Combining minimal risk stratification and prediction of obstructive CAD – clinical utility of a dual pre-test probability model

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Funding Acknowledgement: Type of funding source: Public Institution(s). Main funding source(s): Aarhus University, Health Research Fund of Central Denmark Region

Background: The recently updated pre-test probability (PTP) model for diagnosing chronic coronary syndrome suggested by the European Society of Cardiology (ESC) was designed to predict the presence of obstructive coronary artery disease (CAD). In addition to this model, identification of non-obstructive CAD and utilization of preventive interventions may also lower rates of death and non-fatal myocardial infarction. Opposite to the ESC PTP, the minimal risk tool (MRT) is a new model developed to identify individuals without CAD but symptoms suggestive of CAD. We explored a combined use of the 2 models to predict the absence or presence of obstructive CAD.

Methods: This was a sub-study of the Danish study of Non-Invasive testing in Coronary Artery Disease (Dan-NICAD) which included patients with low-intermediate PTP of CAD. Minimal risk was defined as having a coronary calcium score of 0, no evidence of coronary atherosclerosis at coronary computed tomography angiography, and no cardiovascular (CV) events defined as myocardial infarction, death or revascularization in the mean observation period of 3.1 [2.7–3.4] years. Obstructive CAD was defined as a fractional flow reserve <0.80 in a major vessel during invasive coronary angiography (ICA) or a high-grade stenosis by visual assessment ($>90\%$ lumen reduction).

The risk factors included in the MRT were age, sex, smoking history, diabetes mellitus, dyslipidaemia, family history of premature CAD, hypertension, symptoms related to stress, and high-density lipoprotein concentration. Based on a point-system ranging from 0–5, the MRT and the ESC PTP were combined (dual-PTP) (figure 1). A dual-PTP ≤ 1 indicated very low risk. Using both minimal risk and obstructive CAD as references, the dual PTP was compared to the MRT and the ESC PTP through tests of model discrimination.

Results: Of the 1544 eligible patients, 710 (46%) had normal coronary arteries and no CV events. Obstructive CAD was diagnosed in 152 (10%). Equivalent to a dual-PTP <1 point, 209 patients with ESC PTP$<5\%$ and MRT$>50\%$ or ESC PTP 5–15% and MRT $>75\%$ were classified as very low risk. Of these patients, 84% were at true minimal risk (red area figure 1). Furthermore, only 6 patients would have been diagnosed with obstructive CAD at ICA, and 0 events would be missed. The dual-PTP was non-inferior to the MRT and the ESC PTP in identifying patients having minimal risk and obstructive CAD, respectively (minimal risk: c-statistics 0.74 (0.72–0.77) vs. 0.76 (0.73–0.78); obstructive CAD: c-statistics 0.66 (0.62–0.70) vs. (0.67 (0.63–0.72)). The dual-PTP was superior to the ESC PTP in discriminating patients at minimal risk (c-statistics 0.74 (0.72–0.77) vs. 0.69 (0.67–0.71).

Conclusions: Combining the ESC PTP and the MRT, the dual-PTP seems to enable accurate prediction of both patients with minimal risk and patients with obstructive CAD. Based on the dual-PTP, patients can safely be deferred from or referred for diagnostic testing

Figure 1: Combined estimation of pre-test probability of obstructive CAD (ESC PTP) and stratification for minimal risk (MRT). Red area is equivalent to a dual PTP ≤1 indicating very low risk.