
Cost-Effectiveness of Upstream Versus Selective Glycoprotein IIb/IIIa Inhibitors for Acute Coronary Syndromes

As a result of extensive clinical research during the past decades, various treatment options are available today that might improve the prognosis of patients with coronary disease. One of the challenges for contemporary medicine is to implement these therapies rationally in clinical practice, in the appropriate patients at the appropriate time. In cost-conscious environments, treatment decisions should not only be based on the suspected benefit/harm ratio, but also on insights into therapy-related costs. Hence, pharmaco-economical analyses are becoming increasingly important in clinical cardiology.

In a recent issue of JACC, Glaser et al. (1) presented the results of a pharmaco-economical analysis in patients presenting with acute coronary syndromes (ACS) with moderate or high risk for cardiovascular events. They concluded that the strategy of routine upstream use of small-molecule (upstream-SM) glycoprotein (GP) IIb/IIIa inhibitors is a more cost-effective approach than the strategy of selective use of abciximab in patients who ultimately undergo percutaneous coronary intervention (PCI).

Glaser et al. (1) performed a decision-tree analysis and used data from clinical trials and a meta-analysis to define the probabilities on the decision nodes. However, several discrepancies exist between the applied probabilities and the data presented in the studies cited, most of which favor the upstream-SM strategy. As an example, Glaser assumes a relative risk (RR) in the range 0 (favoring upstream-SM) to 2.5 (favoring abciximab) for the incidence of death and myocardial infarction (MI) in the PCI setting; yet according to the TARGET (Do Tirofiban and ReoPro Give Similar Efficacy Outcomes?) trial, in ACS patients the 95% confidence intervals (CIs) are 0.4 to 2.5 for MI (2). Interestingly, the RR of 0 implies that the upstream-SM strategy could produce survival for sure, which is unrealistic. Glaser assumes a RR of 1.0 for major bleeding complications in patients undergoing PCI, whereas the TARGET trial reports 1.0% major bleeds after upstream-SM versus 0.7% after abciximab (2). As a final example, Glaser et al. (1) assumes that the upstream-SM strategy, as compared to control therapy, is associated with a RR of 0.88 for death as well as for MI, with ranges varying from 0.41 to 0.47 to 0.95. In fact, the meta-analysis of the corresponding trials showed a 95% CI for the odds ratio of the composite end point of 0.82 to 0.95 (3).

If all variations between the assumptions of Glaser et al. (1) and the original studies are adjusted, results of the pharmaco-economical analysis are reversed: the selective abciximab strategy is then associated with a gain of 83,611 life-years per 100,000 patients, and avoids 173 major bleeds, as compared to upstream-SM. Still, this finding is unreliable. In fact, the presented decision-tree model was insufficiently adjusted for uncertainty because the sensitivity analysis that was applied did not alter all parameters at the same time. Monte-Carlo simulation demonstrates a tremendous uncertainty in any result of this study overall.

Decision-tree analyses might be useful to help clinicians make rational, consistent, and cost-conscious decisions. However, given the fact that average readers of clinical journals, including JACC, are not specialists in medical decision making and pharmaco-economics, authors of such analyses should be highly transparent in their choices, and they should emphasize the uncertainties of their conclusions. I am afraid that Glaser and colleagues missed opportunities in this respect.

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