
Letters to the Editor

Same-Day Discharge After Percutaneous Coronary Intervention

Trial Sequential Analysis of Outcomes

In the comparison made between same-day discharge and routine overnight observation by Brayton et al. (1), the best level of evidence was that derived from randomized controlled trial (RCT) studies. With regard to the composite outcome of death, myocardial infarction, or target lesion revascularization, the analysis of 7 RCTs showed no significant differences between the 2 approaches (pooled odds ratio: 0.90; 95% confidence interval: 0.43 to 1.87; p = 0.78). While this result supports the conclusion of no proven difference, the main question is whether or not the available data support a conclusion in terms of proof of no difference (or proof of noninferiority) rather than the mere demonstration of no proof of difference.

One problem in exploring these methodological questions is that the degree of consensus on how noninferiority meta-analysis can be conducted is still modest (2). On the other hand, the advantages of trial sequential analysis (TSA) are being recognized increasingly not only for handling questions of superiority (3,4) but also with regard to those of noninferiority (3–5); in fact, TSA aims at classifying each meta-analysis into one of only 4 categories (superiority, inferiority, futility/noninferiority, inconclusive result).

We applied TSA to the same 7 RCTs examined by Brayton et al. (1). Our assumptions included 2-sided testing, type 1 error of 5%, and a power of 80%. With respect to the above-mentioned composite outcome, the intervention effect was set at a relative risk reduction (RRR) of 50% or 33%. The expected absolute event rate in the controls was 7.6% (i.e., the cumulative arithmetic rate in the control groups of the 7 RCTs). The main result of TSA was expressed through the graph of a cumulative z-curve; the boundaries in this graph for concluding superiority or inferiority or futility were determined according to the O’Brien–Fleming alpha-spending function. All calculations were carried out using a specific statistical software (User Manual for TSA, TSA, Copenhagen Trial Unit 2011).

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Our results indicate that current information from RCTs does not allow us to draw any firm conclusion about the outcome comparison between the two approaches (i.e., "inconclusive result" of TSA). In fact, while the overall number of patients enrolled in the 6 trials was 2,555, our TSA estimated that the optimal information size would be 10,752 patients (assuming RRR = 50%) or 27,243 patients (assuming RRR = 33%).

In summary, the number of patients studied in the RCTs presently available is only one-fourth or one-tenth in comparison with the ideal sample size required to draw a firm conclusion. Therefore, the comparison between the 2 discharge strategies remains open.

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References

Statistical Uncertainty in 10-Year Framingham Risk of Coronary Heart Disease and Cardiovascular Disease

In a recent study, Ford (1) presents an important analysis, with implications for public health prioritization. However, we believe some of the findings should be interpreted with caution. The Framingham Heart Study has contributed immeasurably to our understanding of cardiovascular disease in the United States and internationally, but the published regression equations for 10-year risk of coronary heart disease (CHD) and cardiovascular disease (CVD) were developed for clinical use, and variance-covariance matrices were not reported (2,3). Thus, it is impossible to quantify uncertainty or estimate confidence intervals for any patient’s 10-year risk of CHD or CVD. In other words, while the mean of the risk is known, its variance is unknown.

For this reason, the standard errors for the population-level 10-year risk of CHD and CVD that Ford (1) presents in Table 1 in his article are misleading. The same method is used to estimate these standard errors as used for measures such as age, blood pressure, and cholesterol level. The difference between them is that, unlike Framingham risk scores, these characteristics can be measured with certainty (or are assumed to be measured with negligible error and thus are treated as “certain”); thus, their standard errors are appropriate and accurate. On the other hand, the standard errors reported for population-level 10-year risk of CHD and CVD are inappropriate because they capture only between-person variability in predicted risk but do not account for the fact

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