Oncological Safety of Breast Conservation Surgery in Young Females

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Abstract Breast conservation surgery (BCS) is the standard of care in early breast cancer. The oncological safety of this procedure has been proven beyond doubt in several randomised control trials. But there are concerns regarding the safety of this procedure in young females. The concern is regarding increased risk of local recurrence. This issue has not been addressed in any major trial. In this prospective study we intend to look into the oncological safety of BCS in young patients who are less than forty years of age.

Keywords Breast conservation surgery · Young females · Local recurrence · Survival

Introduction

Several randomized control trials have confirmed the oncological safety of breast conservation surgery (BCS) in early stage breast cancers. But there have been concern regarding the safety of this procedure in young patients. This is mainly because of the fact that malignancies in younger patients are more aggressive when compared to malignancies in the elderly postmenopausal patients [1]. Young age is considered to be a poor prognostic factor and a determinant for the development of local recurrence following BCS for invasive

carcinomas of the breast. Several studies have questioned the safety of BCS in young females [2, 3]. But there are reports to the contrary, confirming the safety of breast conservation in young patients [4].

Breast cancer patients would like their breast to be conserved and a mutilating surgery like modified radical mastectomy would have long term psychological impact on their lives. We at Regional Cancer Centre (RCC) have been offering breast conservation surgery for all possible patients for the past two decades. This includes a large number of young patients as well. We decided to analyze the oncological safety of breast conservation in young females who underwent treatment at our centre.

Patients and Methods

Medical records of all patients below forty years of age who underwent Breast Conservation Surgery (BCS) at Regional Cancer Centre, Trivandrum, Kerala, India during the period July 2005 to June 2008 were analyzed.

Those patients being offered BCS after neoadjuvant chemotherapy, bilateral breast cancers, and other previous tumors were excluded from the analysis. Patients having positive margins on histopathological analysis were offered re-excision to negative margins or mastectomy. Patients being offered mastectomy were excluded from the study.

Preoperative Evaluation

Preoperative evaluation included routine blood tests, mammography with breast ultrasound and chest X-ray. MRI of the breast was not performed as a standard protocol in these patients. Staging evaluation was done as per the standard guidelines.

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Treatment

All patients underwent wide excision of the tumour bearing area to negative margins. Patients referred to our centre after a biopsy underwent a wide excision of the scar bearing area or the residual tumour in all cases. Frozen section evaluation of the margins was done in most patients. Some of the patients underwent partial reconstruction of the breast. In cases where the final histopathology report showed positivity of the margin a re-excision was done. Those patients who opted for mastectomy for positive margins were excluded from the study. Axillary dissection was done in all patients as a standard procedure. Post operatively all the patients received adjuvant systemic therapy according to the stage of the disease. All patients received whole breast irradiation and a boost dose(50 Gy of WBI followed by a 10 Gy boost) to the tumour bed.

Followup

Patients were followed up with clinical breast examination every three months for the first year, every four months for the next two years and every six months for the next two years. Annual bilateral mammography was done in all patients. Other investigations were done according to the symptoms of the patients. Recurrences in the ipsilateral breast or regional nodes were considered as local events. All other recurrences were considered to be systemic recurrences. These recurrences were cytologically or histologically confirmed whenever possible.

Results

Over the study period 3099 breast cancer surgeries were done at the centre which included 2514 modified radical mastectomies and 585 breast conservation surgeries. 620 patients were less than 40 years of age and of them One hundred and seventy five young patients underwent breast conservation surgery during the study period. Thirteen of the patients were lost to follow- up. A total of one hundred and sixty two patients were available for analysis. Median follow up in our analysis was 3.8 years (2.6 years - 6.20 years).

Table 1 summarizes the tumour characteristics of the patients included in the analysis. The mean age was 35.3 yrs. (Range 22–40 yrs). All patients had invasive ductal carcinomas of the breast. More than 80 % of the patients had tumors more than 2 cm in size. A significant number of patients had node positive disease and majority of the patients had high grade and hormone receptor negative disease – all poor prognostic factors for local and systemic control. Node positivity was seen in 42 % of the patients with 13 % having four or

Table 1 Profile of the patients

Variable	No of patients <i>n</i> = 162	Percentage
Age	35.34 years	(22–40)
TUMOUR SIZE		
T1 (<2 cm)	52	32.1 %
T2(2-5 cm)	106	65.4 %
T3(>5 cm)	4	2.5 %
NODAL STATUS		
N 0	91	56.2 %
N 1(1–3)	49	30.2 %
N 2(4–9)	14	8.6 %
N 3 (>10)	8	4.9 %
GRADE		
Grade 1	05	11.11 %
Grade 2	44	32.54 %
Grade 3	113	56.35 %
RESECTION MARGINS		
Positive	0	0
Close(<0.5)	13	8.00 %
Negative	149	92.00 %
OTHER FACTORS		
LymphoVascular invasion (LVI)	17	11.11 %
Extracapsular spread (ECS)	28	17.3 %
HORMONE RECEPTOR STATUS		
Positive	55	34 %
Negative	107	66 %
HER-2 OVER EXPRESSION		
Positive	40	24.7 %
Negative	33	20.4 %
Unknown	89	54.9 %

more nodes positive. 56 % of the patients had grade III disease and 66 % had receptor negative tumours.

Margins were considered to be negative if the distance from the edge of the tumour to the inked surface was more than 10 mm and the margins were considered to be close if it was 5-10 mm. Anything less than 5 mm was considered as positive margin. 92 % of the patients had negative margins and 8 % of the patients had close margins. As mentioned earlier patients with positive margins were taken up for re-wide excision or mastectomy. Those patients who underwent mastectomy were excluded from the study.

Table 2 Oncological events

Event	Number	%
Local recurrence only	4	2.46 %
Local recurrence with systemic metastasis	3	1.85 %
Systemic metastasis only	23	14.19 %
Contralateral primary	1	0.61 %

Table 3 Published data on young breast cancer

Variable	RCC	Milan data	Mayo clinic,2012
Number	162	201	175
Local recurrence	9(4.3 %)	18(9 %)	11.4 %
Distant metastasis	23(14.19 %)	25(12.5 %)	NA
Survival	87.9 %	88.6 %	89.6 %
Significant Factors	Close margins N status Stage		

Table 2 describes the events that occurred in the patients. Seven patients (4.3 %) developed a local recurrence. Four off these patients had local disease as the only site of recurrence. The remaining three patients with local recurrence had associated systemic recurrence as well. Twenty three patients had systemic metastasis (14.19 %) and one patient had a contralateral invasive breast cancer. The 5 year cumulative survival was 87.9 %.

We did a univariate analysis to look at the variables affecting local recurrence. Among the various factors analyzed only the stage of the disease ($p = 0.045$) and close margins ($p = 0.04$) defined as less than 10 mm but more than 5 mm, were found to be statistically significant predictors of local recurrence. The T status, N status, HER2 status and ECS were not found to be predictors of local recurrence. There were more local recurrences in hormone receptor negative patients and in very young patients but these were not statistically significant. 18 patients were found to have a triple negative disease, but this was not found to be a predictor of local recurrence.

As far as the distant metastasis is concerned, N status ($p = 0.009$), stage of the disease ($p = 0.006$) and close margins ($p = 0.09$) were found to be significant predictors. And as expected local recurrence was a predictor of distant metastasis ($p = 0.02$).

Discussion

Breast cancer in young patients has shown an increasing trend globally. Treating these patients can be emotionally and technically demanding. There has been a lot of data looking at the locoregional recurrence in young patients. A large number of studies have come out with the conclusion that young age is an independent predictor of local recurrence [2, 3]. It is the concerns regarding increased risk of local recurrence that makes young age a relative contraindication for BCS. Based on these observations many authors recommend a more radical approach [5] towards treating breast cancer in the young.

Ours is a large series from a tertiary cancer centre, in which 162 patients received breast conservation followed by whole breast irradiation and adjuvant therapy. There has been

adherence to treatment guidelines with all efforts to attain a negative margin to 10 mm. We perform a wide local excision which is just short of a quadrantectomy as this offers a better chance of attaining a negative margin. It has been proven by the Milan 2 trial [6] that wide local excision or quadrantectomy can achieve a statistically significant better local control than a limited conservative procedure such as lumpectomy. Frozen section was used to ascertain the negativity of the margins in most patients. The patients in whom the margins were inadequate were taken up for re-excision or mastectomy.

The most important finding in our study is that the cumulative incidence of isolated IBTR after conservative surgery appears to be acceptable (2.46 % at five years). Our results seem to be at par or even better than that reported from other major centres on breast conservation in young patients (Table 3). The largest published data on the oncological safety of breast conservation in young patients comes from Veronesi's group [7]. In their study the locoregional recurrence rate was 9 %.

In our opinion, if strict treatment protocols are adhered to and if margin negativity to 10 mm can be ensured, local recurrence after BCS in young can be kept at acceptable low limits. We do not find any justification in recommending mastectomy for all young patients. The choice of surgery should depend on tumor/breast ratio and ability to achieve a margin free resection rather than age factors.

The small number of local events might have limited the statistical analysis. In conclusion, breast conservation surgery achieves a good local control in young patients and it needs to be the treatment of choice in young patients.

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