Cognitive decline after off-pump versus on-pump coronary artery bypass graft surgery: Meta-analysis of randomized controlled trials

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Supplemental material is available online.

In the randomized Octopus Study that compared off-pump with on-pump coronary artery bypass graft (CABG) surgery, van Dijk and associates¹ found that avoiding the use of cardiopulmonary bypass had no effect on 5-year cognitive outcomes. On the other hand, in the same trial, off-pump CABG surgery resulted in a trend toward better cognitive outcomes 3 months after the procedure, but the effect became negligible at 12 months.² Although the meta-analysis by Cheng and colleagues³ of 37 randomized trials showed significantly reduced neurocognitive decline at 2 to 6 months (number of trials [N] = 3), significant reductions were not found at 1 month (N = 3) or 12 months (N = 2). Inasmuch as only 4 studies that met their inclusion criteria contributed data to this outcome at any time point, however, the results are not inclusive enough to rule out clinically important differences.³ Therefore, to compare the effect of off-pump and on-pump CABG surgery on cognitive outcomes, we performed a meta-analysis of currently available randomized controlled trials.

Materials and Methods

All prospective randomized controlled trials of off-pump versus on-pump CABG surgery reporting the incidence of cognitive decline were identified by a 2-level search strategy. First, a public domain database (MEDLINE) was searched with a Web-based search engine (PubMed). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries. The MEDLINE database was searched from January 1966 to February 2007. Keywords included “cognitive,” “neurocognitive (neuro-cognitive),” “off pump (off-pump),” “OPCAB,” and “randomized controlled trial.” Studies considered for inclusion met the following criteria: the design was a prospective randomized controlled clinical trial; patients were randomly assigned to

off-pump versus on-pump CABG surgery; and main outcomes included the incidence of cognitive decline at any time point. Data regarding detailed inclusion criteria and the incidence of cognitive decline were abstracted (as available) from each individual study. For each study, data regarding the incidence of cognitive decline in both the off-pump and on-pump CABG groups were used to generate risk differences (RDs) (<0 , favors off-pump CABG surgery; >0 , favors on-pump CABG surgery) and 95% confidence intervals (CIs). Study-specific estimates were combined using inverse variance-weighted averages of logarithmic RDs in a random-effects model. Between-study heterogeneity was analyzed by standard χ^2 tests. Publication bias was assessed graphically with a funnel plot and mathematically with an adjusted rank-correlation test.

Results

Our search identified 8 prospective randomized controlled clinical trials of off-pump versus on-pump CABG surgery reporting the incidence of cognitive decline at any time point. Although only the Octopus Study¹ assessed the 5-year added to within-1-year outcomes,^{2,E1} the remaining 7 trials reported the within-1-year outcomes. In total, our meta-analysis included data on 811 patients. Pooled analysis of the 5 trials^{E1-E5} reporting the within-2-week incidence of cognitive decline demonstrated a statistically nonsignificant benefit of off-pump over on-pump CABG surgery for cognitive decline (RD, -26.8% ; 95% CI, -67.1% to 13.6% ; $P = .1935$). There was significant trial heterogeneity of results. When data from the 6 trials^{2,E3,E5-E8} reporting the 1-month to 3-month incidence of cognitive decline were pooled, off-pump CABG surgery was associated with a statistically significant reduction in cognitive decline relative to on-pump CABG surgery (RD, -8.8% ; 95% CI, -16.0% to -1.6% ; $P = .0162$). There was no trial heterogeneity of results. Pooled analysis of the 4 trials^{2,E4,E5,E7} reporting the 6-month to 12-month incidence of cognitive decline demonstrated a statistically nonsignificant benefit of off-pump over on-pump CABG for cognitive decline (RD, -0.9% ; 95% CI, -8.7% to 6.8% ; $P = .8127$). There was no trial heterogeneity of results. In all the above-mentioned 3 meta-analyses, there was no evidence of significant publication bias.

Discussion

We found, on the basis of the present meta-analysis of the currently available 8 randomized controlled trials enrolling 811 patients, better cognitive outcomes 1 month to 3 months but negligible effects within 2 weeks and 6 months to 12 months after the procedure in off-pump than in on-pump CABG surgery. Our findings strengthened the inadequately proven results of the previous meta-analysis by Cheng and coworkers.³ Furthermore, according to the Octopus Study,¹ better cognitive outcomes in off-

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pump CABG surgery appeared to remain absent at 5 years. These findings suggest that factors other than cardiopulmonary bypass may be responsible for cognitive decline, such as anesthesia and the generalized inflammatory response that is associated with major surgical procedures.^{1,4}

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