[18] Eagle KA, Rihal CS, Foster ED, Mickel MC, Gersh BJ; the Coronary Artery Surgery Study (CASS) Investigators. Long-term survival in patients with coronary artery disease: importance of peripheral vascular disease. J Am Coll Cardiol 1994;23:1091–5.
[19] Gersh BJ, Frye RL. Methods of coronary revascularization–things may not be as they seem. N Engl J Med 2005;352:2235–7.
[20] Chaitman BR, Hardison RM, Adler D, Gebhart S, Grogan M, Ocampo S et al.; Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Study Group. The Bypass Angioplasty Revascularization Investigation 2 Diabetes randomized trial of different treatment strategies in type 2 diabetes mellitus with stable ischemic heart disease: impact of treatment strategy on cardiac mortality and myocardial infarction. Circulation 2009;120:2529–40.
[21] Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M et al.; FREEDOM Trial Investigators. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med 2012;367:2375–84.
[22] Athappan G, Chacko P, Patvardhan E, Gajulapalli RD, Tuzcu EM, Kapadia SR. Late stroke: comparison of percutaneous coronary intervention versus coronary artery bypass grafting in patients with multivessel disease and unprotected left main disease: a meta-analysis and review of literature. Stroke 2014;45:185–93.
[23] Marui A, Kimura T, Tanaka S, Okabayashi H, Komiya T, Furukawa Y et al.; CREDO-Kyoto Investigators. Comparison of frequency of postoperative stroke in off-pump coronary artery bypass grafting versus on-pump coronary artery bypass grafting versus percutaneous coronary intervention. Am J Cardiol 2012;110:1773–8.

**EDITORIAL COMMENT**

Cite this article as: Piccolo R, Windecker S, Kolh P Myocardial revascularization in patients with left main or multivessel coronary artery disease at high surgical risk: conventional wisdom versus risk prediction model. Eur J Cardiothorac Surg 2017; doi:10.1093/ejcts/ezw370.

# Myocardial revascularization in patients with left main or multivessel coronary artery disease at high surgical risk: conventional wisdom versus risk prediction model

**Raffaele Piccolo[a], Stephan Windecker[a] and Philippe Kolh[b,*]**

[a] Department of Cardiology, Bern University Hospital—Inselspital, Bern, Switzerland
[b] Department of Cardiovascular Surgery, University Hospital (CHU, ULg) of Liege, CHU Sart Tilman, Liège, Belgium

* Corresponding author. Department of Cardiovascular Surgery, University Hospital (CHU, ULg) of Liege, Sart Tilman B 35, 4000 Liege, Belgium. Tel: +32-4-3665196; fax: +32-4-3668318; e-mail: philippe.kolh@chu.ulg.ac.be (P. Kolh).

**Keywords:** Coronary artery bypass grafting • Coronary artery disease • Guidelines • Heart Team • Percutaneous coronary intervention • Risk scores

Risk prediction models applied to patients with coronary artery disease constitute an indispensable resource for the multidisciplinary decision-making process in the Heart Team as they allow estimating the risk–benefit ratio associated with different treatment options [1]. Among patients with left main or advanced multivessel disease, coronary artery bypass grafting (CABG) has represented the standard of care, whereas percutaneous coronary intervention (PCI) was reserved to less complex anatomical settings until recently [2]. However, when the operative mortality risk is factored in, common sense suggests that the pendulum between CABG and PCI has to shift towards the less invasive percutaneous approach as cardiac surgical risk increases.

In this issue of the Journal, Chang and colleagues challenged the conventional wisdom by providing an individual participant data analysis of 3 randomized trials comparing CABG vs PCI among patients with multivessel disease (BEST trial), left main disease (PRECOMBAT trial) or with either of these 2 conditions (SYNTAX trial) [3]. Using the additive European System for Cardiac Operative Risk Evaluation (EuroSCORE), the authors evaluated the long-term safety and efficacy of CABG compared with PCI among 598 patients at high risk of perioperative surgical death (EuroSCORE ≥6). Major adverse cardiovascular and cerebrovascular events (MACCE), a composite of all-cause death, myocardial infarction, stroke or repeat revascularization, were decreased through 5 years among patients assigned to CABG compared with those who underwent PCI (29.4% vs 43.8%, $P = 0.001$). The difference was largely related to a 50% and 70% relative reduction in the risk of myocardial infarction and repeat revascularization, respectively, associated with CABG. Interestingly, at 30 days, the rate of MACCE was similar between CABG and PCI (8.3% vs 8.6%), while cumulative event curves for MACCE began to diverge thereafter (25.1% vs 39.5%, $P < 0.001$).

The study findings pose the question whether the EuroSCORE should be considered as a treatment modifier in the selection between CABG and PCI. To solve this issue, we used published data from a recent pooled analysis of the same 3 trials [4], derived with very close approximation the hazard ratios with 95% confidence intervals for patients with a EuroSCORE <6 and, finally, calculated the $P$-value for interaction in the treatment effect of CABG vs PCI between low-to-moderate risk (EuroSCORE <6) and high-risk (EuroSCORE ≥6) patients. The results are summarized in Fig. 1. Of note, the risk-by-treatment interaction did not reveal significant differences for any of the tested clinical outcomes, suggesting the lack of heterogeneity in the treatment effect between CABG and PCI according to surgical
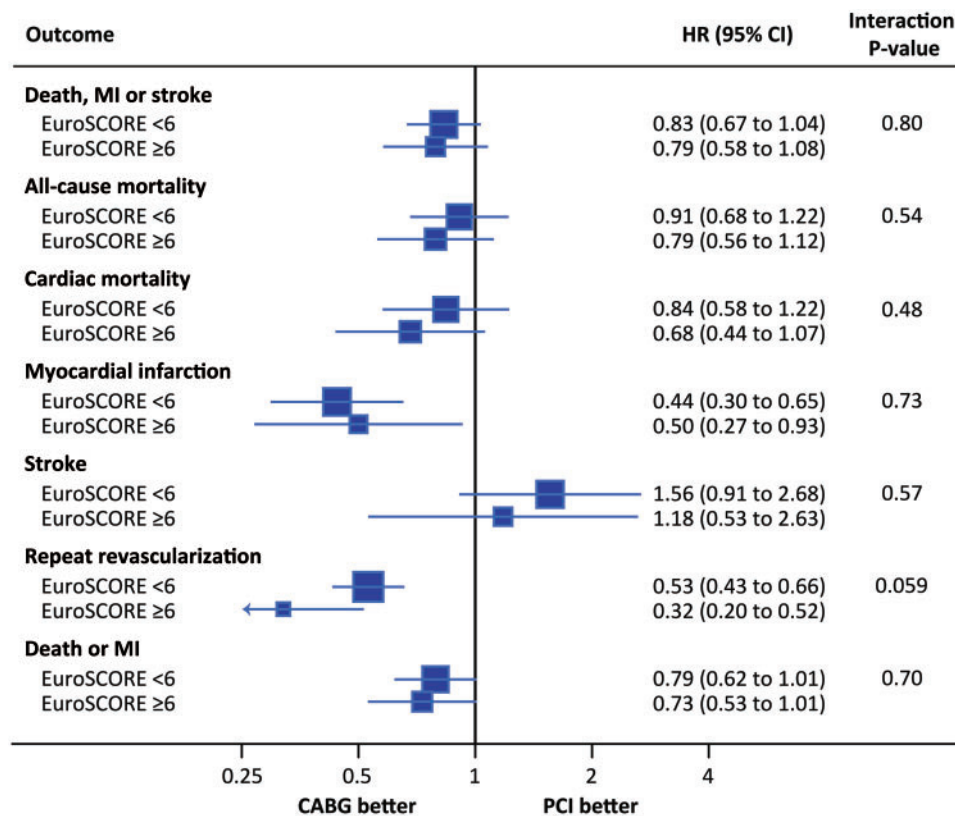
**Figure 1** Efficacy and safety of coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI) stratified by EuroSCORE. Hazard ratios (HRs) with 95% confidence intervals (95% CIs) for patients with EuroSCORE <6 were indirectly derived using a fixed-effect meta-analysis according to the inverse-variance method. MI: myocardial infarction.

risk estimate by the EuroSCORE. Moreover, when repeat revascularization was removed from the MACCE end-point, there was no significant difference between CABG and PCI in the composite of death, myocardial infarction or stroke (hazards ratio 0.79, 95% confidence interval 0.58–1.08, *P*-value for interaction = 0.80).

Several aspects deserve further consideration. The additive EuroSCORE is an outdated tool to predict surgical mortality, and its use for the assessment of short-term outcomes is no longer recommended by societal guidelines (Class III, level of evidence B for CABG and C for PCI) [1]. Instead, a higher level of evidence is conferred to the Society of Thoracic Surgeons score and the EuroSCORE II [1]. As a main limitation, the additive EuroSCORE displays poor calibration and the observed mortality is invariably higher than the predicted mortality [5]. Such disconnect is explained by the fact that at the time of its validation, about 20 years ago, mortality rates in the aftermath of cardiac surgery were at least two-fold higher than those observed in contemporary practice. The present study is not an exception to this rule and, arguably, the visual assessment of Kaplan–Meier curves for mortality indicates that rate of mortality at 30 days was far from reaching 6% in both PCI and CABG arms.

A common feature to all trials included in the present study is that participants had to be suitable for both CABG and PCI according to the local Heart Team. Therefore, it is not surprising

that the mean EuroSCORE was relatively low and amounted to 7.2 ± 1.6 in the CABG group and 7.2 ± 1.5 in the PCI group. By assuming a normal distribution of the score across trials, this means that 95% of the included population had a score <10.5, despite the fact that the upper range value of the additive EuroSCORE is 39. Therefore, although formally fulfilling the criteria for high risk, the study cohort was not really at high risk for early mortality after CABG.

Notwithstanding these limitations, the study has interesting implications in clinical practice as it indirectly underscores the importance of the Heart Team, whose decision-making process should not be overruled by the use of risk prediction models [6]. It is worth to note that a EuroSCORE ≥6 was relatively frequent, as it was found in approximately 1 of 5 patients enrolled across the 3 trials (598 of 3280 or 18%). In conclusion, based on the favourable long-term outcomes associated with CABG, patients at high surgical risk should not be denied CABG by solely focusing on risk scores if deemed suitable for surgery in the overall clinical context by the Heart Team.

## REFERENCES

[1] Kolh P, Windecker S, Alfonso F, Collet JP, Cremer J, Falk V *et al.* 2014 ESC/EACTS Guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur J Cardiothorac Surg 2014;46:517–92.

[2] Piccolo R, Giustino G, Mehran R, Windecker S. Stable coronary artery disease: revascularisation and invasive strategies. Lancet 2015;386:702–13.

[3] Chang M, Lee CW, Ahn JM, Cavalcante R, Sotomi Y, Onuma Y *et al.* Coronary artery bypass surgery versus drug-eluting stent implantation for high surgical risk patients with left main or multivessel coronary artery disease. Eur J Cardiothorac Surg 2017;51:943–9.

[4] Lee CW, Ahn JM, Cavalcante R, Sotomi Y, Onuma Y, Suwannasom P *et al.* Coronary artery bypass surgery versus drug-eluting stent implantation for left main or multivessel coronary artery disease: a meta-analysis of individual patient data. JACC Cardiovasc Interv 2016;9:2481–9.

[5] Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR *et al.* EuroSCORE II. Eur J Cardiothorac Surg 2012;41:734–44; discussion 44–5.

[6] Kolh P, Kurlansky P, Cremer J, Lawton J, Siepe M, Fremes S. Transatlantic editorial: a comparison between European and North American guidelines on myocardial revascularization. Eur J Cardiothorac Surg 2016;49: 1307–17.