ORIGINAL ARTICLE

Association of comorbidities with breast cancer: An observational study

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Abstract

Background: The aim of this study was to describe the prevalence of comorbidity in newly diagnosed female breast cancer patients in north-west India. The second end point of the study was compliance for multimodality treatment. Comorbidity assessed by counting the number of coexisting diseases diagnosed in a cancer patient or by using a comorbidity index that combines the number and severity of the diseases. The most widely used index is the Charlson Comorbidity Index (CCI). **Materials and Methods:** The data of female patients with breast cancer were recorded, having comorbidities during the cancer registration or comorbidities diagnosed during the treatment at the host institute between January and December 2012. The patients were distributed on the basis of physical parameters such as age, stage, tumor grade, hormone receptor status, ECOG status at diagnosis and CCI. Scores of CCI are summed to provide a total score to predict mortality. **Results:** During the period of January to December 2012, 156 biopsy-proven breast cancer patients were included in the study. During this period, female breast cancer patients enrolled were 13.94% out of total patient enrollment. The most prevalent comorbidities associated with breast cancer are hypertension (21.8%), chronic obstructive pulmonary disease (COPD) (19.9%), rheumatologic disease (18.6%), and diabetes mellitus (16.7%), all four conditions have been reported in around 75% of the cases. The planning of multimodality management in comorbidity arm was significantly lower ($P > 0.01$) as compared to patients without comorbidity. **Conclusions:** The planning of multimodality management in comorbidity arm was significantly lower as compared to patients without comorbidity. Because of the comorbid condition, the definitive treatment of breast cancer was not given so this will also affect the treatment of breast cancer. When the CCI score increases with an increase in the number of comorbidities will decrease survival.

Keywords: Breast cancer, Charlson Comorbidity Index, comorbidity, north-west India

Introduction

Comorbidity is defined as "any additional clinical condition that has existed simultaneously or that may occur during the clinical course of a patient with an index disease under study."[1,2] Comorbidity must also be distinguished from complications that arise as a consequence of cancer or its treatment. A number of studies have examined the prognostic impact of patients' "performance status" at the time of cancer diagnosis. Performance status is a measure of a cancer patient's well-being, defined as the amount of normal daily activity the patient can maintain.[3-5] However, the performance status is affected by cancer, complications of cancer, and comorbid conditions.[6] The aim of this study was to describe the prevalence of comorbidity, deviation from

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standard treatment because of comorbidity, and in newly diagnosed breast cancer patients in north-west India. The second end point of the study was comparison of progression free survival with noncomorbid breast cancer patients.

Materials and Methods

The patients with histologically proven malignancy attending the Department of Oncology, at Regional Cancer Treatment, during the period January 2012 to December 2012. During this period, female breast cancer patients enrolled were 13.94% (976/7001) out of total patient enrollment. Out of these 976 (13.94%) patients, 156 (15.98%) patients were associated with comorbidities. The treatment planning done for 156 randomly selected patients without any co morbidity was compared with that done for patients with co morbidity. All patients were examined clinically and requisite investigations (e.g., hematological, biochemical, and imaging) to have an assessment of the extent of malignancy were done. The attendants of the patients were subjected to a counseling session regarding the nature of disease, associated co-morbidities, treatment options, and prognosis. All the patients were assessed by taking a detailed history with complete general physical examination. The performance was determined as per the Eastern Cooperative Oncology Group (ECOG) scale and the co-morbidity score was calculated by Charlson Comorbidity Index (CCI). Hematological, biochemical, and radiological investigations were performed before the actual treatment started, during treatment, and at the follow-up. Clinical staging and stage grouping were done according to the tumor node metastasis (TNM) [Union for International Cancer Control—American Joint Committee on Cancer (UICC—AJCC) staging] classification. The comorbidities were searched by detailed history; complete general physical examination; and required biochemical, hematological, and radiological investigations [*viz*. blood pressure test, electrocardiogram (ECG), echocardiography, color Doppler, joint X-rays, ultrasound (abdomen + pelvis)]. The detected comorbidities were treated accordingly by respective specialized specialists. Based on the ECOG performance status, the site of the disease, stage, and affordability, the patients were treated with either combined chemotherapy and radiotherapy ± surgery, or chemotherapy ± surgery, or radiotherapy ± surgery, or surgery alone. The drugs used were cyclophosphamide, methotrexate, 5-fluorouracil, doxorubicin, platinum agents, paclitaxel, etc., as per the chemotherapy schedule chosen. Nursing care was taken for proper drug route selection, preparation of the patient, pretreatment evaluation, and assessment of the hematological and clinical parameters. The patients were monitored after the treatment to detect any toxicity. Radiotherapy was delivered using appropriate portals, the radiotherapy planning was done on the simulator, and the treatment planning system was Co_{60} teletherapy unit (Theratron 780E/C, Best Theratronics Canada). Toxicity monitoring was done. The definitions of complete and partial response, stable disease, and progressive disease were based on the standardized response definitions of the World Health Organization (WHO).

Results

During the period of January 2012 and December 2012, 156 biopsy-proven breast cancer patients with associated comorbidity were included in the study. In this study the comorbidities prevalent in female breast cancer patients was studied. The demographic profile is shown in Table 1, and the patients were arranged according to the associated comorbid condition. Most prevalent associated comorbidities related to breast cancer are hypertension [34 (21.8%)], chronic obstructive pulmonary disease (COPD) [31 (19.9%)], rheumatologic disease [29 (18.6%)] and diabetes mellitus [26 (16.7%)], all four conditions were reported in more than 75% of the cases [Table 2]. Another finding was that patients with comorbidity do not receive standard cancer treatments such as surgery, chemotherapy, and radiation therapy as often as patients without comorbidity. The planning of multimodality management in comorbidity arm was significantly lower (Complete Response (CR) = 68.3% *vs* Partial Response (PR)/ Stable disease (SD)/Progressive disease (PD) 37.4% $P >$

Table 1: Demographic characteristics of the breast cancer patients

Characteristic	Breast cancer patients *N*=156 (%)
Age (years)	
Median 48 (26-75) ≤40	33 (21.1)
41-60	97 (62.2)
>60	26 (16.7)
Stage	
I	17 (10.9)
II	39 (25.0)
III	60 (38.5)
IV	40 (25.6)
Tumor grade	
Well differentiated	36 (23.1)
Moderately differentiated	50 (32.0)
Poorly differentiated	33 (21.2)
Undifferentiated	37 (23.7)
Unknown	
ER/PR status	
Positive	99 (63.5)
Negative	24 (15.4)
Unknown	33 (21.1)
ECOG	
0	59 (37.8)
1	67 (42.9)
2	30 (19.2)

TNM=Tumor node metastasis, ECOG=Eastern cooperative oncology group

0.01) as compare to patients without co-morbidity [Table 3]. This study shows that older women (>60 years), at the time of breast cancer diagnosis, have more prevalence of comorbid conditions than the younger population. In addition, the stage at diagnosis is associated with the variability in the prevalence of many conditions. The CCI score is depends upon number of comorbidities and age. According to CCI score mortality at 12 months and survival at 10 years can be calculated. When the CCI score increases due to increase in number of comorbidities, It affects survival at 12 months year as well as at 10 year survival outcome. Similarly when CCI score increases because of age group (i.e. <40, 41–50 years) than the 12 months survival is remains same for all age group but only 10-year survival outcome affected [Table 4].[7-9] These results are calculated by using the CCI.

Table 2: Prevalence proportions for comorbid conditions in breast cancer patients

Comorbid condition	Breast cancer patients
Cardiac/vascular	
Coronary artery disease/myocardial infarction	8 (5.1)
Congestive heart failure	4 (2.6)
Cerebrovascular disease	4 (2.6)
Hypertension	34 (21.8)
Peripheral vascular disease	3 (1.9)
Gastrointestinal	
Gastric ulcers	18 (11.5)
Metabolic	
Diabetes	26 (16.7)
Musculoskeletal/rheumatic	
Rheumatologic disease	29 (18.6)
Pulmonary	
Chronic obstructive pulmonary disease	31 (19.9)

Table 3: Treatment profiles: Treatment compliance, type of treatment received, and treatment response

Treatment compliance	*N*=156 (%)		
Complete	138 (88.46)		
Incomplete	18 (11.5) (8,10missed)		
Type of treatment given			
CT and RT both±Sx	69 (44.2)		
RT±Sx	66 (42.3)		
CT±Sx	6 (13)		
Surgery alone	2 (5)		
Treatment response*			
Complete response	Partial response	No response	Progressive disease
91 (58.3)	9 (5.7)	17 (10.9)	21 (13.5+11.5*)

CT=Chemotherapy, RT=Radiotherapy, Sx=Surgery. *11.5% patients missed treatment or lost to the follow-up

Discussion

Due to the presence of comorbidities, the complexities have influenced the cancer patient's preferences for the treatment and treatment outcomes. Comorbidity generally increases with increasing age, and it may be the cause behind age-related differences in cancer diagnosis, treatment, and outcome. The significant findings of the study that patients with comorbidities were aged >60 years mostly. Seventy-five percent of the comorbid conditions are chronic diseases such as hypertension (21.8%), COPD (19.9%), rheumatoid arthritis (18.6%), diabetes mellitus (16.7%). All of the above-mentioned diseases are partly associated with the lifestyle behavior. Because the incidence of most cancers increases with advancing age, it is not surprising that comorbidity has been frequently found among patients with cancer.[10] Comorbidity has often been associated with less aggressive treatment and poor cancer outcomes even after the treatment.[11-17] The 1-year survival across the demographic age group in the study is not significantly altered, although it has a significant effect on the 10-year survival and overall quality of life. The comorbidity could also serve as a competing demand for primary care physicians, decreasing the likelihood of cancer screening recommendations.[18] The CCI (Co-morbidity-Adjusted Life Expectancy) predicts the 10-year mortality for a patient who may have a range of comorbid conditions.

Table 4: Distribution of the patients according to the CCI score, with 12-month mortality and 10-year survival analysis

Charlson comorbidity index score	*N*=156 (%)	12-month mortality# (%)		10-year survival$ (%)
Non-metastatic disease	106 (74.4)	(No. of comorbidity)	(No. of comorbidity)	
3	21 (13.5)	19.27 (1/2)	-	77.48
4	37 (23.7)	19.27 (1/2)	-	53.39
5	42 (26.9)	19.27 (1/2)	32.55 (3)	21.36
6	14 (9.0)	19.27 (1/2)	32.55 (3)	2.25
7	3 (1.9)	19.27 (1/2)	32.55 (3)	0.01
Metastatic disease	40 (25.6)			
7	13 (8.3)	37.12		0.01
8	9 (5.8)	37.12		0.00
9	8 (5.1)	37.12		0.00
10	10 (6.4)	37.12		0.00

#12-month mortality (does not utilize age and is based on 1996 article). $10-year survival (utilizes age and is based on 1994 article). CCI=Charlson comorbidity index

Each condition is assigned a score of 1, 2, 3, or 6, depending on the risk of dying associated with each one. In contrast, the incidence rates of co-morbid conditions; stratified by stage at diagnosis, show that most advanced cancer stage is associated with a greater likelihood of new comorbid conditions. Because of the comorbid condition, the definitive treatment of breast cancer was not given so this will also affect the cure of breast cancer. The strength of this study lies in its detailed information of the patient complaints, obtained through work-up, proper questionnaire, nursing care, psychological counseling, regular follow-up, work-up at every phase of treatment for adverse events if any at any point of the study was taken. The limitation of the study is the analysis of the study using CCI. The limitations of CCI, potentially resulting in bias and confounding are as follows: First, it incorporates 48 available information about comorbid conditions into an aggregate index, which precludes estimation of effects of individual comorbid diseases. Second, it does not include all medical conditions and psychiatric diseases that can confer substantial morbidity even in patients with diagnosis of index diseases. Third, duration is not accounted for, and severity is only considered to a very limited extent. As an example, consider the effect of diabetes, which increases risk of death with duration, whereas the effect of cancer diseases often decreases with survival beyond 5 years. In the CCI, only diabetes and liver disease are divided into only two severity groups, both disease types can be more finely parsed, and other CCI diseases have important severity grades, for example COPD. Fourth, the CCI diseases can be measured using several methods, 133 patients with varying weaknesses and no gold standard. This study highlights the effect of comorbidities on the treatment of the patient. In rural centers where the patients are not able for regular follow-ups, the comorbidities can further deter the compliance of the patients. As enumerated in this study, there are considerable modifications in the treatment of the patients and this further delay the definitive treatment. This study further raises a question on the protocols as per the comorbidities that are encountered in the practice. Studies in larger groups need to be undertaken to establish best possible guidelines to improve the quality of care, the quality of life, and the quality of treatment in such patients.

Abbreviations

CCI = Charlson Comorbidity Index.

ECOG = Eastern Cooperative Oncology Group.

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Conflicts of interest

There are no conflicts of interest.

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