

A retrospective analysis of clinical features, treatment related complications and outcome of postmenopausal females with oestrogen receptor positive breast cancer treated at National Cancer Institute, Maharagama

C R B Gunarathne

MD (Clinical Oncology),


Post Graduate Institute of Medicine,

University of Colombo

Date of submission 2018.06.01

Statement of Originality

I confirm that this is an original research done by me and this has not been presented or published beforehand for any other journal, conference or as a dissertation for any other degree.


Candidate – Dr. C R B Gunarathne

Supervisor – Dr. Sujeeva Weerasinghe



Dr. SUJEEVA WEERASINGHE
(MBBS.MD)
Consultant Clinical Oncologist
National Cancer Institute
Maharagama

Abstract

Introduction –Breast cancer is the commonest cancer in the world and this holds true for Sri Lanka as well. Post menopausal hormone receptor positive patients makes up a significant portion of breast cancer patients. These patients have some unique characteristics and challenges that has not been described in the Sri Lankan context before.

Objectives – To describe the demographic, clinical and pathological features, side effects of hormonal treatment and long term outcome of post menopausal hormone receptor positive patients treated at the National Cancer Institute, Sri Lanka.

Method –All patients fitting the above criteria registered with the National Cancer Institute, Sri Lanka (NCISL) from 1st January 2008 to 30th April 2008 were included. Patients who had incomplete records were excluded. An event was considered as any death, relapse or loss to further follow up. All details were obtained from the patient clinic records using a data extraction form. All data were analysed using SPSS version 16 software.

Results -Out of the 155 patients registered at the NCISL during this period 20 patients were excluded due to incomplete records, wrong diagnosis and duplication .Mean age at diagnosis was 63 years. Most patients belonged to Stage II. Commonest treatment modalities were Modified Radical Mastectomy, Anthracycline and cyclophosphamide chemotherapy and conventional radiotherapy. Tamoxifen was the most used anti hormonal agent. Thromboembolic episodes and endometrial hyperplasia were commonly associated with tamoxifen while osteoporosis was the commonest side effect of Aromatase Inhibitors. 5 year Event Free Survival (EFS)for the entire cohort was the 63.4% and use of aromatase inhibitor as the initial ant hormonal agent contributed to a significantly better 5 year EFS ($P < 0.03$)

Conclusions –Demographic and clinic pathological data are similar to data from neighbouring countries. Significantly low side effects have been reported compared to accepted standards. 5 year EFS is inferior to published data from developed countries. Use of Aromatase Inhibitors conferred a better EFS compared to tamoxifen.

Table of Contents

Abstract	3
List of tables	4
List of Figures	5
Introduction	7
Objectives	9
Literature Review	10
Materials and Methods	12
Results	14
Discussion	25
Conclusions	27
Limitations	29
Recommendations	30
Acknowledgment	30
References	31
Annexures	33

List of tables

Table 1 – Distribution of age in patients -----	14
Table 2 - Distribution of patients according to tumour size.-----	15
Table 3 -Distribution of patients according to Lymph node involvement -----	16
Table 4 -Distribution of patients according to metastatic status-----	16
Table 5 -Distribution of patients according to Stage -----	16
Table 6-Distribution of patients according to tumour grade -----	17
Table 7 - Distribution of patients according to histology type-----	17
Table 8 - Common chemotherapy regimens used -----	18
Table 9 -Initial anti hormonal agent used -----	19
Table 10 -Major side effects seen during anti hormonal treatment -----	23
Table 11 -Association of side effects with type of anti hormonal therapy -----	24

List of Figures

Figure 1 Distribution of age in patients -----	14
Figure 2 - Distribution of patients according to metastatic status -----	16
Figure 3 – Distribution of patients according to Stage -----	17
Figure 4 – 5 year EFS of post menopausal, hormone receptor positive breast cancer patients at NCISL -----	23
Figure 5 – Comparison of 5 year EFS between Tamoxifen and Aromatase Inhibitors -----	24

Introduction

Breast cancer is the most common malignancy among females in Sri Lanka as well as in the world. In 2012, the estimated age-adjusted annual incidence of breast cancer in 40 European countries was 94.2/100 000 and the mortality 23.1/100 000 [1]. The mortality rate has decreased in recent years, because of the improved treatment and the earlier detection [2, 3]. However, breast cancer is still the leading cause of the cancer related deaths in the world. There are over 800 new breast cancer patients diagnosed in the National Cancer Institute, Sri Lanka each year.

Management of breast cancer has become evolved over the years. Treatment can be subdivided to 2 main components. Local treatment (surgery, radiotherapy) and systemic treatments (chemotherapy, hormones and targeted therapy). However in recent times as in all cancers more and more attention is being focused on molecular biology of cancer cell. This has resulted in treatment being highly individualized according to risk factors expressed by the individual cancer cells.

Oestrogen (ER), progesterone (PgR) and Epidermal Growth Factor HER 2 status plays a very important role in this individualization of therapy. Tumors with any detectable (>1%) expression of ER and/or PgR by Immunohistochemistry are considered as hormone- receptor positive breast cancer [4, 5]. Approximately 70% breast cancers express ER/PR and 20% show over expression of HER-2 receptors. Hormone receptor positivity generally carries a good prognosis when it comes to final outcome in breast cancer. In the presence of uncertainty of endocrine responsiveness indicated by low levels of steroid hormone receptor immune reactivity other features like grade, Ki67 assessment genomic tests such as MammaPrint, Oncotype DX, Prosigna ROR and Endopredict [6,7] plays a bigger role in deciding treatment options.

In postmenopausal ER positive breast cancers Aromatase Inhibitors (both non-steroidal and steroidal) and tamoxifen plays a central role in treatment. Aromatase Inhibitors allow for prolongation of the DFS, with no significant impact on OS (1%–2%, depending on the choice of an upfront or sequential strategy) [8–11]. They can be used upfront (nonsteroidal Aromatase Inhibitors and exemestane), after 2–3 years of

tamoxifen (non-steroidal Aromatase Inhibitors and exemestane) or after 5 years of tamoxifen (letrozole and anastrozole) as extended adjuvant therapy[12, 13].

Although there is no question of the use of aromatase inhibitors and tamoxifen in post-menopausal hormone receptor positive breast cancer patients there is still significant debate about the choice of aromatase inhibitor, sequence of treatment options and duration of treatment. The choice might depend on the morbidity pattern of the patient, patient or physician preferences and availability of drugs.

Justification -

Patients above 55 years makes up the largest subset of the breast cancer population in Sri Lanka. Out of these majority will be hormone receptor positive breast cancer. However the clinic pathological features or outcome of their treatment has not been described before.

Breast cancer in its presentation, progression and biological features are known to widely vary according to race, locality and even environment exposure. Therefore it's important to properly describe the Lankan patient profile rather than extrapolating world or regional data to Sri Lanka.

The commonest therapeutic regimen in post menopausal breast cancer patients who are hormone receptor positive will be tamoxifen or Aromatase Inhibitors. Therefore its important to adequately describe the outcome as well as the toxicity profile of these treatment regimens for the first time in Sri Lanka.

Although there are a number of regional and world studies published regarding the ideal anti hormonal drug in hormone sensitive breast cancer, there is a significant gap when it comes to Sri Lankan context. Our study aims to address this issue as well.

This study will provide baseline data for any future research carried out on post menopausal hormone receptor positive breast cancer in Sri Lanka

Objectives

General objective

- To describe the clinical features and long term outcome of patients presenting with oestrogen receptor positive breast cancer in post-menopausal patients presenting to the National Cancer Institute, Maharagama.

Specific objectives

- To describe the clinical features of patients of oestrogen receptor positive breast cancer in post-menopausal patients presenting to National Cancer Institute, Maharagama.
- To describe the different modalities of treatment in above patients.
- To analyse the 5 year overall survival of above patients.
- To analyse the 5 year event free survival of the patients.
- To describe the side effect profile of hormonal therapy used in post-menopausal breast cancer patients.
- To compare the survival rates of patients on different types of hormonal therapy.

Literature Review

Breast cancer is by far the commonest cancer in females all over the world. Jaques Ferlay et al reviewed population/hospital based cancer registries of 184 countries and described incidence and mortality of 27 major cancers in 2012. There were 1,677,000 new breast cancer patients in a year with an age standardized rate of 25.2 per 100,000. This made up 12% of all new cancer cases and 25% of all cancers in females. He also found out although in developed countries the mortality is significantly dropping, breast cancer is by far the commonest cause of death due to cancer in women in developing countries. The Sri Lankan data is also more or less similar. The most comprehensive data can be elicited from the cancer registry maintained by the National Cancer Control Program and the latest data is available from 2010 and it shows 2401 new cases diagnosed with an Age Standardized Rate (ASR) of 23 per 100,000. Breast cancer accounted for the highest number of deaths in females due to cancer with an ASR of 6.3 per 100,000. Out of all breast cancer patients 1101 (45%) were over the age of 55 years.

Hormone receptor positivity breast cancer can vary due to many factors. Ethnicity plays a major role in this. In Western countries it's as high as 77% while in Malaysia it's 56.4%

Hormone receptor positivity is a good prognostic sign in breast cancer. A SEER review done taking it to account all patients diagnosed between 1975 – 2010 by Howlader N et al found that hormone receptor positive breast cancer patients had a 5 year survival of 87.8%.

Anderson WF et al in a review of the SEER database found out hormone receptor-positive (HR-positive) breast cancer comprises approximately 75% to 80% of all breast cancers majority of them are Oestrogen receptor-positive and a lesser number are progesterone receptor-positive. Hormonal treatment for breast cancer has been used as far back as in the late 19th century when Beatson described oophorectomy as a form of treatment for advanced breast cancer. Tamoxifen was the first hormone therapy medicine to be used in breast cancer initially with advanced breast cancer and then even in early disease. The utility of tamoxifen was further enhanced by discovery

of Oestrogen Receptors in breast cancer cells by Manni et al in 1980. The National Surgical Adjuvant Breast And Bowel Project (NSABP) and the Nolvadex Adjuvant Trial Organisation (NATO) trials established beyond doubt of place of tamoxifen in post-menopausal breast cancer patients as an adjuvant therapy. Multiple trials subsequently reinforced this concept in the next few years.

Arimidex Study Group of 1996 established the place of anastrozole in relapsed patients while on tamoxifen and letrozole soon followed suit as described by Dombernowsky P et al. This led to investigation of Aromatase Inhibitors as first line treatment of breast cancer and studies done by ATAC trialist group (Anastrozole) and Mouridsen H et al (Letrozole) helped to make Aromatase Inhibitors as a first line hormone therapy in breast cancer.

Natural progression of these trials was to see if combination of tamoxifen and Aromatase Inhibitors were useful and a number of trials have examined the efficacy of switching treatments from tamoxifen to aromatase inhibitors. The favourable results of a meta-analysis of three randomised trials – the Austrian Breast and Colorectal Study Group (ABCSCG-8), Arimidex–Nolvadex (ARNO-95) and the Italian Tamoxifen Anastrozole (ITA) studies was instrumental in confirming the advantage of switch therapy.

Tamoxifen and Aromatase Inhibitors although well tolerated has their own significant side effects. Major side effects of tamoxifen being blood clots, strokes and endometrial cancers. Aromatase Inhibitors can cause cardiovascular disease, bone loss, depression etc.

Materials and Methods

This is a retrospective, cohort study conducted at the National Cancer Institute, Maharagama.(NCIM). At NCIM new patients who were referred or transferred from other hospitals or self-admitted for the first time will be and given a clinic file. This file contains patient's clinical history, investigations and all the details of treatment of the patient. The statistic unit of the NCIM maintains a database of all the patients registered at the hospital and from this data base we could identify the clinic numbers of all the breast cancer patients registered in a given period of time.

The list of the patient's clinic numbers were obtained from the statistics department after obtaining the permission of the Director, National Cancer Institute. Files of the patients who have died are kept separately and can be identified using the database of the statics department. After all the breast cancer patient clinic files were collected using the above method, clinic files of those who fit our inclusion and exclusion criteria will be selected manually by going through each and every file. Data collection from the clinic files will be carried out using a data collection form by the investigators. Participant will not be interviewed and will not be filling the data collection forms.

Patients-

There were 155 Oestrogen receptor positive postmenopausal females diagnosed with breast cancer referred to National Cancer Institute Maharagama from 01.01. 2008 to 30.04.2008. However 10 patients had to be excluded as they were duplications. Further 5 patients did not have Immuno histochemical evidence of oestrogen receptor positivity and were excluded. 7 patient records were determined to be incomplete to obtain the information needed for this study and were not included either. Therefore total number of patients included in this study for the purpose of analyzing was 133.

Data collection –

Data was collected from the patient records described above using a structured questionnaire by the investigator. (Annexure I). Extracted data included demographic data, dates of registration, treatment and clinically significant events, disease details (Histology, site of primary, metastatic status and site), treatment details (Form of local treatments, chemotherapy regimens, agents of hormonal treatment etc), comorbidities, follow up details etc.

Statistical analysis –

All the patients who conformed to the inclusion and exclusion criteria of this study were included in the final analysis. (Annexure II) Data were analysed using the SPSS version 18 software. All survival data was calculated using the Kaplan Meier curves. The significance of differences of survival was measured using the Log Rank test. The difference between 2 variables were calculated using the Pearson's Chi square test and Fischer's exact test. The level of significance was considered as 0.05.

Ethical Considerations –

During the course of this study no person identifying information was collected. Investigators took every precaution to minimise any disturbance to the day to day management of patients by accessing records only during non-clinic hours. The confidentiality of the records was further enhanced since at no point they were taken out of the clinic rooms. Ethical clearance was obtained from the Ethical Review Board of the Faculty of Medicine, University of Colombo.

Results

Demographic data –

Age –

Commonest age group in our cohort was 61 – 65 years with ≤ 60 being a close second. Mean age of the patient group was 63.92 years with a standard deviation of 5.93. The oldest patient was 81 years.

Table 1 :Distribution of age in patients

	Frequency	Percent
Valid ≤ 60 years	44	33.1
61 - 65 years	47	35.3
65 - 70 years	25	18.8
71 - 75 years	10	7.5
>75 years	7	5.3
Total	133	100.0

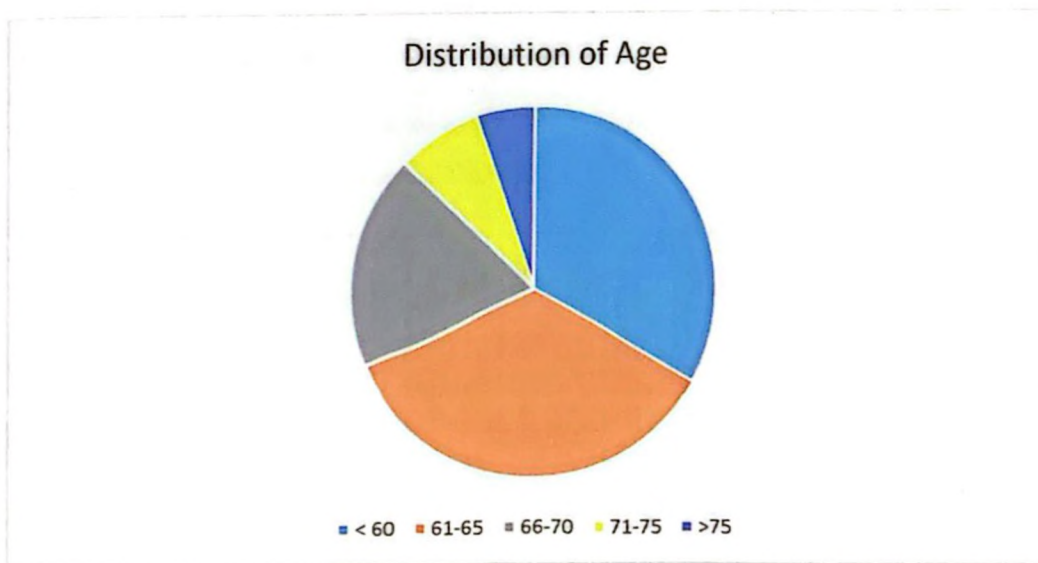


Figure 1 :Distribution of age in patients

Clinico- Pathological details –

Stage of tumour –

Size -

Majority of the patients had tumours which were 2- 5cm in size (T 2). This was followed by T 3 tumours.

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid T 1	6	4.5	4.5	4.5
T 2	61	45.9	45.9	50.4
T 3	46	34.6	34.6	85.0
T 4	20	15.0	15.0	100.0
Total	133	100.0	100.0	

Table 2 : Distribution of patients according to tumour size.

Lymph node involvement –

More than 60% had lymphnodal involvement (N 1 and above) and the extent of involvement can be characterised as follows.

	Frequency	Percent
Valid N 0	52	39.1
N 1	63	47.4
N 2	18	13.5
Total	133	100.0

Table 3 : Distribution of patients according to Lymph node involvement.

Metastatic status –

Only 21 patients (15.8%) had metastasis at presentation and most of the metastasis was seen in the lungs (64%), bone (44%) and liver (12%). 20% had metastasis at more than one site.

		Frequency	Percent
Valid	M 0	112	84.2
	M 1	21	15.8
	Total	133	100.0

Table 4 : Distribution of patients according to metastatic status.

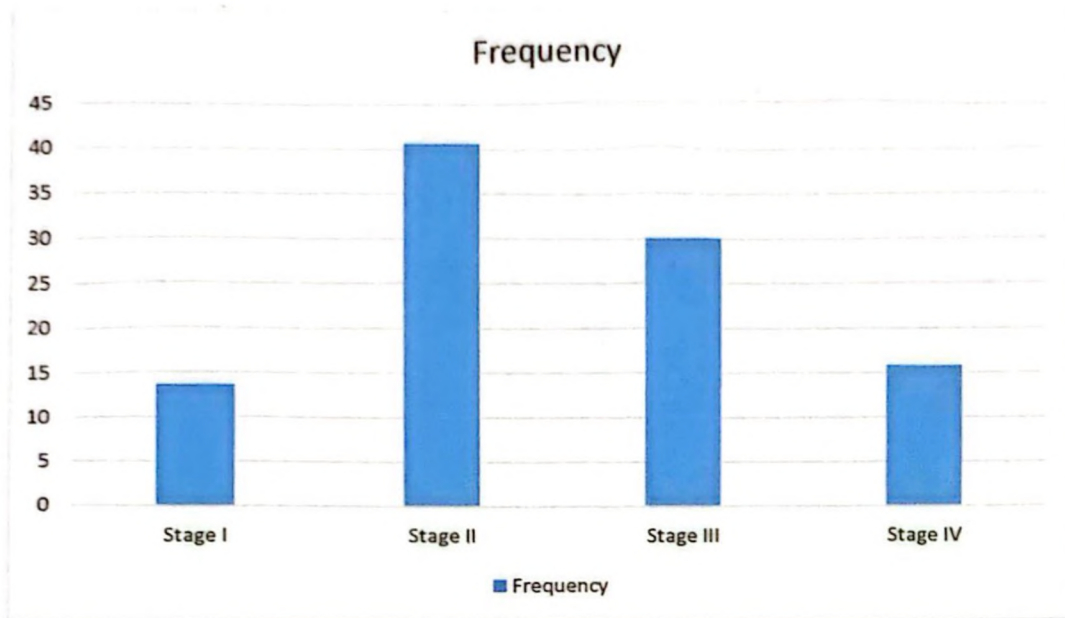
Stage (AJCC 7th Edition) –

Most of the patients belong to stage II and III while Stage I had the least number. Stage II patients numbered 54 while there were 40 patients in Stage III. Only 18 patients were in Stage I.

	Frequency	Percentage
Stage I	18	13.6
Stage II	54	40.6
Stage III	40	30
Stage IV	21	15.8
	133	100%

Table 5 : Distribution of patients according to Stage

Figure 2: Distribution of patients according to Stage



Grade of tumour –

85(63%) of patients had Grade 11 tumours and rest were almost divided equally with Grade I and III tumours.

		Frequency	Percent
Valid	Grade 1	23	17.3
	Grade 2	85	63.9
	Grade 3	25	18.8
	Total	133	100.0

Table 6 : Distribution of patients according to tumour grade.

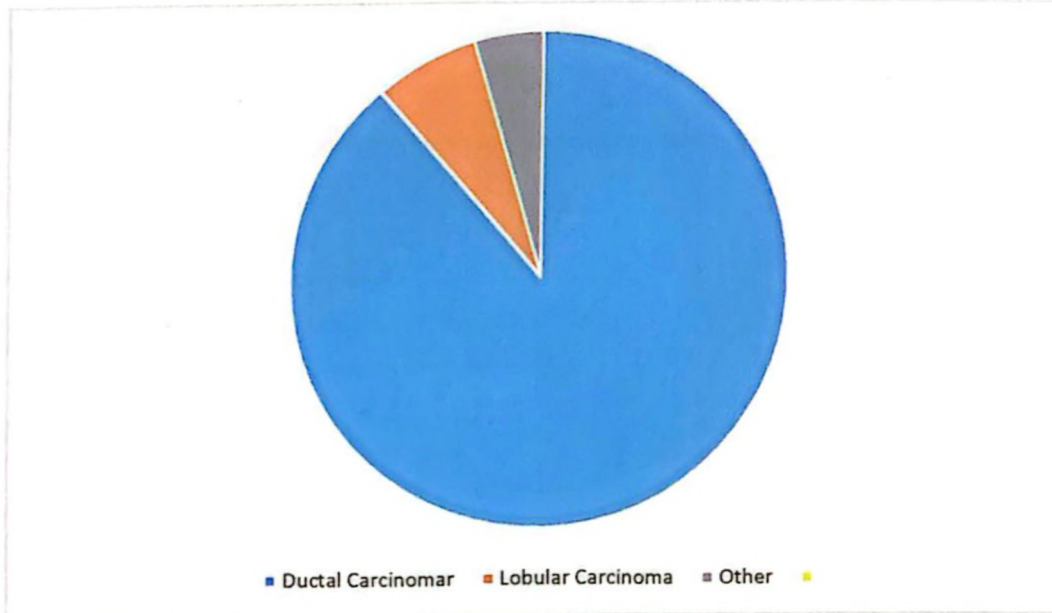
Histology -

Ductal carcinomas were the histology of the vast majority of tumours with the rest making up only a very small component. There were 118 patients (88.7%) with ductal carcinoma in this cohort.

	Frequency	Percent
Valid Ductal carcinoma	118	88.7
Lobular carcinoma	9	6.8
Others	6	4.5
Total	133	100.0

Table 7: Distribution of patients according to histology type

Figure 3: Distribution of patients according to histology type



Form of local treatment –

Surgery –

Details were not available for 22 patients regarding the type of surgery they had.

From the rest of the 111 patients 96 had Modified radical Mastectomy with Axillary Clearance and 15 had Wide Local Excision with Axillary Clearance.

Chemotherapy –

80 had chemotherapy with curative intent while 22 had with palliative intent. Most frequently used chemotherapy regime was Adriamycine with Cyclophosphamide(AC) and 5 Fluro uracil, Adriamycinee with Cyclophosphamide was the second commonest. (FEC)

	Number	%
AC +/- Taxanes	37	46.25
FEC	15	18.75
CMF	24	30
TAC	4	5
	80	100

Table 8: Common curative chemotherapy regimens used

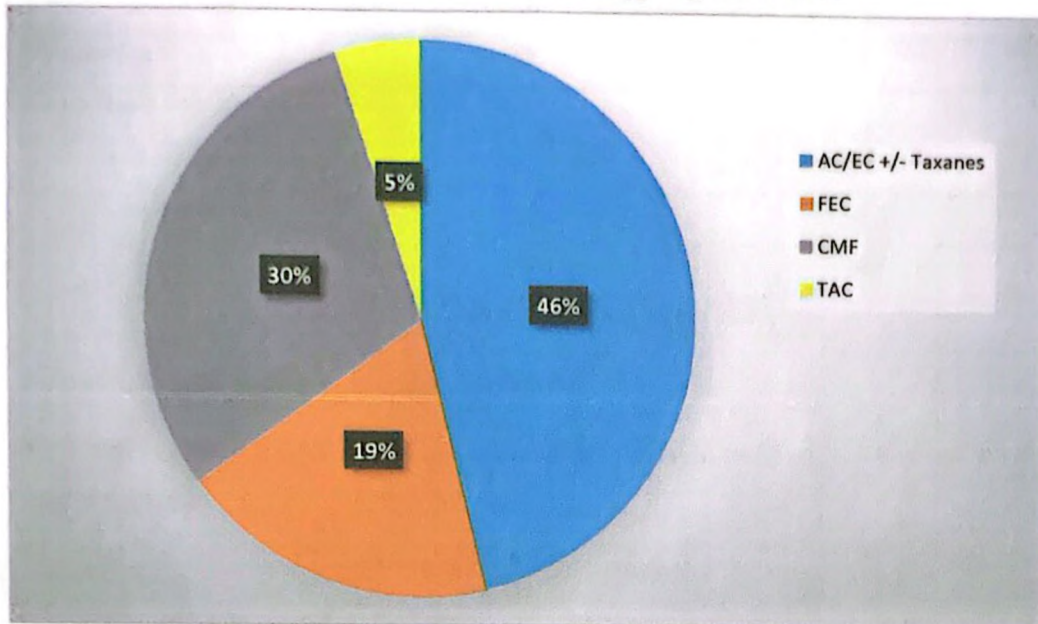
AC = Adriamycine + Cyclophosphamide

FEC = 5 Fluro Uracil + Epirubicin + Cyclophosphamide

CMF = Cyclophosphamide + Methotrexate + 5 Fluro Uracil

TAC = Taxol + Adriamycine+ Cyclophosphamide

Figure 4: Common chemotherapy regimens used



Radiotherapy –

Out of the 133 patients in the cohort 100 had radiotherapy as part of their treatment and 83 were treated using conventional radiotherapy and 17 were treated conformally.

Anti Hormonal Treatment –

All patients in the cohort had anti hormonal treatment. Tamoxifen by far the commonest agent used. More than one hormone therapy agents were used in 65 patients within 5 years of starting treatment. Out of this 40 were at relapse. From the total number of patients who had more than one anti hormonal agent, tamoxifen was the initial hormonal agent used in 42 patients, Anastrozole in 12 and Letrozole in 11.

Tamoxifen was used on average for 3.74 years (SD 1.064, Range 1- 5 years)
Anastrozole for 3.65 years (SD 1.427, Range 1-5 years) and Letrozole for 3.95 years (SD 1.129, Range 2-5 years)

	Number	%
Tamoxifen	82	61.6
Aromatase Inhibitors		
Anastrozole	32	24
Letrozole	19	14.4
	133	100

Table 9: Initial anti hormonal agent used

Side effects seen with anti hormonal treatment –

Vast majority did not report any major side effects (67%). Commonest side effect seen was osteoporosis.

Side effect	Number	%
Thrombo embolic episodes	11	8.3
Endometrial hyperplasia	12	9
Osteoporosis	13	9.7
Liver dysfunction	8	6.1
No major side effect	89	65.9
	133	100

Table 10: Major side effects seen during anti hormonal treatment –

Association of side effects with type of anti hormonal therapy –

Tamoxifen use was significantly associated with thromboembolic episodes when compared with aromatase inhibitors. Aromatase Inhibitors were significantly associated with osteoporosis. Endometrial hyperplasia and liver dysfunction was not significantly associated with any of the agents.

Agent	Side Effect seen	Side Effect not seen	
Thrombo embolism			
Tamoxifen	10	72	82
Aromatase Inhibitors	1	50	51
	11	122	133
$X^2 = 4.3411, p = 0.03722$			
Endometrial hyperplasia			
Tamoxifen	10	72	82
Aromatase Inhibitors	2	49	51
	12	121	133
$X^2 = 2.6211, p = 0.10538$			
Osteoporosis			
Tamoxifen	3	79	82
Aromatase Inhibitors	10	41	51
	13	120	133
$X^2 = 9.0697, p = 0.00259$			
Liver dysfunction			
Tamoxifen	4	78	82
Aromatase Inhibitors	4	47	51
	8	125	133
$X^2 = 0.489, p = 0.48473$			

Table 11: Association of side effects with type of anti hormonal therapy

Survival –

Event Free survival (EFS) –

5 year EFS for the entire cohort was 62.4%. A recurrence, death and loss for follow up was considered as an event.

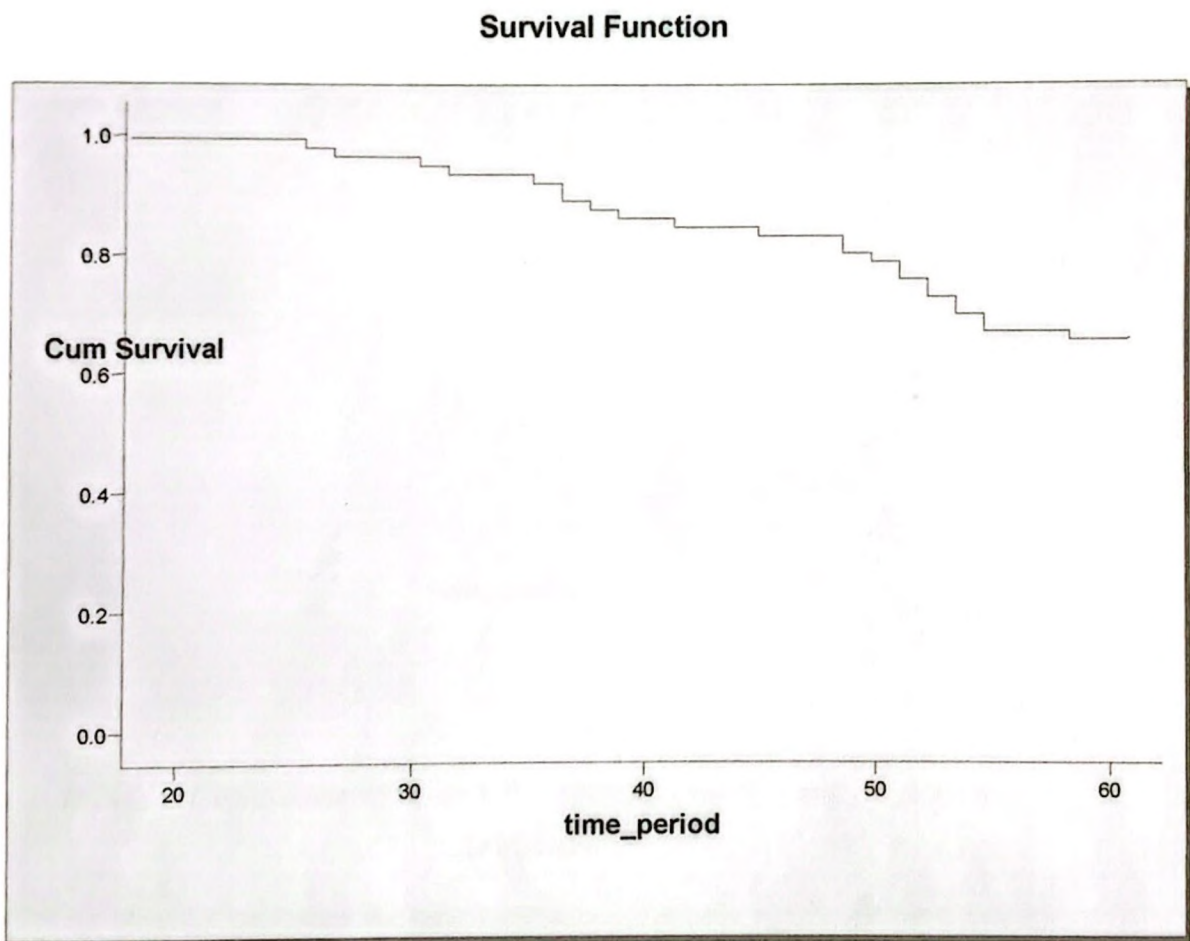


Figure 4: 5 year EFS of post menopausal, hormone receptor positive breast cancer patients at NCISL

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	4.447	1	.035

5 year EFS Tamoxifen Vs Aromatase Inhibitors -

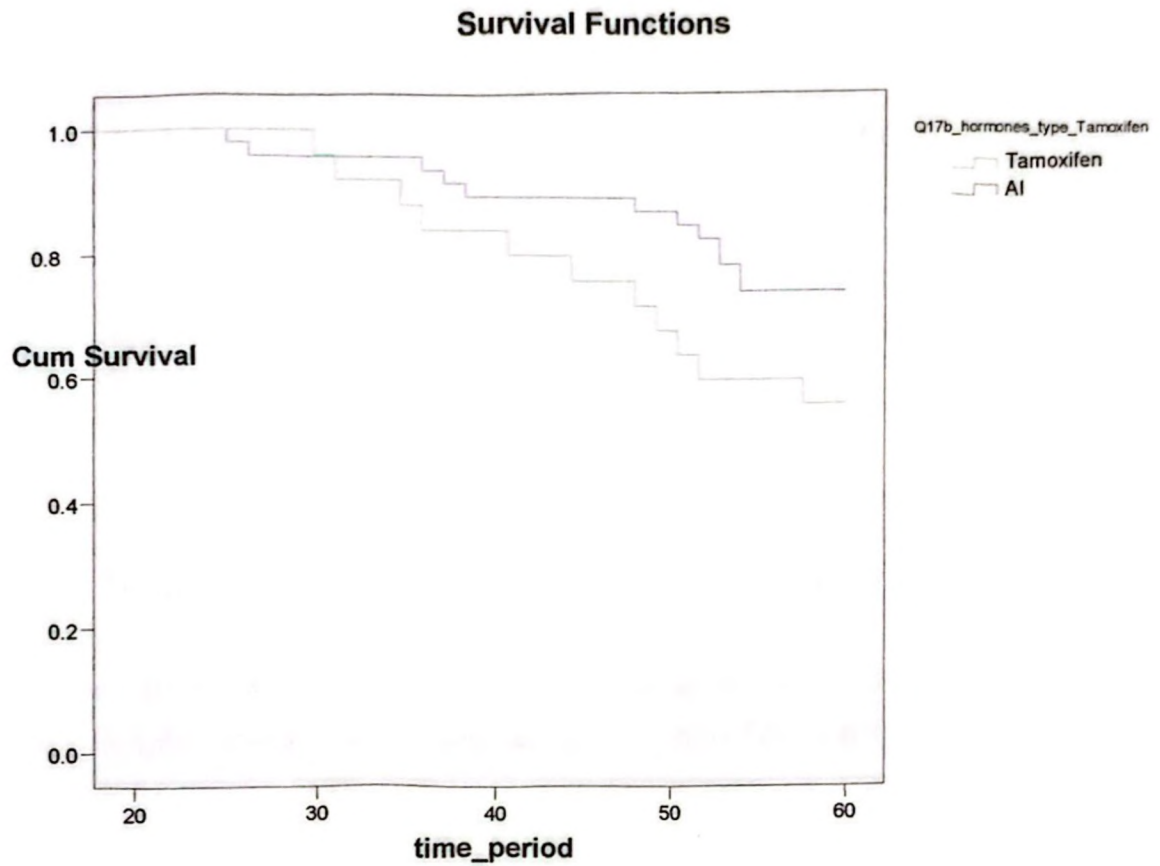


Figure 5: Comparison of 5 year EFS between Tamoxifen and Aromatase Inhibitors

Patients who were on Aromatase Inhibitors had a statistically significant better 5 year EFS compared to patients on Tamoxifen. (76% vs 59%) For this analysis patients who were on switch therapy and therefore who had both agents before an event occurred were excluded.

Discussion

Demographic data –

In this study the commonest age group of patients seen was 60-65 years with age group 55-59 coming a close second. This is somewhat similar to the other published Sri Lankan data(1) where these age groups generally have the highest incidence. Mean age of diagnosis of in our cohort was 63 years. This is similar to the international data as seen by the SEER database review by Howlander et al in 2014(2). Unfortunately, we couldn't find any similar studies coming from Asia where only women above 55 years were included.

Stage –

Although from 2018 staging of breast cancer has changed we have used the previous (AJCC 7th edition) (3) staging system as the patients under study have been staged according to the old system.

In the developed world due to various factors like screening programs, availability of medical care etc more early breast cancers are detected (2). In Asia there is a large disparity as in countries like India, Stage III breast cancers accounted for over 50% of breast cancers in post menopausal women while Stage I accounting for only 4%. Compared to Hongkong where Stage II was the commonest with 43% and Stage I being a close second with 30%. (4) Although genetic make up might play a role in this difference factors like access to health care, health seeking behaviours etc would be playing a major role. Sri Lankan situation seem to be in between these two extremities with commonest being Stage II cancers with 40.3% and Stage I being 13.3%. This probably implies also patients presents relatively early, lack of a formal screening system means very early disease is missed.

Grade –

In the University of Malay, Malaysia registry 55% of patients had Grade II cancers. (4) how ever in our population although Grade II was the commonest it had a much higher proportion of 63.9%. The reason for this difference cannot be clearly explained.

Treatment –

Surgery – In our cohort 86% of had modified radical mastectomy as the preferred method of surgery. In western countries Wide Local Excision accounts for 70-80% of surgeries for breast cancer.(5) Although higher percentage of patients presenting with bigger tumours may be a reason for this, fact that even in other Asian developed countries like Singapore where patients present early has a high mastectomy rate (60-70%)(6) suggests other issues such as cultural factors like Asian women being less concerned about body image, risk averse behaviour might be important as well.

Radiotherapy – From all the patients who were treated with radiotherapy 83% had conventional radiotherapy. This reflects the demand in NCISL for the Linear Accelerator. Due to the long waiting period and the relative ease of planning chest wall radiotherapy vast majority of patients had their radiotherapy in the Cobalt 60 machines.

Chemotherapy – As expected anthracycline based chemotherapy (46%) was the commonest regimen employed in treating patients. However, CMF regimen was 2nd commonest with 30%. This may be due to that this is a relatively aging population with multiple comorbidities.

Anti-Hormonal agents – There is clear evidence to suggest that in post-menopausal women aromatase inhibitors is the preferred form of anti-hormonal agents. (7) However surprisingly in our cohort tamoxifen was the starting agent in 61.6% patients. This might be due to wider availability of tamoxifen and perceived better side effect profile might be reasons for this. There is evidence to suggest that letrozole has a better efficacy and side effect profile compared to anastrozole.(8) However the preferred aromatase inhibitor in this cohort was anastrozole. (62.7%) Without tumour recurrence switch therapy was used in 61.5% of the patients only. Again this might be due to unavailability of Aromatase Inhibitors.

Side effects seen after initiation of hormonal therapy –

As expected number of side effects were seen with the starting of anti-hormonal treatment. However reported incidence of all the side effects was significantly less than reported. (9) This might be due to poor reporting of these side effects and some of the investigations to detect those side effects not being widely available. (Dexa scans). Majority of patients did not have a screening at the onset of hormonal therapy to look for baseline status of these side effects. With tamoxifen thromboembolic episode and endometrial hyperplasia (with 2 reported incidences of endometrial adenocarcinoma) were the commonest and osteoporosis with aromatase inhibitors was the commonest side effect seen.

Event free survival –

Overall 5year EFS for the entire cohort was 62.4%. This is far inferior than 80% described in wester literature. (10), (7) The reason for this deficit is multi factorial and cannot be described from the data obtained from this study. We don't have enough subject numbers to do a regression analysis to assess the impact of hormonal therapy on this deficit.

In the ATAC trial where 6247 patients were studied Aromatase Inhibitors displayed a significantly better EFS compared to tamoxifen with a p value of less than 0.03(11) Our cohort also showed similar results but with almost similar p value of 0.035.

Conclusions

- Mean age of diagnosis for patients who were hormone receptor positive and above 55 years was 63 years.
- Commonest Stage of presentation of the above patients was Stage II
- Majority of the patients had Modified Radical Mastectomy as the preferred surgery, Anthracycline based chemotherapy regimens was the commonest chemotherapy used and conventional radiotherapy was the most frequent radiotherapy technique.
- Commonest side effect for patients on tamoxifen was thrombo embolic episodes while for aromatase inhibitors it was osteoporosis.
- The 5 year event free survival of this cohort was 62.4%.
- Patients on aromatase inhibitors had a significantly better 5 year EFS compared to tamoxifen

Limitations

This was a study done in only one institution. Although this is the largest cancer center in Sri Lanka the data gathered from one unit possibly cannot be generalised to the whole Sri Lankan population. Also due to logistical reasons data was gathered on patients who were registered with the NCISL during 3 months only. If more subjects were included in the study the power of the conclusions could have been increased and further sub group analysis could have been done to make this study more meaningful.

All the data was obtained solely from clinic records retrospectively. However NCISL has only a written clinic records and some of these records are incomplete. This would have an impact on the accuracy of the findings. Death was hardly ever recorded in the clinic files. Therefore although Overall Survival measurement was one of our objectives this could not be achieved.

When we analysed side effects of different hormonal agents we considered only the initial agent used. However, in patients who were on switch therapy would have been on more than one hormonal agent. Therefore when comparing side effects between hormonal agents the findings are diluted by this switch.

In this study we have assumed all patients above 55 years are post-menopausal women.

Recommendations

To establish a database with prospective collection of information regarding patient demographics, treatment modalities, side effects, outcomes etc to improve accuracy and reliability of data collected for future studies. Such a database is important from quality improvement perspective as well.

To conduct a similar study covering all cancer treatment units in Sri Lanka to gather national level data.

Establishing breast cancer investigation and treatment protocols based on the available standard guidelines to ensure standardized treatment of all breast cancer patients.

Acknowledgment

Dr.Sujeewa Weerasinghe MD, for all the guidance given while supervising this project.

The director and all the consultants at NCISL for granting permission to access their patient's records.

Mr. SithumManjika of the Community Medicine department of Sri Jayawardenapura Medical Faculty for help with the statistical analysis.

Dr.Rathnasena and staff of NCISL who helped in extracting information from clinic files.

References

1. National Cancer Control Program. Cancer Incidence Data Sri Lanka 2010. 2010.
2. Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ CK (eds). SEER Cancer Statistics Review 1975-2014 National Cancer Institute SEER Cancer Statistics Review 1975-2014 National Cancer Institute. 2017;(April):2012–4.
3. Hortobagyi GN, Connolly JL, D’Orsi CJ, Edge SB, Mittendorf EA, Rugo HS, et al. AJCC Cancer Staging Manual, Eighth Edition: Breast. 2017. 589-636 p.
4. Agarwal G, Pradeep P V., Aggarwal V, Yip CH, Cheung PSY. Spectrum of breast cancer in Asian women. *World J Surg.* 2007;31(5):1031–40.
5. Agarwal S, Pappas L, Neumayer L, Kokeny K, Agarwal J. Effect of breast conservation therapy vs mastectomy on disease-specific survival for early-stage breast cancer. *JAMA Surg.* 2014;149(3):267–74.
6. Chan PMY, Choo BA, Zhang T, Seah MDW, Chen JJC, Lu SQH, et al. Mastectomy rates remain high in Singapore and are not associated with poorer survival after adjusting for age. *Springerplus.* 2015;4(1):1–10.
7. Monnier A. Refining the postmenopausal breast cancer treatment paradigm: The FACE trial. *Expert Rev Anticancer Ther* [Internet]. 2006;6(10):1355–9. Available from:
<http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L44697161%5Cnhttp://dx.doi.org/10.1586/14737140.6.10.1355%5Cnhttp://sfx.library.uu.nl/utrecht?sid=EMBASE&issn=14737140&id=doi:10.1586/14737140.6.10.1355&atitle=Refining+the+postmenop>
8. Smith I, Yardley D, Burris H, De Boer R, Amadori D, McIntyre K, et al. Comparative efficacy and safety of adjuvant letrozole versus anastrozole in

postmenopausal patients with hormone receptor-positive, node-positive early breast cancer: Final results of the randomized phase III femara versus anastrozole clinical evaluation . *J Clin Oncol*. 2017;35(10):1041–8.

9. Sainsbury R. The development of endocrine therapy for women with breast cancer. *Cancer Treat Rev* [Internet]. 2013;39(5):507–17. Available from: <http://dx.doi.org/10.1016/j.ctrv.2012.07.006>
10. Boccardo F, Guglielmini P, Bordonaro R, Fini A, Massidda B, Porpiglia M, et al. Switching to anastrozole versus continued tamoxifen treatment of early breast cancer: Long term results of the Italian Tamoxifen Anastrozole trial. *Eur J Cancer* [Internet]. 2013;49(7):1546–54. Available from: <http://dx.doi.org/10.1016/j.ejca.2012.12.025>
11. Cuzick J, Sestak I, Baum M, Buzdar A, Howell A, Dowsett M, et al. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 10-year analysis of the ATAC trial. *Lancet Oncol* [Internet]. 2010;11(12):1135–41. Available from: [http://dx.doi.org/10.1016/S1470-2045\(10\)70257-6](http://dx.doi.org/10.1016/S1470-2045(10)70257-6)

Annexure I

A retrospective analysis of clinical features, treatment related complications and outcome of postmenopausal females with oestrogen receptor positive breast cancer treated at National Cancer Institute, Maharagama

1. Serial No :
2. Clinic No :
3. Name :
4. Age (Years) :
5. Home Town / District :
6. TNM :

T		N		M	
---	--	---	--	---	--
7. Grade :

i.		ii.		iii.	
----	--	-----	--	------	--
8. Date of First Presentation to NCIM

Year	Month	Date

9. Histological Type

Ductal Carcinoma		
Lobular carcinoma		
Others		

10. Metastatic Screening

	Yes	No	Result
CXR			
USS			
Bone Scan			
CT Scan			

If metastatic the site / s-

11. Co Morbidities

	Yes	No
DM		
HT		
IHD		
BA		
Renal Failure		
Other		

12. Treatment Sequence

Surgery	
Chemotherapy	
Radiotherapy	
Hormones	
Target Therapy	

13. Surgery

MRM / AC / SLE	
WLE/AC/SLB	
Palliative Surgery	

14. Chemotherapy

Neo Adjuvant Chemo	
Adjuvant Chemo	
Palliative Chemo	

15. Type of Chemotherapy

CMF	
FAC / FEC	

TAC	
AC / EC	
Paclitaxol	
Docetaxol	
Others	

16. Radiotherapy

Cobolt 60	
3 D Comformal	
Dose	
Boost	

17. Hormones

Started on

Finished on

Year	Month	Date

Year	Month	Date

Type	Duration (Years)
Tamoxifen	
Aromatase inhibitors	
1. Letrazole	
2. Anastrozole	
3. Aromocin	
Tamoxifen → Aromatase Inhibitors	
Aromatase inhibitors → Tamoxifen	

18. Side Effects of Hormones

Thromboembolism / DVT	
IHD / CVA	
Endometrial hyperplasia	
Endometrial adenocarcinoma	
Osteoporosis / Osteopenia	
Liver functions	
Others	

19. Target therapy

Yes / No	Type	Duration

20. Date of the detection of local recurrence / Metastasis/ Progression / Death

Year	Month	Date

- How it was detected
- Site

21. Time since initiation of Hormones

Year	Month

22. Next line of treatment

23. Out - come

24. Special remarks

Annexure II

Inclusion criteria

- New postmenopausal females or above 55 years of age with breast cancer with positive estrogen receptor status.
- Registered with the National Cancer Institute Sri Lanka from 01.01.2008 to 30.04.2008.

Exclusion criteria

- ER/PR status not available patients are excluded.
- Those who have been treated previously for breast cancer at other hospitals will be excluded.
- Patients should not be on GNRH Agonist or Antagonist.