A Biomarker Assay Predicts Women Diagnosed with DCIS without Microinvasion at Increased Risk for Breast Cancer Specific Death

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Background

- While rare, patients diagnosed with ductal carcinoma in situ (DCIS) can die from breast cancer.
- We investigated the association of DCISionRT® test results with breast cancer mortality (BCM). DCISionRT is a validated test to assess 10-year breast cancer recurrence risk for patients with DCIS.
- Due to the very low incidence of death in patients with DCIS, a prior nested case control study was used.

Materials and Methods

- The case control study identified 96 women who died of breast cancer and 318 controls from a population of 6,964 in Sweden diagnosed with DCIS without microinvasion (1992-2012).
- DCISionRT testing was performed on a subset of patients with FFPE microarray tissue while blinded to outcome.
- Conditional logistic regression was used to calculate odds ratios (OR) for the risk of BCM accounting for clinicopathologic factors, treatment, and continuous and categorical Decision Score (DS).

Results

- DS results were available for 157 of the 414 women in the original case control study[1]
- Primary DCIS was treated with Breast Conserving Surgery (BCS) alone (34%), BCS plus radiotherapy (RT) (29%) or mastectomy (37%).
- Clinicopathologic factors and treatment distributions were consistent with those in the original case control study, except there were 15% fewer patients that had larger tumors (>2.5 cm).
- Continuous and categorial DS were independently associated with BCM in multivariate analyses, accounting for treatment differences and clinicopathology.
- Patients with increasing continuous DS had increasing BCM (OR=10 per 5 DS units, p=0.004), and patients with high categorical DS (>6) were at greater risk of BCM (OR=19, p=0.007).
- Treatment was not independently associated with decreased BCM risk in this study.
- Patients selected for treatment with mastectomy tended to have increased BCM compared to those who were treated with BCS.
- Young age (<50 years), tumor size (>1 cm), and grade 3 were not statistically associated with BCM.

(1) C. Wadsten, BJS, Aug 2017.

- The DCISionRT score, DS, was significantly associated with breast cancer mortality, while clinicopathologic factors were not.

- High Decision Scores (DS>6) were strongly associated with increased risk for breast cancer mortality (BCM).

- DCISionRT may help to identify women with more aggressive disease that warrants more aggressive upfront treatment

Table 1. Clinicopathologic Factors in Cases vs. Controls

	Cases N	Cases %	Controls N	Controls %	All N	All %
Age <50	17	34.7%	30	29.1%	47	29.9%
Size >1 cm or Multifocal	38	77.6%	69	67.0%	107	68.2%
Grade 3	19	38.8%	33	32.0%	52	33.1%
Positive Margin	9	18.4%	2	1.9%	11	7.0%
Clinical Detection	15	30.6%	29	28.2%	44	28.0%
BCS and RT	12	24.5%	32	31.1%	44	28.0%
Mastectomy	22	44.9%	35	34.0%	57	36.3%
DS>6	**17**	**34.7%**	**16**	**15.5%**	**33**	**21.0%**

Figure 1. Odds Ratio of Decision Score and Mastectomy

OR (95% CI) for categorical DS

Table 2. Multivariate Analysis of Factors Affecting the Risk of Death from Breast Cancer

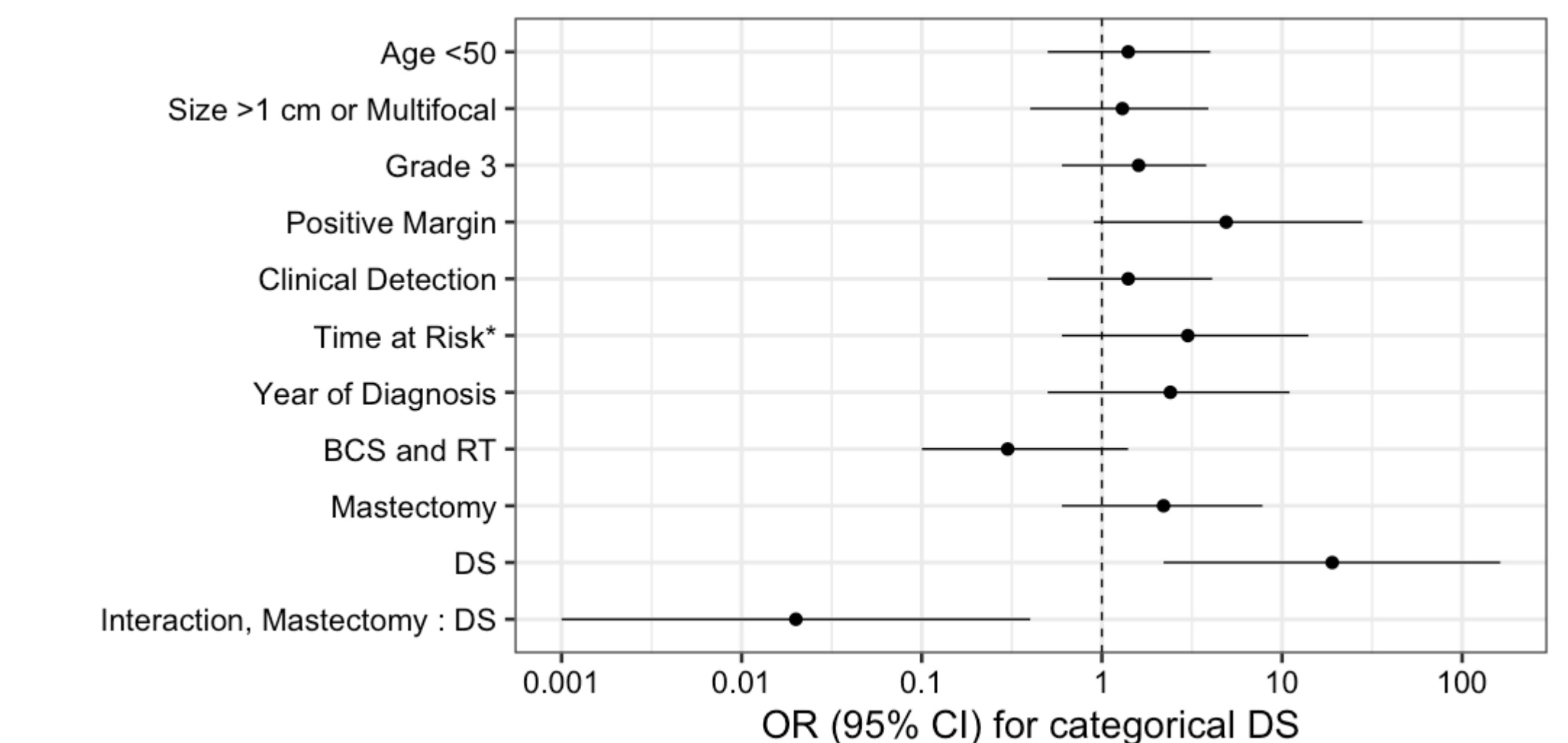|	Continuous DS (DS per 5 units) OR	95% CI	p-value	Categorical DS (DS≤6 vs DS>6) OR	95% CI	p-value
Age <50	1.6	0.60 - 4.4	0.36	1.4	0.50 - 4.0	0.51
Size >1 cm or Multifocal	1.3	0.40 - 3.8	0.68	1.3	0.40 - 3.9	0.65
Grade 3	1.1	0.40 - 2.7	0.86	1.6	0.60 - 3.8	0.34
Positive Margin	3.8	0.70 - 19.0	0.11	4.9	0.90 - 28.0	0.08
Clinical Detection	0.8	0.30 - 2.4	0.68	1.4	0.50 - 4.1	0.57
Time at Risk*	3.0	0.60 - 14.0	0.16	3	0.60 - 14.0	0.18
Year of Diagnosis	2.5	0.50 - 12.0	0.24	2.4	0.50 - 11.0	0.27
BCS and RT	0.3	0.07 - 1.2	0.09	0.3	0.07 - 1.4	0.13
Mastectomy	6.5	1.00 - 42.0	0.05	2.2	0.60 - 7.8	0.23
DS	**10.0**	**2.10 - 50.0**	**0.004**	**19**	**2.20 - 163.0**	**0.007**
Interaction, Mastectomy : DS	**0.1**	**0.02 - 0.7**	**0.02**	**0.02**	**0.001 - 0.4**	**0.008**

*Time at risk = months from date of diagnosis to date of death for cases and corresponding controls selected by incidence density sampling to have the same follow-up time. N=157, cases=49, controls=108.

Conclusions

- Patients with higher DCISionRT scores had an increased risk of BCM.
- DCISionRT may help to identify patients with the potential to develop more aggressive subsequent disease that warrants more aggressive upfront treatment, such as mastectomy.
- Additional data are needed to further validate these findings.