

Exact logrank tests for analyses of gene expression profiles

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The asymptotic log rank and generalized Wilcoxon tests are the standard procedures for comparing samples of possibly censored survival times. For comparison of samples of very different sizes, an exact test is available that is based on a complete permutation of log rank or Wilcoxon scores. While the asymptotic tests do not keep their nominal sizes if sample sizes differ substantially, the Exact Complete Permutation test (ECP) requires equal follow-up of the samples. We have developed a new permutation test that does not require equal follow-up time distributions because survival times are permuted while conditioning on the realized follow-up in each group (the Exact log rank test Conditioning on Follow-up, ECF). Size and power of ECP and ECF have been explored by means of Monte Carlo simulation of survival studies, assuming the same and different distributions of follow-up times in the two groups to be compared. It can be shown that ECF is superior to ECP in the latter situation, while the relative power of ECF compared to ECP is high (>90%) if the groups have the same follow-up time distributions. Our permutation test is exemplified by means of analysis of two cancer studies. In the first example, unequal distributions of follow-up times are a consequence of the study's experimental design. In the second example, a gene expression study, a large number of hypotheses are to be tested, and group sizes are partly very unbalanced. In such settings the assumption of equal follow-up time distributions cannot be verified, and a test not requiring equal follow-up distributions is preferred.