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Prognostic value and incremental benefit of ischaemic myocardial burden subtended by non-invasive CT-derived fractional flow reserve (FFRCT) significant stenoses

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Background: Fractional flow reserve derived from CT-coronary angiography (FFRCT) accurately identifies ischaemic vessels which may be associated with clinical outcomes. Its predictive value in grey zone FFRCT values between 0.7–0.8 is not defined. The technique permits estimation of burden of ischaemic myocardium subtended by FFRCT significant vessels.

Purpose: To evaluate the prognostic value and incremental benefit of FFRCT defined ischaemic myocardial burden when compared to FFRCT alone.

Methods: This is a subanalysis of NXT (Analysis of Coronary Blood-Flow Using CTA:Next-Steps), a prospective study of stable coronary artery disease (CAD) patients referred for invasive angiography (ICA) undergoing invasive FFR, CTA and FFRCT in whom treating physicians had been blinded to FFRCT results. Primary endpoint, defined as a composite of non-fatal myocardial infarction and any revascularisation, was determined in 206 patients (age 64±9.5 years, 64% male) and 618 vessels. Burden of ischaemic myocardium was defined as percentage of myocardium subtended beyond the point at which a vessel's FFRCT becomes $\leq$0.8 as estimated by APPROACH score (FFRCT-APPROACH). In significant FFRCT vessels, the predictive value and incremental benefit of FFRCT-APPROACH was compared with significant FFRCT ($\leq$0.8) for primary endpoint as measured by area under the receiver operator characteristic curve (AUC). Significant ischaemic myocardial burden was defined as $>$10%. The incidence and relationship between the primary endpoint with each 10% increase in FFRCT-APPROACH and 0.05-unit decrease in FFRCT values $\leq$0.8 was determined.

Results: Significant FFRCT was identified in 52.9% of patients (109/206) and 29.3% of vessels (181/618). At 4.7 years median follow-up the incidence of the primary endpoint in vessels with significant FFRCT-APPROACH was 58.9% (96/163) which was comparable with vessels with significant FFRCT (55.2%,100/181; P=0.50). The predictive value of FFRCT-APPROACH for the primary endpoint was comparable with FFRCT (AUC 0.72 [95% CI 0.65–0.79] vs 0.71 [0.63–0.78], P=0.79). When combined, there was significant predictive improvement compared with FFRCT alone (AUC 0.77 [0.70–0.84]; P=0.01). The largest incremental benefit upon FFRCT was observed in vessels with FFRCT values in the grey zone between 0.70–0.80 (AUC 0.76 [0.65–0.86] vs 0.62 [0.48–0.74]; P$<$0.01). Each 10% increase in FFRCT-APPROACH (Adjusted-HR 1.36; 95% CI 1.16–1.60; P$<$0.001) and each 0.05-unit FFRCT decrease (Adjusted-HR 1.42; 1.19–1.70; P$<$0.001) were independently associated with significant increase in the incidence of the primary-endpoint.

Conclusion: In patients with stable CAD referred for ICA, the burden of ischaemic myocardium subtended by FFRCT significant vessels predicted non-fatal myocardial infarction and future revascularisation. This provided significant incremental benefit when used in combination with FFRCT particularly at FFRCT values in the grey zone between 0.7 to 0.8.