A Method for Comparing Survival Duration in the Presence of Strong Intraclass Correlation

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ABSTRACT

In some animal survival studies, the experimental animals (e.g. mice) are raised in small clusters (e.g. 5 mice per cage). Certain mice may also share similar genetic background (littermate for sample) or the nature of the experiment may give rise to other form of clustering, as in the example described on page 7. Therefore the survival times of the individuals from the same cluster may be correlated with each other. When comparing the survival time distributions between different treatment groups, one major problem for the pooled log-rank test is that is does not incorporate this intraclass correlation in the analysis. We surveyed different conditions using computer simulation and found that the approach of using the restricted mean followed by a Wilcoxon rank test has substantial advantages over the log-rank test, particularly for the case of small sample size and strong intraclass correlation. This new approach compares favorably with log rank test with respect to type-I error when intraclass correlation increases. The trade off is a modest loss of power when the correlation is small or zero.