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COMPUTED-TOMOGRAPHY STAGING OF BREAST CANCER AND IT'S ROLE IN PATIENT MANAGEMENT IN A RESOURCE-LIMITED SETTING: A RETROSPECTIVE STUDY FROM FIJI

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ABSTRACT:

Breast cancer is now the leading cause of mortality from cancer in Women in Fiji. State of the art diagnostic measures such as MRI, PET scanning and advanced tumour markers are unavailable in many LMIC countries including Fiji, but CT is becoming more widely available. The aim of the study was to determine the association between CT/anatomical staging and prognosis in a resource-limited setting, and its role in planning appropriate treatment strategies. This was a retrospective, analytical study of the data from the Colonial War Memorial Hospital Oncology department tumour register recorded between 2013 and 2018. The mean age of the breast cancer patients with confirmed diagnosis was 54.93 years with SD of 12.4 years. There was a 40% 3 year mortality rate. CT reports were available for 196 patients. Poor prognosis was very closely associated with Tumour size ($p=0.002$, OR 0.26 (0.10-0.63)), Nodes ($p<0.001$, OR 0.25 (0.13-0.48.)) and Metastases ($p<0.001$, OR 0.13 (0.07-0.25)).The lungs were the most frequent site of metastases. CT staging enables accurate TNM classification, which is closely associated with prognosis. In the absence of advanced cytopathological and imaging modalities CT staging has an important part to play in planning appropriate treatment.

Keywords: CT/anatomical staging, breast cancer, prognosis, Fiji.

INTRODUCTION:

Breast cancer is a major cause of mortality and morbidity worldwide with 1 in 8 women developing an invasive breast cancer during their lifetime [1,2]. In 2018 WHO reported that breast cancer accounted for 1.81% of total

deaths in Fiji with an age-adjusted death rate of 26.21 per 100,000 of population, which ranks Fiji number 12 in the world [3]. A recent survey reported 187 breast cancer cases between January 2019 and August 2020; 63% of whom did not receive any treatment [4].

Facilities for diagnosing and treating patients with breast cancer in Fiji are limited. There are no Magnetic Resonance Imaging (MRI) or Positron Emission Tomography (PET) scanning facilities. Hormone receptor status tests are only sporadically available and other tumour marker and genetic testing is not routinely available. There is limited access to CT scans and mammography. Staging CT can be done but timely interpretation and reporting is a significant hurdle. These constraints make the role of breast cancer staging unclear. There is no set protocol or consensus on how and when to stage and on which patients.

In Fiji, as in many other Low Middle Income Countries (LMIC), many patients present late, with large fungating breast masses or evidence of metastasis (bone pain, shortness of breath, cachexia) when palliative care is all that can be offered. Early diagnosis is key to good outcome and this is particularly the case where access to and quality of chemotherapy is limited and radiotherapy unavailable.

Clinical TNM staging describes the local involvement of the breast (T), regional lymph nodes (N) and distant metastases (M). This incorporates imaging findings. Clinical staging can then be incorporated into anatomical staging which ideally includes histologic grade for invasive cancers and the status of the human epidermal growth factor receptor-2 (HER2), estrogen receptor (ER), and progesterone receptor (PR) expression.

Prognosis is related to stage.

The aim of the study was to determine the association between CT/anatomical staging results in breast cancer and prognosis in a resource-limited setting

METHODOLOGY:

This was a retrospective, analytical study exploring the association of CT staging of breast cancer with patient outcome 3 years post diagnosis. It was conducted in Colonial War Memorial Hospital (CWMH) in Suva, the central referral hospital of Fiji,

The Oncology Department Cancer Registry was searched for the details of all patients listed with a diagnosis of Breast Cancer between 2013 and 2018. Clinical records including outcome 3 years post diagnosis were obtained from the Hospital Patient Information system (PATIS). Of the 440 patients listed 348 (79.1%) were confirmed and of these 40.2% (140/348) had no record of CT.

Recorded CT results were not available for 12 of the 208 patients leaving a study group of 196 patients. Details of pathological classification, presence of receptors and details of chemotherapy and surgical treatment were documented where available. Tumour size and presence of Nodes and Metastases were recorded using standard TNM classification [5]. Data was entered onto an Excel spread sheet. Excel was used to derive basic demographic data and Open Epi software was used to determine differences in binary data with Chi squared tests and to calculate Odds Ratios and

95% confidence intervals for the associations between TNM characteristic and outcome at 3 years.

Ethics approval was granted by the post-graduate ethical committee of the CWMH and the University of Papua New Guinea (UPNG) School of Medicine and Health Sciences (SMHS) Research and Ethics committee. Approval to use the data in the oncology registry and hospital PATIS system was given by the Superintendent of CWMH.

RESULTS:

Of the initial 440 patients, four (0.9%) were males. Two of them were excluded from the study due to refusal of further treatment and unavailability of pathological confirmation whilst the other 2 did not have staging CT scan. Eighty four (19.1%) patients did not turn up for clinics or refused treatment after initial diagnosis. and 34 (7.7%) patients were listed for palliative care.

Demographic data was available for 348 (79.1%) patients. Age ranged from 24-87 years with a mean (SD) of 54.9 (12.4) years and a normal distribution across age groups as shown in Figure 1. The youngest patient was one of several patients with bilateral breast cancer.

Of the 348 patients, 207 (59.5%) were alive at the end of 3 years. Laterality of the tumour site was recorded in 186 of the 207 patients.

Ninety two (49.5%) affected the right, 90 (48.4%) the left and 4 (2.2%) both breasts.

Data concerning treatment given to the patients was not adequately entered in the hospital PATIS records and data in the oncology records was insufficient for analysis. Histopathology reports on PATIS were sporadic and when present diagnosis was usually "carcinoma". Only 4 (1%) patients had reports on ER and PR status. Three of these four patients were ER/PR positive and died within 3 years. The fourth patient who was ER/PR negative had CT staging of T₃N₁M₁ also died within 3 years. No one had a record of an HER2 result.

Whist CT was available for 196 (56%) of the 348 patients Tumour grade was not indicated in 84 (43%) and presence of Nodes was not indicated in 6 (3%).

Patient outcome (survival at 3 years after initial diagnosis) is shown for those with available data in Table 1. The Association between the TNM classifications and survival is shown in Table 2. In the absence of other prognostic factors, the CT staging shows very close associations between larger tumours, the presence of nodes and the presence of metastases with poor outcome. The presence of metastases was the strongest association with mortality. Metastases were in the lungs (plus or minus other sites) in 77 of 80 patients as shown in Table 3.

Table 1: TNM classification and survival

Tumour	Alive N (%)	Deceased N (%)	Node	Alive N (%)	Deceased N (%)	Metastases	Alive N (%)	Deceased N (%)
0	1 (2)	0 (0)	0	62 (55)	18 (23)	0	90 (79)	27 (33)
1	7 (11)	3 (6)	1	46 (41)	49 (64)	1	24 (21)	55 (67)
2	20 (31)	5 (10)	2	2 (2)	4 (5)			
3	15 (23)	8 (17)	3	3 (3)	6 (8)			
4	21 (33)	32 (67)						
Total	64 (100)	48 (100)	Total	113 (100)	77 (100)	Total	114 (100)	82 (100)

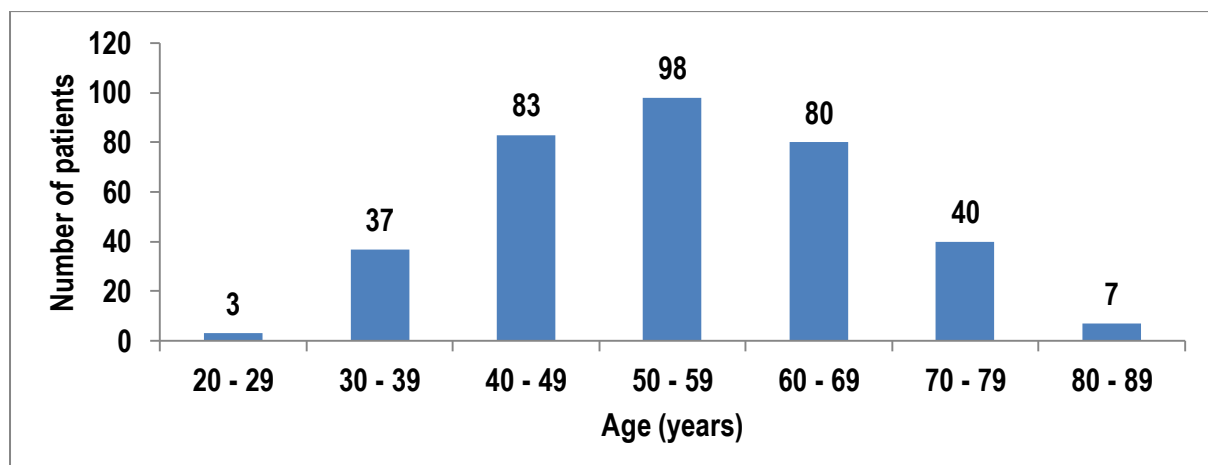
Table 2: Association between tumour grading (TNM classification) and survival at 3 years

TNM stage and survival at 3 years.	p-Value	Odds-Ratio	95% Confidence interval
Tumour (T3 +T4 vs. T1 +T2)	0.002	0.26	0.10-0.63
Node (N1-3 vs. N0)	<0.001	0.25	0.13-0.48
Metastasis (M1 vs. M0)	<0.001	0.13	0.07-0.25

Table 3 Sites of Metastatic Breast Cancer.

Metastases	Number of Cases N (%)
Lungs only	46 (57.5)
Lungs and others	31 (38.8)
Lungs total	77 (96.3)
Not lungs-brain, head	3 (3.7)
Total	80 (100)

Figure 1: Age distribution of the 348 breast cancer patients (2013-2018)



DISCUSSION:

To our knowledge this is the first report of the use of CT staging of patients with breast cancer in the Pacific Islands. The study is limited by lack of adequate information on histology, the presence of tumour markers, details of treatment modalities and in some cases details of tumour staging. Nevertheless the study clearly shows the value of CT as a predictor of prognosis.

The age demographics of our study population showed a mean age at 54.9 years. This is younger than that in the United States (median of 63.0 years in white and 60.0 years in black patients) and older than that reported in India (mean of 50.1 years) and Africa (mean of 50.0 years) [6-8].

The prevalence of breast cancer in males (0.9%) in our study is comparable to that reported from the USA [9].

The 3 years survival rate of 60.0%, in our study compares very poorly with the over 85% age standardised 5 year survival reported from industrialized nations [10]. Breast cancer survival remains lower in Eastern Europe and Africa [11]. The 5-year survival estimates range from less than 20% survival in Mali and the Gambia, to 35–50% in Uganda [12].

In contrast to other studies which reported a higher proportion of cancer's in the left than the right breast there was no difference in the present study and the prevalence of bilateral

involvement (2%) was similar to that reported elsewhere [13,14].

Fiji provides a manageable population for data collection and analysis. Almost every citizen is registered either with a birth certificate or voter identification card. Patients have hospital numbers allocated with the capacity for recording their admissions, clinic attendance, pharmacy records, radiology and pathology results, surgical reports, allergy reports, personal profile and discharge/referral summaries. However the quantitative and qualitative data available for this study has highlighted the urgent need for major improvement in documenting important information.

Mammography and ultrasonography are available in Fiji. They are less costly than CT but their diagnostic capability is limited and the role of the different imaging modalities in a country with limited resources remains to be determined.

A disturbing incidental finding of the study was that more than 19% of the diagnosed breast cancer patients did not get any form of treatment simply by not coming back to the hospital. The oncology register recorded them as "did not turn up for clinic" or "refused treatment".

Reasons for this high refusal of treatment may include belief in breast cancer as a "custom" rather than a medical event, ignorance of treatment options, fear of the effects of

treatment or, in a country with a very strong religious background, belief in prayer to heal. This clearly is an area for further research.

CONCLUSION:

The age related incidence of breast cancer in Fiji appears to be lower than in industrialized countries. In the absence of detailed histopathological and molecular diagnosis, CT predicted 3 year survival. Early diagnosis of breast cancer is key to planning appropriate treatment options and CT has an important role to play.

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