Statistical Methods: Tests of Associations Between BRCA Groups, Their Clinical Variables, and Tumor Characteristics

Michael Radmacher
Rich Simon

mdradmac@helix.nih.gov
RSimon@nih.gov

SUMMARY

We tested for associations between BRCA group and a variety of clinical variables and tumor characteristics on a collection of 7 BRCA1 cases and 7 BRCA2 cases (one of the original eight BRCA2 samples, #14486, was removed from the analysis because the same patient was already represented by another sample). For categorical variables we created a contingency table and used Fisher's exact test to compute a p-value (the Chi-square test was not used because each table had at least one expected cell frequency less than 5). For continuous and ordered variables, we used the Wilcoxon two-sample (rank-sum) test, a non-parametric alternative to the two-sample *t* test. Tests were performed in S-plus 4.5 and StatXact 3.1.

Only 3 variables were found to have significant ($p<0.05$) associations with BRCA group. The three variables are: ER expression, PGR expression and number of mitoses per 10 hpf. It should be noted that this was an exploratory analysis and the p-values cited have not been corrected for multiple comparisons. Therefore, the results for the three variables with significant associations with BRCA group require confirmation by independent studies.

Also, the lack of significance for the remaining variables does not necessarily mean associations do not exist between BRCA group and these variables. The power of the tests we performed is limited by the amount of data available for each variable—the data set is comprised of only 7 specimens for each of the BRCA groups. The power of the tests would increase by the addition of new specimens to the data set.

Group A = BRCA1 (7 cases); Group B = BRCA2 (7 cases)

WILCOXON RANK-SUM TESTS
W = rank-sum statistic (exact)
alternative hypothesis: two-sided

AGE AT DIAGNOSIS
W = 17.0, n=7, m=7, p-value = 0.3829

T STAGE
W = 25.5, n=7, m=7, p-value = 1.0

TUMOR SIZE
W = 26.5, n=7, m=7, p-value = 0.8304

NUMBER OF POSITIVE NODES
W = 10.5, n=7, m=6, p-value = 0.1375

STAGE
W = 17.0, n=7, m=6, p-value = 0.5594

ER EXPRESSION (*see -/+ test below*)
W = 0.0, n=7, m=7, p-value = 0.0006
(Means: BRCA1=0.9, BRCA2=159.3)

PGR EXPRESSION (*see -/+ test below*)
W = 1.5, n=7, m=7, p-value = 0.0023
(Means: BRCA1=0.4, BRCA2=138.4)

NON-INVASIVE CANCER TYPE (*1=DCIS,Low; 2=DCIS,Medium; 3=DCIS,High*)
W = 16.5, n=4, m=6, p-value = 0.3810

TUBULES (DEGREE OF DIFFERENTIATION)
W = 15.0, n=6, m=6, p-value = 1.0

PLEOMORPHISMS (GENETIC INSTABILITY)
W = 24.0, n=6, m=6, p-value = 0.5455

MITOSES
W = 27.0, n=6, m=6, p-value = 0.1818

 # OF MITOSES PER 10 HPF
W = 34.0, n=6, m=6, p-value = 0.0087
(Means: BRCA1=64.7, BRCA2=17.0)

GRADE (*GRADE = TUBULES + PLEOMORPH + MITOSES*)
W = 24.0, n=6, m=6, p-value = 0.3182

SOLID SHEETS? (*0 = <25%; 1 = 25-75%; 2 = >75%*)
W = 24.0, n=6, m=6, p-value = 0.5671

PUSHING MARGINS? (*0 = NO; 1 = Yes,<25%; 2 = Yes,25-75%; 3 = Yes,>75%*)
W = 21.5, n=5, m=6, p-value = 0.2814

NECROSIS? (*0 = NO; 1 = Yes,<10%; 2 = Yes,10-30%; 3 = Yes,>30%*)
W = 19.5, n=5, m=6, p-value = 0.3030

LYMPH? (*0 = NO; 1 = Yes,mild; 2 = Yes,prominent*)
W = 25.5, n=6, m=6, p-value = 0.3636

FISHER'S EXACT TESTS: CONTINGENCY TABLES

INVASIVE CANCER HISTOLOGY

	Ductal	Lobular	Medullary
Group A	5	0	1
Group B	5	1	0

p-value = 1.0

PLOIDY (*D=diploid; ND=non-diploid*)

	D	ND
Group A	0	7
Group B	2	4

p-value = 0.1923

N STAGE

	0	1
Group A	2	5
Group B	0	6

p-value = 0.4615

PERIGLANDULAR TUMOR GROWTH IN NODES? (*0 = NO, 1=YES*)

	0	1
Group A	5	2
Group B	3	3

p-value = 0.5921

M STAGE

	0	1
Group A	6	1
Group B	5	2

p-value = 1.0

PAGET

	0	1
Group A	7	0
Group B	5	2

p-value = 0.4615

ER EXPRESSION (-/+: *<25 -> -, >25 -> +*)

	-	+
Group A	7	0
Group B	2	5

p-value = 0.021

PGR EXPRESSION (-/+: *<25 -> -, >25 -> +*)

	-	+
Group A	7	0
Group B	4	3

p-value = 0.1923

S.PHASE (HI/LO)
Diploid: <7% -> LO, >7% -> HI; Non-diploid: <12% -> LO, >12% -> HI

	LO	HI
Group A	0	6
Group B	3	3

p-value = 0.1818

VASCULAR PERMEATION (*0=Not Seen; 1=Seen*)

	0	1
Group A	3	1
Group B	6	0

p-value = 0.4

BORDERS (*0 = Not Discernible; 1 = Discernible*)

	0	1
Group A	5	0
Group B	6	0

p-value = 1.0

NUCLEI (*0 = Non-Vesicular; 1 = Vesicular*)

	0	1
Group A	1	4
Group B	0	6

p-value = 0.4545

NUCLEOLI (*0 = Not Prominent; 1 = Prominent*)

	0	1
Group A	2	3
Group B	2	4

p-value = 1.0

LOG-RANK TESTS: SURVIVAL ANALYSIS

Chi-square=0.4, p-value=0.5426