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Letter to the Editor

Off-pump versus on-pump coronary artery bypass grafting: Quantifying information size by trial sequential analysis

Coronary artery bypass surgery (CABG) has traditionally been performed with cardio-pulmonary bypass and an arrested heart (on-pump CABG). Conducting the operation on the beating heart (off-pump CABG) has been made possible by cardiac stabilisers, thereby avoiding cardiac arrest and cardiopulmonary bypass.

Several studies have been done to evaluate off-pump versus on-pump CABG, but results are quite conflicting. In 2012, the meta-analysis by Möller and co-workers [1] reported that off-pump increased all-cause mortality compared with on-pump CABG; in particular, trial sequential analysis (TSA) of the 10 trials with low risk of bias showed a significantly increased risk of all-cause mortality with off-pump compared with on-pump CABG [1]. More recently, the large randomised-controlled trial by Lamy et al. 2013 [2] has found no difference between off-pump and on-pump in death rates at 1 year (122/2375 versus 119/2377, respectively; RR, 1.03; 95%CI, 0.80 to 1.32; p > 0.05).

We applied TSA to re-examine, on the basis of all-cause mortality, the 10 trials included by Möller et al. in the above-mentioned analysis plus the trial by Lamy et al. (i.e. a total of 11 trials for 9702 patients).

Our TSA (random-effect model) employed the following assumptions: type 1 error = 5% (two-sided); power = 80%; event frequency for controls = 5.1%; expected relative difference = 18% (in favour of on-pump technique). The boundaries for concluding superiority or inferiority or futility were calculated according to the O’Brien-Fleming alpha-spending function. A specific statistical software was used [User Manual for TSA, Copenhagen Trial Unit 2011, see www.ctu.dk/tsa].

Fig. 1 shows the results of our TSA. In examining the 11 trials (including the one by Lamy et al.), the cumulative z-curve did not cross the superiority boundary and remained quite far from it, in contrast to the finding reported by Möller et al. [1]. More importantly,
the optimal information size, determined by our TSA on the basis of these trials, was estimated at $N = 18,689$, which is much more than the total number of 9702 patients included so far in the 11 trials.

In conclusion, although a quite large number of clinical studies have been completed and despite the availability of a recent large-scale randomised trial, the question of whether off-pump and on-pump approaches imply different mortality rates remains open, and further research in this area is still needed. As this example of application confirms, the main advantage of TSA [3,4] is that this statistical technique contributes to determine whether the available evidence on a given therapeutic problem is conclusive (with demonstration of superiority or inferiority or futility) or inconclusive and, in inconclusive cases, indicates which information size would be needed to draw a statistically sound conclusion.

**Conflict of interests**

The authors state that they have no conflicts of interest.

**References**


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