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## Deep learning in quantitative PET myocardial perfusion imaging to predict adverse cardiovascular events

Juarez-Orozco LE.1; Martinez-Manzanera O.2; Van Der Zant FM.3; Knol RJJ3; Knuuti J.2

**Background:** Deep Learning (DL) is an innovative approach that allows for complex image recognition and analysis. Cardiovascular imaging constitutes a well-suited target for DL implementation but data on the improvement of prognostic estimates is lacking. Quantitative PET myocardial polar maps provide a topological summary of absolute perfusion measurements across the left ventricle in patients with known or suspected coronary artery disease (CAD). As we foresee the generation of machine learning-based systems that support risk characterization in individual patients, we aimed to evaluate the feasibility and performance of DL in direct PET myocardial perfusion polar maps analysis for the identification of patients who experienced major adverse cardiovascular events (MACE) during follow-up.

**Methods:** We analyzed data from 1185 patients who underwent 13N-ammonia PET for suspected ischemia. A tailored DL model constructed through transfer learning in order to process three quantitative perfusion polar maps per patient (rest, stress and reserve) was built, trained, cross-validated and tested in the identification of patients who developed a MACE composite of cardiac death, myocardial infarction, revascularization or heart failure. DL performance was evaluated through sensitivity, specificity and accuracy. ROC AUCs were used to compare DL with clinical, ventricular function, absolute perfusion quantification, and integrated models built through a simpler machine learning method.

**Results:** Patients were followed for a median of 13 months follow-up (range 2-28). There were 27% of patients with positive family history for CAD, 16% with a previous MI, 14% were smokers, 16% had diabetes, 33% had dyslipidemia and 51% had arterial hypertension. Overall incidence of MACE was 13%. DL identified patients who developed MACE during follow-up with a sensitivity, specificity, accuracy, precision and ROC AUC of 87%, 77%, 82.0%, 79.3% and  $0.90 \pm 0.02$ , respectively. DL outperformed the clinical (AUC =  $0.78 \pm 0.09$ ), ventricular function (AUC =  $0.74 \pm 0.07$ ), absolute perfusion quantification (AUC =  $0.84 \pm 0.03$ ), and integrated (AUC =  $0.85 \pm 0.06$ ) models.

**Conclusion:** Deep Learning is feasible in the direct evaluation of quantitative myocardial perfusion polar maps and significantly improves the identification of patients who develop major adverse cardiovascular events at the individual level. Deep Learning-based analysis outperforms simpler machine learning methodology considering clinical, functional and quantitative flow variables. Further research into the clinical value of DL estimations in the comprehensive risk evaluation of patients suspected with myocardial ischemia is warranted.

<sup>&</sup>lt;sup>1</sup>Turku PET Centre, Turku, Finland

<sup>&</sup>lt;sup>2</sup>Turku University Hospital, PET Center, Turku, Finland

<sup>&</sup>lt;sup>3</sup>Medical Center Alkmaar, Cardiac Imaging Division Alkmaar, Northwest Clinics, Alkmaar, Netherlands (The)