Clinical Utility of Bone Scan Index (BSI) for Breast Cancer Patients with Bone Metastasis
-Multi-Institutional Prospective Cohort Study-

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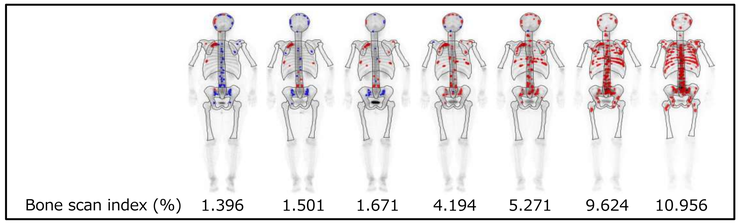
Comprehensive Support Project for Oncological Research of Breast Cancer (CSPOR-BC)

Background

- The bone is the most frequent site of metastasis from breast cancer. However, evaluation for the response to systemic therapy in bone lesion is troublesome.
- The bone scan index (BSI) is a quantitative tool for improving the interpretability and clinical relevance of bone scans[1)].
- The BSI describes the tumor burden in bone as a percent of the total skeletal mass based on reference man skeletal masses[1)].

1) Koizumi M et al. Ann Nucl Med. 2015 Oct;29(8):659-65.



Study Design

- **Study design :** Multi-institutional prospective cohort study
- **Purpose:**
  (1) To investigate the correlation between the BSI and prognosis (progression-free survival, PFS; overall survival, OS).
  (2) To investigate the correlation between the BSI and skeletal-related events (SREs).
- **Primary endpoint :** PFS
- **Secondary endpoint :** OS and SREs
- **Eligibility criteria :**
  (1) Histologically or cytologically diagnosed breast cancer
  (2) Bone metastasis(confirmed by biopsy, Xp, computed tomography, or magnetic resonance imaging)
  (3) Less than 3 prior systemic treatments (chemotherapy, endocrine therapy, or both) for metastatic disease
  (4) Zoledronate or denosumab will be administered
- **Treatment and evaluation :**
  (1) Standard treatment according to guidelines will be delivered to every participant.
  (2) The target accrual is 200 patients with metastatic breast cancer.
  (3) A bone scan will be performed periodically (before treatment and 12 and 24 weeks after registration).
  (4) BSI was calculated by determining the percentage of each bone that is involved by the tracer in relationship to the total skeletal mass, as determined from reference man, which is using the BONEVAVI® automated method (FUJIFILM RI Pharma Co., Ltd., Tokyo, Japan).

Statistical Analysis

- The study is aimed at conducting an exploratory analysis of the relation between BSI and prognosis or skeletal-related events.
- A landmarking Cox model was used to predict PFS and OS by baseline and on-treatment BSI changes. Because on-treatment BSI changes could be observed 12 or 24 weeks, the origin of PFS/OS was set to 12 or 24 weeks and analysis set was defined those who are at risk at 12 or 24 weeks, respectively.
- P value of <0.05 is considered to be statistically significant.

Patient Characteristics

Total patients		N=153
Age	median(range)	63.0(54-70)
Subtype	ER+/HER2-	125 (81.7%)
	ER+/HER2+	9 (5.9%)
	ER-/HER2+	6 (3.9%)
	ER-/HER2-	9 (5.9%)
	unknown	4 (2.6)
PS	0	107 (69.9%)
	1	35 (22.9%)
	2	11 (7.2%)
Site of metastasis	bone	153 (100%)
	Lung	26 (17.0%)
	liver	7 (4.6%)

Prior endocrine therapy	No	75 (49.0%)
	Yes	78 (51.0%)
Prior chemotherapy	No	126 (82.9%)
	Yes	26 (17.1%)
Prior anti-HER2 therapy	No	143 (94.7%)
	Yes	8 (5.3)
Type of treatment	endocrine therapy#	109 (71.2%)
	chemotherapy	27 (17.6%)
	anti-HER2 therapy	17 (11.1%)
	bone modifying agent	153 (100%)

: 56Pts had only bone metastasis and 53 pts showed metastasis to not only bones but also other organs.

Results

- During the follow-up period (median: 22.5 month, IQR:16.8-29.5), 124 events of disease progression and 51 events of death were observed.

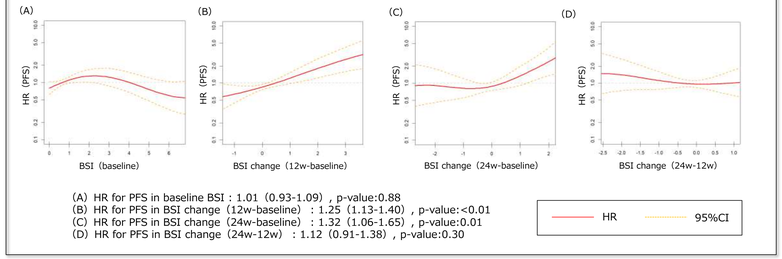
	Base line (N=153)	After 12weeks (N=130)	After 24weeks (N=109)
BSI	0.85 (0.25-19.2)	1.03 (0.23-2.93)	0.79 (0.25-2.63)

BSI (12w) - BSI (Base line)
0.11 (-0.12-0.80)
(N=130)

BSI (24w) - BSI (12w)
-0.04 (-0.60-0.15)
(N=99)

BSI (24w) - BSI (Base line)
-0.01 (-0.38-0.46)
(N=109)

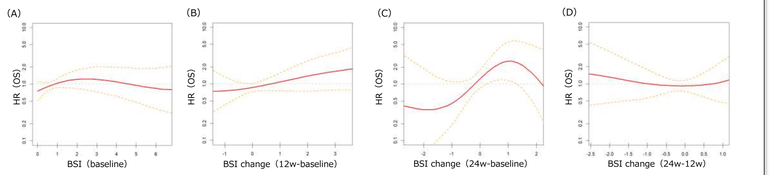
Estimated Cubic Spline Transformation of the Association Between BSI and the Risk of Progression Free Suvrival



(A) HR for PFS in baseline BSI : 1.01 (0.93-1.09) , p-value:0.88
(B) HR for PFS in BSI change (12w-baseline) : 1.25 (1.13-1.40) , p-value:<0.01
(C) HR for PFS in BSI change (24w-baseline) : 1.32 (1.06-1.65) , p-value:0.01
(D) HR for PFS in BSI change (24w-12w) : 1.12 (0.91-1.38) , p-value:0.30

HR 95%CI

Estimated Cubic Spline Transformation of the Association Between BSI and the Risk of Overall Survival



(A) HR for OS in baseline BSI : 1.07 (0.95-1.21) , p-value:0.23
(B) HR for OS in BSI change (12w-baseline) : 1.26 (1.08-1.47) , p-value:<0.01
(C) HR for OS in BSI change (24w-baseline) : 1.47 (1.11-1.95) , p-value:<0.01
(D) HR for OS in BSI change (24w-12w) : 1.02 (0.78-1.35) , p-value:0.87

HR 95%CI

Conclusions

- This study is the first to report the clinical significance of evaluating BSI for metastatic breast cancer patients with bone metastasis. Changes in BSI from baseline to 12 weeks and 24 weeks are associated with PFS and OS, which could help us evaluate whether the systemic therapy is effective against the bone metastasis.

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