. Non parametric test of Spearmann was used to test for correlation. The results revealed no significant correlation between the markers of subclinical cardiotoxicity and doses to cardiac substructures as well as heart. However, there was significant correlation between Mean heart dose and Mean Left Anterior descending artery dose, Mean Left circumflex artery dose, Mean Left Coronary artery dose and Left Anterior descending artery V25.(P=.000). Moreover the doses received by heart and cardiac structures are as expected more for left sided cancers compared to right in the range of 2299.48 cGy and 146.31 cGy for Mean Left Anterior Descending artery dose to 797.07 cGy and 243.99 cGy for Mean heart dose and 413.96 cGy and 97.62 cGy for Mean Left coronary artey dose. However other sufficiently powered studies have demonstrated the role of Myocardial performance index and Left ventricular ejection fraction in predicting subclinical cardiotoxicity.(92) The strong correlation between the mean cardiac doses and various doses to LAD can be further studied as it may show that the simpler segmentation and constraints on heart can continue to be the standard radiation planning procedure instead of more difficult segmentation and constraints of LAD.

CONCLUSION

The most prevalent cancer diagnosed worldwide is now female breast cancer, surpassing lung cancer in prevalence. Among Indian women, breast cancer is the most prevalent type of cancer. With the increasing cases of cancer worldwide, comes our responsibility to further dissect and understand the enigma constituting the same.

This study was aimed at assessing the clinicopathological profile and its effects on the survival outcomes of patients of Breast cancer treated with curative intent at our centre. Although the study was underpowered to test for effect of many variables on the survival outcomes due to lesser number of events and limitations of sample size, it successfully demonstrates the general trend of prognostic effects of different clinicopathological variables on outcomes as well as an epidemiological profile mirroring that of real-world data as evidenced by other similar trials.

With the advent of newer, safer modalities of treatment, the general prognosis of breast cancer in India is good. But due to lack of a standard screening and treatment guideline throughout the country, there are wide discrepancies in workup and management of patients. This in addition to the delay in presentation, prevalence of local herbal, folk remedies which are sought after by the rural populace and sometimes the Provider delay due to large patient load results in an apparently poorer prognosis for a comparatively controllable malignancy.

Our study also brings to light the high prevalence of Obesity and Comorbidities like Hypertension, Diabetes mellitus in the populace which might also have hidden associations with breast cancer risk and even prognosis, prompting further prospective research on the same as well as fleshing out well thought out mechanisms aimed at targeting awareness of lifestyle habits as well as its implications on Cancer risk and prognosis along with its effect on other the traditional Non communicable diseases such as Coronary artery disease, Stroke, etc.

Absence of proper post treatment follow up also seems to be a major factor which prevents the timely diagnosis of relapses or metastasis, which either stem from a lack of proper counselling from the care-giver or due to the lack of compliance from the patient side.

In conclusion, attempts to tackle breast cancer burden should be started at its roots from:

1. Screening of young females with an emphasis on those with a family history of breast cancer or other related cancers. This should in fact start from a younger age than those reported in western guidelines due to the younger age of presentation of Indian breast cancer patients and the poorer outcome of the same.
2. Timely treatment with minimal Provider delay should be targeted by decreasing the burden on existing health care institutions. Either by increasing the number of health care providers or by developing new Cancer centres equipped with the latest Radiation, Systemic therapy and Surgical treatment options under government schemes which will help in both data accrual as well as ease economic burden of cancer patients.
3. Proper streamlined process for long term follow up of treated patients.

LIMITATIONS OF THE STUDY

The study was not sufficiently powered to test for significant differences in outcomes as a result of various demographic and pathological as well as treatment related variables. There were lesser number of events which resulted in subgroup analysis failure because of all events being censored in the groups. Being retrospective in nature, this study does not include patients treated with a homogeneous treatment regimen which accounts for a lot of confounding results.

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ANNEXURES

ANNEXURE-1

PROFORMA FOR DATA COLLECTION

ALL INDIA INSTITUTE OF MEDICAL SCIENCES, JODHPUR

(DEPARTMENT OF RADIATION ONCOLOGY)

PROFORMA FOR DATA COLLECTION

NAME OF THE PATIENT: AGE: SEX:

REG. ID:

RELIGION:

RESIDENCE:

MOBILE NO:

HT: WT: BMI: (AT START OF TREATMENT)

SYMPTOMS AT PRESENTATION:

DURATION OF SYMPTOMS:

ADDICTION HISTORY: NEVER/ FORMER/ CURRENT

MENSTRUAL STATUS:-

PARITY:

HISTORY OF CO-MORBIDITIES: DM TYPE2 / HTN / IHD / CKD / COPD /DYSLIPIDEMIA/ PAD/STROKE. THERS.....

RESPONSE ASSESSMENT

A) DATE:

B) CURRENT DISEASE STATUS:

RELAPSE/PROGRESSION:

A) DISTAL/LOCAL(SITE AND NUMBER):

B) TREATMENT OFFERED:

DATE OF DEATH/DATE OF THE LAST FOLLOW-UP:

CAUSE OF DEATH:

ANNEXURE-2

CARDIAC ASSESSMENT AT FOLLOW UP

DEPT OF RADIATION ONCOLOGY AND DEPT OF CARDIOLOGY

"SURVIVORSHIP ISSUES IN BREAST CANCER SURVIVORS TREATED AT OUR CENTRE"

NAME OF THE PATIENT: AGE: SEX:

REG. ID:

ELECTRO-CARDIOGRAPHY:

HEART RATE-

Q_{TC} -_____MS

$T_{WAVE\ PEAK} - T_{WAVE\ END}$ =_____

$(T_{WAVE\ PEAK} - T_{WAVE\ END})/Q_{TC}$ =_____

ECHOCARDIOGRAPHY:

LVEF (%)-

LV DIASTOLIC FUNCTION-

LV SYSTOLIC FUNCTION-

MYOCARDIAL PERFUSION INDEX-

ANNEXURE-3

AJCC 8TH TNM PROGNOSTIC CLASSIFICATION

T CATEGORY	T CRITERIA
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis (DCIS)[a]	Ductal carcinoma in situ (DCIS)
Tis (Paget)	Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted.
T1	Tumor $\leq$ 20 mm in greatest dimension
T1mi	Tumor $\leq$ 1 mm in greatest dimension
T1a	Tumor $>$ 1 mm but $\leq$ 5 mm in greatest dimension (round any measurement from $>$1.0-1.9 mm to 2 mm)
T1b	Tumor $>$ 5 mm but $\leq$ 10 mm in greatest dimension
T1c	Tumor $>$ 10 mm but $\leq$ 20 mm in greatest dimension
T2	Tumor $>$ 20 mm but $\leq$ 50 mm in greatest dimension
T3	Tumor $>$ 50 mm in greatest dimension
T4	Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or macroscopic nodules); invasion of the dermis alone does not qualify as T4
T4a	Extension to the chest wall; invasion or adherence to pectoralis muscle in the absence of invasion of chest wall structures does not qualify as T4
T4b	Ulceration and/or ipsilateral macroscopic satellite nodules and/or edema (including peau d'orange) of the skin that does not meet the criteria for inflammatory carcinoma
T4c	Both T4a and T4b are present
T4d	Inflammatory carcinoma (see "Rules for Classification")

CATEGORY	CRITERIA
cN[a]	
cNX[b]	Regional lymph nodes cannot be assessed (eg, previously removed)
cN0	No regional lymph node metastases (by imaging or clinical examination)
cN1	Metastases to movable ipsilateral level I and II axillary lymph node(s)
cN1mi[c]	Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm)
cN2	Metastases in ipsilateral level I and II axillary lymph nodes that are clinically fixed or matted;
	or in ipsilateral internal mammary lymph nodes in the absence of axillary lymph node metastases
cN2a	Metastases in ipsilateral level I and II axillary lymph nodes fixed to one another (matted) or to other structures
cN2b	Metastases only in ipsilateral internal mammary lymph nodes in the absence of axillary lymph node metastases
cN3	Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I and II axillary lymph node involvement;
	or in ipsilateral internal mammary lymph node(s) with level I and II axillary lymph node metastases;
	or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
cN3a	Metastases in ipsilateral infraclavicular lymph node(s)
cN3b	Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
cN3c	Metastases in ipsilateral supraclavicular lymph node(s)

pN[d]	
pNX	Regional lymph nodes cannot be assessed (eg, not removed for pathological study or previously removed)
pN0	No regional lymph node metastasis identified or ITCs only
pN0(i+)	ITCs only (malignant cell clusters no larger than 0.2 mm) in regional lymph node(s)
pN0(mol+)	Positive molecular findings by reverse transcriptase-polymerase chain reaction (RT-PCR); no ITCs detected
pN1	Micrometastases; or metastases in 1-3 axillary lymph nodes; and/or clinically negative internal mammary lymph nodes with micrometastases or macrometastases by sentinel lymph node biopsy
pN1mi	Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm)
pN1a	Metastases in 1-3 axillary lymph nodes, at least one metastasis larger than 2.0 mm
pN1b	Metastases in ipsilateral internal mammary sentinel lymph nodes, excluding ITCs
pN1c	pN1a and pN1b combined
pN2	Metastases in 4-9 axillary lymph nodes; or positive ipsilateral internal mammary lymph nodes by imaging in the absence of axillary lymph node metastases
pN2a	Metastases in 4-9 axillary lymph nodes (at least one tumor deposit larger than 2.0 mm)
pN2b	Metastases in clinically detected internal mammary lymph nodes with or without microscopic confirmation; with pathologically negative axillary lymph nodes
pN3	Metastases in 10 or more axillary lymph nodes;
	or in infraclavicular (level III axillary) lymph nodes;
	or positive ipsilateral internal mammary lymph nodes by imaging in the presence of one or more positive level I and II axillary lymph nodes;
	or in more than 3 axillary lymph nodes and micrometastases or macrometastases by sentinel lymph node biopsy in clinically negative ipsilateral internal mammary lymph nodes;
	or in ipsilateral supraclavicular lymph nodes
pN3a	Metastases in 10 or more axillary lymph nodes (at least one tumor deposit larger than 2.0 mm);
	or metastases to the infraclavicular (level III axillary lymph) nodes
pN3b	pN1a or pN2a in the presence of cN2b (positive internal mammary lymph nodes by imaging);
	or pN2a in the presence of pN1b
pN3c	Metastases in ipsilateral supraclavicular lymph nodes

CATEGORIES FOR DISTANT METASTASES—CLINICAL AND PATHOLOGICAL (CM0, CM1, PM1)

M CATEGORY	M CRITERIA
M0	No clinical or radiographic evidence of distant metastases[a]
cM0(i+)	No clinical or radiographic evidence of distant metastases in the presence of tumor cells or and no deposits no greater than 0.2 mm detected microscopically or by using molecular techniques in circulating blood, bone marrow, or other nonregional lymph node tissue in a patient without symptoms or signs of metastases
M1	Distant metastases detected by clinical and radiographic means (cM) and/or histologically proven metastases larger than 0.2 mm (pM)

WHEN T IS...	AND N IS...	AND M IS...	THEN THE STAGE GROUP IS...[b]
Tis	N0	M0	0
T1	N0	M0	IA
T0	N1mi	M0	IB
T1	N1mi	M0	IB
T0	N1	M0	IIA
T1	N1	M0	IIA
T2	N0	M0	IIA
T2	N1	M0	IIB
T3	N0	M0	IIB
T1	N2	M0	IIIA
T2	N2	M0	IIIA
T3	N1	M0	IIIA
T3	N2	M0	IIIA
T4	N0	M0	IIIB
T4	N1	M0	IIIB
T4	N2	M0	IIIB
Any T	N3	M0	IIIC
Any T	Any N	M1	IV

ANNEXURE-4

ETHICAL COMMITTEE CERTIFICATE

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2021/ 3559 **Date: 12/03/2021**

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2021/3394**

Project title: **"To study of survival outcomes, prognostic and treatment related factors in patients of breast cancer treated with post-operative radiation therapy"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**D.M. Dissertation**
Student Name:	**Dr.Rishi P Nair**
Guide:	**Dr. Puneet Pareek**
Co-Guide:	**Dr. Jeewan Ram Vishnoi, Dr. Surendra Deora & Dr. Poonam Elhence**

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation.

If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary
Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur