

Dear Sir

The paper by Takahashi et al [1] attempts to revitalise the SYNTAX score and argues that it has a place in clinical practice. Unfortunately flaws and weaknesses in the derivation of the score predicate against such use.

First, the concordance characteristics of the new model are at best modest, with point estimates of only $C=0.65$ (CABG) and $C=0.71$ (PCI) for 10 year mortality, and $C=0.62$ (CABG) and $C=0.67$ (PCI) for 5 year major adverse cardiac events.

Second, and more fundamentally, the authors exerted bias in the choice of unrepresentative and suboptimal data sets for the creation of their new score. In the SYNTAX[2] trial a *post hoc* finding of no difference between PCI and CABG in patients with left main disease created the rationale for the confirmatory EXCEL[3] and NOBLE[4] Trials. EXCEL, for which two of the authors of this new analysis were joint Chief Investigators, found a significant mortality benefit for CABG over PCI in left main disease at 5 years, and a benefit for CABG for major adverse cardiac events at 3 and 5 years when (eventually) analysed using the prespecified conventional Universal Definition of Myocardial Infarction.[5] So why have the authors developed their model using data which are known to be biased towards PCI for left main disease, and validated the analyses on two highly positive trials for multivessel disease and one small neutral study for left main disease? The authors of EXCEL declared that they have full access to the trial data set, so what is their motivation in using earlier and unrepresentative data and to ignore large and available datasets in the creation and validation of their models? This latest study may be best read as a cynical attempt by the authors to hold back the tide of long term evidence that left main disease is different in response to CABG or PCI.[6]

Nick Freemantle PhD

Professor of Clinical Epidemiology & Biostatistics, University College London, UK

Domenico Pagano MD

Professor of Cardio-Thoracic Surgery, Secretary General European Association of Cardio-Thoracic Surgery

COI

NF: UCL receives a grant from EACTS for methodological and educational activity from UCL.

DP: is Secretary General EACTS and Board Member STS.

References

1. Takahashi K, Serruys PW, Fuster V, Farkouh ME, Spertus JA, Cohen DJ, et al. Redevelopment and validation of the SYNTAX score II to individualise decision making between percutaneous and surgical revascularisation in patients with complex coronary artery disease: secondary analysis of the multicentre randomised controlled SYNTAXES trial with external cohort validation. *Lancet* 2020; 396: 1399–412

2. Serruys PW, Morice M-C, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009; 360: 961-72.
3. Stone GW, Sabik JF, Serruys PW, Simonton CA, Généreux P, Puskas J, et al. Everolimus-eluting stents or bypass surgery for left main coronary artery disease. *New Eng J Med* 2016 DOI: 10.1056/NEJMoa1610227.
4. Holm NR, Mäkikallio T, Lindsay MM, Spence MS, Erglis A, Menown IBA, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: updated 5-year outcomes from the randomised, non-inferiority NOBLE trial. *Lancet* 2019 doi.org/10.1016/S0140-6736(19)32972-1
5. Gregson J, Stone GW, Ben-Yehuda O, Redfors B, Kandzari DE, Morice M-C, et al. Implications of alternative definitions of peri-procedural myocardial infarction after coronary revascularization. *J Am Coll Cardiol* 2020; 76: 1609–21.
6. Freemantle N, Pagano D. Interpretation of results of pooled analysis of individual patient data. *Lancet* doi.org/10.1016/S0140-6736(18)31786-0