The end of all our exploring...

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For over half a century, only a handful of subjects in the field of cardiovascular surgery have consistently attracted intense research interests, cardiopulmonary bypass (CPB) being one of them. Few would argue that the numerous investigations to date focusing on the occurrence of systemic inflammatory response syndrome (SIRS) after open-heart surgery have had positive impacts on the healthy development of CPB technology and techniques [1]. However, a number of surgical approaches that do not involve CPB have also been in widespread practice over the past two decades. A prominent example is off-pump coronary artery bypass grafting (CABG). Because it avoids CPB, and thus cardioplegic arrest, many believe off-pump CABG to be ‘minimally invasive’ (and thus advocate the procedure), as SIRS appears to no longer be a major burden. In the current era of evidence-based medicine, however, this belief is yet to be convincingly proven.

In this issue of the journal, Galeone et al. [2] demonstrate that both the on-pump and off-pump CABG approaches are associated with similar degrees of inflammatory response, as reflected by the activation of the receptor activator of the nuclear factor-κB pathway and enhanced postoperative cellular expression of the nuclear factor-κB p50 subunit. Conversely, the blood osteoprotegerin concentration reached peak levels slightly later in their off-pump group than in the on-pump group, but remained higher than the baseline until postoperative day 6. As far as SIRS is concerned, their study reveals little meaningful intergroup difference. Their lack of exploration of participants’ anti-inflammatory response simultaneously, however, means that it is difficult to form a definitive view [3]. Although the puzzle remains unresolved and the jury is still out, Galeone and colleagues’ observation does indeed provide us with some food for thought. In particular, their finding may stimulate readers to reapproach the ongoing debate on whether CABG should be performed with or without the pump (even though the real issue involved is far more complex than the pump alone [4]).

CABG is arguably the most thoroughly investigated operation in the history of surgery. Although much is yet to be learned despite the multiple ‘off-pump vs on-pump’ comparisons made...
over the past decade, at least one thing is clearer now: it is no longer appropriate to simply label the off-pump approach ‘minimally invasive.’ In fact, there is emerging evidence to suggest that, in this off-pump vs on-pump competition, SIRS may actually make little difference in major clinical outcome parameters. In a single-center study involving 6665 consecutive patients undergoing isolated CABG over an 8-year period, the off-pump group \( n = 3266 \) did indeed experience a reduced incidence of postoperative atrial fibrillation, less need for blood transfusions and a shorter duration on mechanical ventilation \[5\]. However, of the 97.6% of the study participants who were followed up for an average of 4.5 years, those in the off-pump group had significantly higher rates of repeat revascularization and major vascular events, as well as more rehospitalization owing to cardiovascular causes (which significantly increased the costs for this group) \[5\]. More importantly, a recent systematic review \[6\] of 86 randomized clinical trials (involving 10,716 patients) of off-pump vs on-pump CABG failed to confirm any significant benefits of the off-pump approach with regard to postoperative mortality, stroke or myocardial infarction. On the contrary, better long-term survival was observed in patients who underwent on-pump CABG \[6\]. Møller et al. \[6\] therefore concluded that ‘based on the current evidence, on-pump CABG should continue to be the standard surgical treatment,’ although ‘off-pump CABG may be acceptable’ when there are contraindications for cannulation of the aorta and CPB. Along the same lines, two additional multicenter randomized trials \[7, 8\] were published after these researchers’ meta-analysis. In the first, the CORONARY Investigators \[7\] reported that fewer grafts were performed, and more repeat revascularization occurred within just 30 days of CABG, in the off-pump group \( n = 2375 \). In the second, the latest GOPCABE trial \[8\] of 2539 patients aged 75 and above (i.e. patients with one of the oft-mentioned high-risk factors) more repeat revascularization was again required following off-pump CABG relative to conventional CABG during the first postoperative month.

To conclude, we could not agree more with T.S. Eliot’s famous lines from the Four Quartets: ‘We must not cease from exploration and the end of all our exploring will be to arrive where we started and know the place for the first time.’ For many (if not all) surgeons, it is unlikely that more randomized clinical trials on this particular subject are desirable in the foreseeable future, as the old question no longer seems relevant. We should be proud that CPB and its related management are far more advanced than they were half a century ago \[1, 9\]. To tailor a procedure to a patient, and not vice versa, we are definitely more confident today in modifying the definition of ‘minimally invasive’ to embrace ‘on a better pump’ rather than simply ‘off pump.’

REFERENCES