Comparing survival outcomes between breast conserving surgery and mastectomy among BRCA carriers and non-carriers

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Introduction

Breast cancer is the most common cancer and third leading cause of cancer deaths among females in Hong Kong. Hereditary cancers account for 5-10% of breast cancers, of which, 60% of hereditary breast cancer is due to BRCA1 and BRCA 2 mutations. The aims of management of breast cancer in BRCA mutation carriers are threefold- curative, risk reduction and good cosmesis. Currently, controversy exists between breast conserving surgery (BCS) and mastectomy for BRCA mutation carriers with some studies suggesting a higher ipsilateral breast cancer recurrence rate for BCS. Survival data is limited, although two studies have shown there is no significant difference between the two surgical options. This study aims to evaluate the survival outcomes between BCS and mastectomy among BRCA and non-BRCA mutation carriers in breast cancer patients.

Table 1. Clinical characteristics by mutation carrier status

	BRCA Carrier (n=142)	Non-carrier (n=2938)	P value
Age ± SD (mean)	42.3 ± 8.7	49.7 ± 12.9	<0.001
Surgery type			
Mastectomy	82 (57.7)	1944 (66.2)	0.048
BCS	60 (42.3)	994 (33.8)	
Histological Type			
IDC	112 (79.4)	2088 (71.4)	0.072
DCIS	9 (6.4)	348 (11.9)	
Others	20 (14.2)	490 (16.7)	
Not stated	1 (-)	12 (-)	
Stage			
0	11 (7.7)	446 (15.2)	0.105
1	59 (41.5)	1088 (37)	
2	53 (37.3)	1009 (34.3)	
3	19 (13.4)	395 (13.4)	
TNBC	44 (33.1)	309 (11)	<0.001
ER positive	84 (61.3)	2157 (75.5)	<0.001
PR positive	61 (44.9)	1744 (61.5)	<0.001
HER2 positive	19 (14.4)	726 (26.8)	0.007

BRCA BReast CAncer, *SD* standard deviation, *BCS* Breast conserving surgery, IDC Invasive ductal carcinoma, *DCIS* Ductal carcinoma in-situ, *TNBC* Triple negative breast cancer, *ER* estrogen receptor, *PR* Progesterone receptor

Table 2. Multivariate analysis of factors influencing the overall survival, disease free survival and local recurrence within carriers and non-carriers

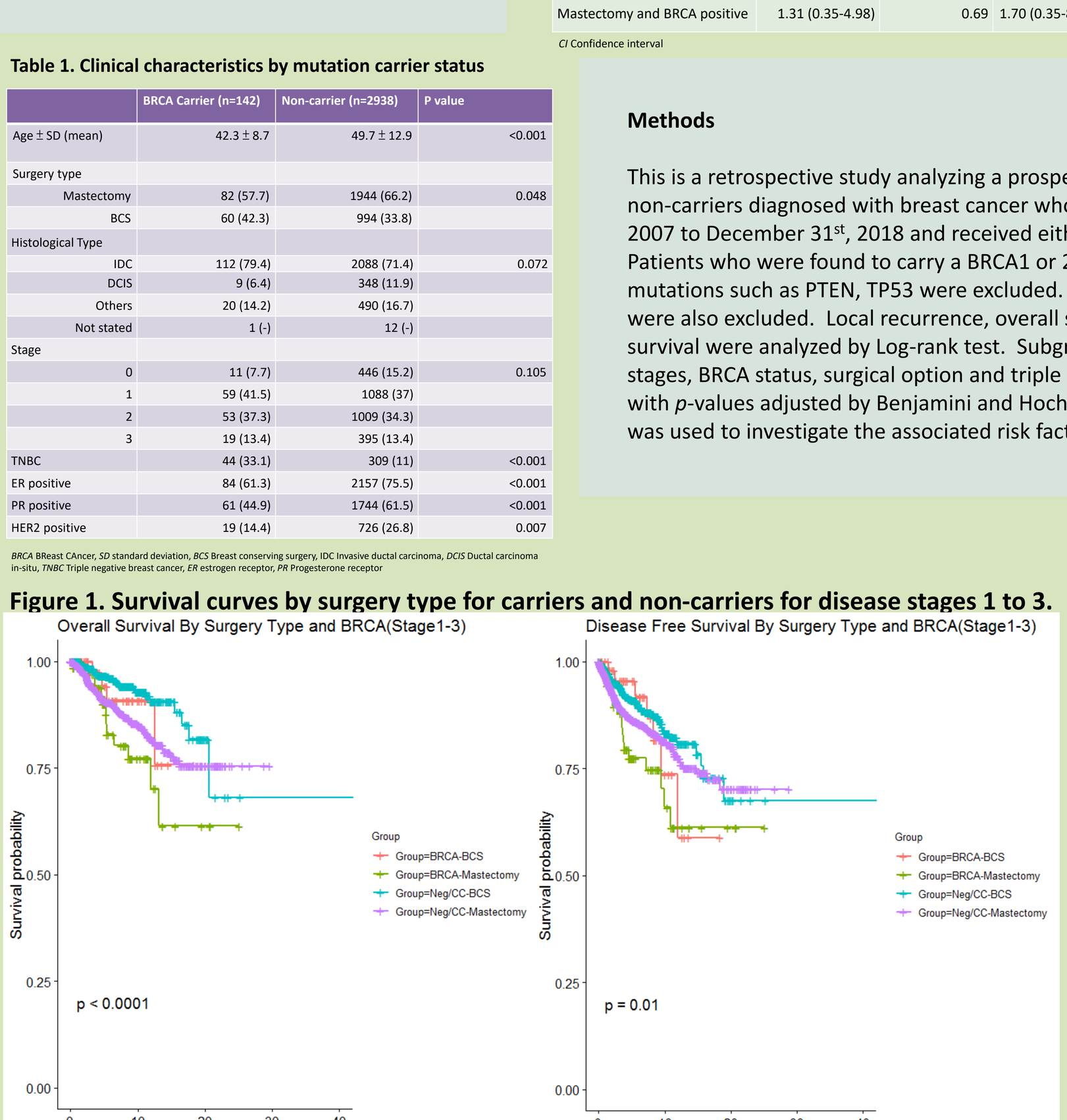
	Overall survival		Cancer free survival		Disease free survival		Local recurrence	
	Hazards ratio (CI 95%)	P value	Hazards ratio (CI 95%)	P value	Hazards ratio (CI 95%)	P value	Hazards ratio (CI 95%)	P value
Stage(with reference to Stage 1)								
Stage 2	2.62 (1.67-4.12)	<0.01	3.58 (1.96-6.54)	<0.01	2.01 (1.43-2.82)	<0.01	2.23 (1.49-3.35)	<0.01
Stage 3	10.47 (6.57-16.7)	<0.01	17.22 (9.46-31.33)	<0.01	6.28 (4.40-8.95)	<0.01	8.58 (5.68-12.96)	<0.01
Age	1.01 (1-1.03)	0.02	1.00 (0.98-1.01)	0.82	0.98 (0.97-0.99)	<0.01	0.98 (0.97-1.00)	0.01
Invasive Grade (with reference to Grade1)								
Grade 2	1.13 (0.68-1.88)	0.64	2.17 (0.99-4.77)	0.05	2.12 (1.30-3.46)	<0.01	1.92 (1.09-3.40)	0.02
Grade 3	1.83 (1.08-3.10)	0.03	3.42 (1.54-7.61)	<0.01	2.55 (1.53-4.24)	<0.01	2.56 (1.43-4.61)	<0.01
TNBC	1.20 (0.76-1.90)	0.44	1.14 (0.67-1.93)	0.63	1.53 (1.03-2.29)	0.04	1.44 (0.93-2.22)	0.11
Radiotherapy	0.97 (0.69-1.37)	0.85	1.06 (0.71-1.59)	0.77	0.96 (0.72-1.28)	0.79	0.86 (0.62-1.20)	0.37
Chemotherapy	0.42 (0.30-0.58)	<0.01	0.42 (0.28-0.61)	<0.01	0.52 (0.39-0.69)	<0.01	0.52 (0.37-0.71)	<0.01
Hormonal Therapy	0.57 (0.40-0.83)	<0.01	0.54 (0.36-0.82)	<0.01	0.82 (0.60-1.13)	0.23	0.66 (0.47-0.95)	0.02
Targeted Therapy	0.64 (0.40-1.03)	0.07	0.54 (0.32-0.82)	0.02	0.91 (0.64-1.29)	0.58	0.73 (0.48-1.12)	0.15
Mastectomy	1.51 (0.98-2.35)	0.06	1.57 (0.96-2.58)	0.07	1.04 (0.76-1.41)	0.82	0.94 (0.66-1.12)	0.72
BRCA positive	1.19 (0.36-3.94)	0.78	0.91 (0.21-3.89)	0.89	0.85 (0.37-1.98)	0.71	0.66 (0.24-1.84)	0.43
Mastectomy and BRCA positive	1.31 (0.35-4.98)	0.69	1.70 (0.35-8.36)	0.51	1.68 (0.63-4.44)	0.30	2.10 (0.65-6.74)	0.21

CI Confidence interval

Methods

This is a retrospective study analyzing a prospectively maintained database for BRCA carriers and non-carriers diagnosed with breast cancer who underwent genetic testing between January 1st, 2007 to December 31st, 2018 and received either a breast conserving surgery (BCS) or mastectomy. Patients who were found to carry a BRCA1 or 2 pathogenic variant were included; other pathogenic mutations such as PTEN, TP53 were excluded. Stage IV disease and bilateral breast cancer patients were also excluded. Local recurrence, overall survival, cancer specific survival and disease-free survival were analyzed by Log-rank test. Subgroup analyses of survival between different disease stages, BRCA status, surgical option and triple negative tumors were conducted by Log-rank test with *p*-values adjusted by Benjamini and Hochberg (BH) method. A Cox proportional hazards model was used to investigate the associated risk factors.

Figure 1. Survival curves by surgery type for carriers and non-carriers for disease stages 1 to 3.



BRCA BReast CAncer gene (carrier group), *BCS* Breast Conserving Surgery, *Neg/CC* negative/cancer control (non-carrier)

Results

A total of 3080 patients were included in the analysis; with 142 BRCA mutation carriers and 2938 non-carriers. The BCS and mastectomy rates in the BRCA mutation group were 42.3 percent and 57.7 percent respectively compared to 33.8 percent and 66.2 percent in the non-carrier group (p=0.048). There was no statistical significance between the different surgical groups and BRCA carrier status regarding local recurrence rate. Log-rank test showed that a poorer disease staging showed significantly worse overall survival, cancer specific survival and disease-free survival (p<0.0001). In a subgroup analysis, BRCA mutation carriers with Stage I disease who received BCS or mastectomy had a worse overall survival compared to non-carrier groups (p=0.0097). This finding was similar for cancer specific survival (p=0.0031). There was no difference in survival for other disease stages, disease-free survival or triple negative breast cancer patients. A Cox proportional hazards model revealed that BRCA mutation status (p=0.71) and type of surgery (p=0.30) were not independent risk factors for poorer survival.

Conclusion

BCS is not associated with adverse long term survival outcomes in BRCA mutation carriers and has no survival benefits over mastectomy. The consideration for BCS should be based on surgical eligibility irrespective of genetic status. With appropriate pre-operative counseling, BCS should be offered as an option to BRCA mutation carriers.