Impaired myocardial flow reserve from 82-rubidium positron emission tomography predicts survival benefit from revascularization: a multicenter registry study


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Background: The identification of patients that may accrue prognostic benefit from revascularization is complex. Myocardial perfusion imaging (MPI) using 82-rubidium positron emission tomography (82Rb-PET) provides information on myocardial perfusion defects, calcium-score, left ventricular ejection fraction (LVEF), and myocardial flow reserve (MFR).

Purpose: To examine if MFR assessed by 82-Rb PET MPI identifies subgroups that benefit from revascularization.

Methods: We included 7462 all-comers suspected of coronary artery disease undergoing 82-Rb-PET MPI at three high-volume nuclear centers in Denmark between January 1, 2018, and August 20, 2020. Patients with reversible perfusion defects <5%, eGFR <30 mL/min/1.73m2, receiving dialysis, left ventricular ejection fraction <35%, and those that died within 90 days of their index 82Rb-PET MPI were excluded. Revascularization was defined as percutaneous coronary intervention (PCI) or coronary artery bypass-graft surgery (CABG) within 90 days of MPI. Patients were followed for major adverse cardiac events (MACE), a composite of all-cause death, acute coronary syndromes, ischemic stroke, or heart failure, and all-cause mortality until July 9, 2022. We analyzed each outcome according to revascularization and MFR (<2 vs. ≥2) using the Kaplan-Meier estimator and proportional hazards Cox regressions adjusted for patient and 82Rb-PET characteristics, including any perfusion defects, using inverse probability weighting.

Results: A total of 1805 patients were included (mean age 69 (SD 10.6), 29.8% females, 27% diabetes), of whom 902 (50%) had MFR <2. The median follow-up was 35.9 months. A total of 480 were revascularized. 58 experienced a MACE; 36 died. Revascularization was associated with a significantly lower risk of all-cause mortality and MACE among patients with MFR <2, whereas there was no survival benefit from revascularization among those with normal MFR (figure 1). After adjustment, HR for revascularization for MACE in the MFR <2 group was 0.51 (95%CI 0.33-0.78) versus 1.19 (95%CI 0.64-2.20) in the MFR ≥2 group (p for interaction 0.042) and for All-cause mortality 0.48 (95%CI 0.30-0.77) in the MFR <2 group versus 1.01 (95%CI 0.43-2.39) in the MFR ≥2 group (p for interaction 0.28). Results were independent of the extent of reversible perfusion defect, consistent across several subgroups, and independent of the mode of revascularization (CABG or PCI), figure 2.

Conclusion: In this observational study, revascularization was associated with improved prognosis, specifically among patients with impaired MFR, whereas among patients with normal MFR, there was no prognostic benefit. Impaired MFR may identify patients with prognostic benefit from revascularization. This novel hypothesis should be tested in a randomized controlled trial.
Figure 1: Kaplan-Meier curves with 95% C.I. by revascularization status for MACE (left panel) and all-cause mortality (right panel) and by MFR<2 (top) and MFR≥2 (bottom) P-values indicate multivariable adjusted significance level. All analyses adjusted for patient and 82Rb-PET characteristics, including any perfusion defects. MFR – myocardial flow reserve.
Figure 2: Forest plot showing hazard ratio for revascularization versus no revascularization in subgroups: Endpoints MACE (left panel) and all-cause mortality (right panel) and by MFR <2 (top) and MFR≥2 (bottom). All analyses adjusted for patient and 82Rb-PET characteristics, including any perfusion defects. MFR = myocardial flow reserve, LVEF = left ventricular ejection fraction etc. Bottom graph indicates hazard ratio given the values of variables. NA: Too few data.