Spline regression
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Comprehensive Support Project

Low body mass index (BMI) is associated with poor survival in Japanese patients with early breast cancer
an exploratory analysis of prospective randomized phase III trials N-SAS BC02 and 03

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Abstract

Background: Obesity is reported to be associated with worse prognosis in early breast cancer. However, there is little data regarding the impact of low BMI on survival in patients with breast cancer. As obesity is rare and low BMI is relatively common in Japanese population compared to Caucasians, Japanese cohort is suitable to assess the impact of low BMI on survival in patients with early breast cancer. Recently an exploratory analysis of a small Japanese randomized phase II trial (JFMC 34-0601) suggested that low BMI was associated with a decreased overall response rate to neoadjuvant endocrine therapy with exemestane. We further explored the impact of low BMI on survival in patients with early breast cancer using a dataset of randomized phase III trials in Japan.

Methods: Patients included in prospective randomized phase III trial N-SAS BC02 or BC03 were retrospectively analyzed. N-SAS BC02 investigated four arms of adjuvant chemotherapy consisted of taxane alone or in combination with anthracycline-containing regimen (median follow up of 6.1 years). NSAS BC03 compared anastorozole with tamoxifen as adjuvant endocrine therapy (median follow up of 6.4 years). The correlation of BMI and overall survival was exploratory analyzed.

Results: A total of 1726 patients were included in our study. Median age was 56 (24 – 82) years, 71.2% of tumors were ER positive, and 9.7% were HER2 overexpressed. Lymph node metastases were observed in 76% of patients. Mean value of BMI was 23.3 and only 4.6% of patients had BMI over 30. 33.1% of patients had BMI under 22 and 4.8% had BMI under 18.5. In the univariate Cox proportional hazard model, lower BMI was significantly associated with worse prognosis (BMI<27 vs >27, HR 0.55, 95% CI 0.32 – 0.93, p = 0.025). The same trend was observed in multivariate analysis (HR 0.61, p = 0.064).

Conclusion: We confirmed that obese patients were relatively rare in Japanese patients with early breast cancer. In this non-obese population, lower BMI was correlated with worse prognosis. However these results should be cautiously interpreted. Our findings suggest that there may be an optimal BMI in patients with early breast cancer; however it should be confirmed by another cohort.

Background

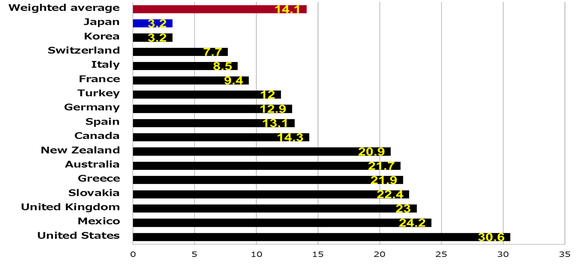
- There is little data regarding the impact of low body mass index (BMI) on overall survival in patients with breast cancer.
- Japanese are relatively in low BMI compared to Caucasian population and therefore suitable to assess the impact of low BMI on survival in patients with early breast cancer.

Objective

To explore the impact of low BMI on overall survival in patients with early breast cancer using a dataset of randomized phase III trials in Japan.

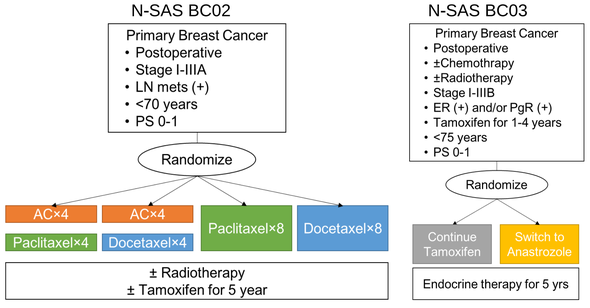
Primary Endpoint：Overall Survival

Percentage of total population who have a BMI greater than 30.
Data from Organisation for Economic Co-operation and Development (OECD).
Data for Australia is from 2002, all other data is from 2003.



Materials & Methods

- Patients included in prospective randomized phase III trial N-SAS BC02 or BC03 were retrospectively analyzed.
- N-SAS BC02[1] was a multicenter phase III trial in which 1,060 patients were randomized to one of four adjuvant regimens: (1) anthracycline-cyclophosphamide followed by paclitaxel (ACP), (2) AC followed by docetaxel (ACD), (3) paclitaxel alone (PTX), or (4) docetaxel alone (DTX).
- N-SAS BC03[2] was a multicenter phase III trial in which anastrozole (ANA) was compared with tamoxifen (TAM) as adjuvant therapy in postmenopausal Japanese patients with hormone-responsive early breast cancer (N = 696).
- This study was supported by the Public Health Research Center Foundation CSPOR.

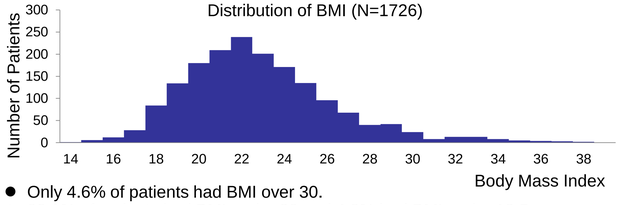


Results

- Median follow up was 6.1 years for N-SAS BC02 and 6.4 years for N-SAS BC03.
- A total of 1726 patients were included in the current study (BC02; 1031, BC03; 695).

	BC02			BC03		
	ACP	ACD	PTX	DTX	TAM	ANA
N	258	260	256	257	351	344
BMI (kg/m2)*	23.3 (3.5)	23.6 (3.7)	23.0 (3.7)	23.2 (3.6)	23.5 (3.4)	23.4 (3.3)
Age (year)+	54 (28-70)	53 (24-70)	54 (26-70)	52 (30-70)	60 (44-82)	60 (45-77)
Stage++						
I	40 (15.5)	18 (6.9)	29 (11.2)	36 (14.0)	147 (41.9)	142 (41.3)
IIA	95 (36.8)	115 (44.2)	98 (38.3)	104 (40.5)	125 (35.6)	126 (36.6)
IIB	85 (32.9)	104 (40.0)	106 (41.4)	93 (36.2)	57 (16.2)	52 (15.1)
IIIA	38 (14.7)	23 (8.8)	23 (9.0)	24 (9.3)	11 (3.1)	10 (2.9)
IIIB	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (3.1)	14 (4.1)
Lymph node mets++						
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	211 (60.1)	208 (59.0)
1-3	154 (59.4)	156 (60.0)	152 (59.4)	154 (59.9)	99 (28.2)	102 (29.7)
4-9	61 (23.6)	61 (23.5)	63 (24.6)	62 (24.1)	31 (8.8)	22 (6.4)
10-	43 (16.7)	43 (16.5)	41 (16.0)	41 (16.0)	10 (2.8)	17 (4.9)
Tumor size++						
<3 cm	166 (64.3)	166 (63.8)	162 (63.3)	165 (64.2)	278 (79.2)	274 (79.7)
≥3 cm	92 (35.7)	94 (36.2)	94 (36.7)	92 (35.8)	73 (20.8)	70 (20.3)
ER(+) ++	148 (57.4)	144 (55.4)	146 (57.0)	145 (56.4)	326 (92.9)	320 (93.0)
PgR(+) ++	104 (42.2)	122 (46.9)	109 (42.6)	114 (44.4)	275 (78.3)	270 (78.5)
HER2 positive ++	36 (14.0)	36 (13.8)	35 (13.7)	34 (13.2)	14 (4.0)	13 (3.8)
Type of surgery++						
Conservation	121 (46.9)	121 (46.5)	119 (46.5)	121 (47.1)	182 (51.9)	181 (52.6)
Mastectomy	137 (53.1)	139 (53.5)	137 (53.5)	136 (52.9)	169 (48.1)	163 (47.4)

*Mean (SD), +Median (Min-Max), ++Freqnency (%)

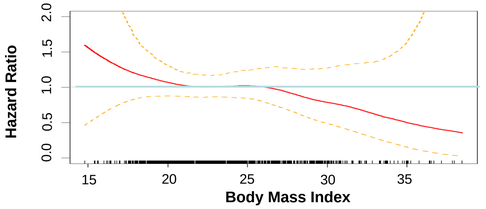


- Only 4.6% of patients had BMI over 30.
- 33.1% of patients had BMI under 22 and 4.8% had BMI under 18.5.

Univariate analysis

Variables	HR	95% CI	p-value
BMI (≥27 vs <27)			
All patients (N = 1726)	**0.55**	**(0.32 – 0.93)**	**0.025**
ER positive (N = 1229)	0.65	(0.29 – 1.42)	0.278
ER negative (N = 497)	0.54	(0.26 – 1.10)	0.089

Effect of BMI for hazards in overall survival (p-spline curve)



Multivariate analysis

Variables	HR	95% CI	p-value
BMI (≥27 vs <27 reference)	**0.61**	**(0.36 – 1.03)**	**0.064**
Stage (vs I)			
IIA	0.98	(0.56 – 1.71)	0.941
IIB	0.70	(0.39 – 1.26)	0.240
IIIA	0.79	(0.41 – 1.54)	0.490
IIIB	4.41	(1.09 – 17.83)	0.037
LN mets (vs 0-3)			
4-9	1.83	(1.27 – 2.62)	0.001
10-	3.05	(2.08 – 4.48)	<0.001
Tumor size (≥3cm vs <3)	2.06	(1.47 – 2.90)	<0.001
HER2	0.94	(0.60 – 1.47)	0.783
ER	0.45	(0.32 – 0.63)	<0.001
PgR	0.61	(0.42 – 0.87)	0.007
Surgery (Mastectomy vs Conservation)	1.08	(0.79 – 1.49)	0.614
Age (by 10 years)	0.92	(0.77 – 1.08)	0.297

Summary

- Obese patients were rare in Japanese patients with early breast cancer, which is dramatically different from Caucasian study.
- Lower BMI was correlated with worse prognosis.
- There may be an optimal BMI in patients with early breast cancer.

References

1. Support Care Cancer. 2012;20:3355.
2. Breast Cancer Res Treat. 2014;148:337.

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