PROJECT 1

DoS: ANTONIO ESPOSITO

Title: Predicting transcatheter aortic valve implantation (TAVI) outcome with a multiparametric imaging approach based on computed tomography (mpCT)

Curriculum: EXPERIMENTAL AND CLINICAL MEDICINE

Residency Program: RADIOLOGY

Link to OSR/UniSR personal page:
https://research.hsr.it/en/core-facilities/preclinical-imaging/antonio-esposito.html
http://www.unisr.it/k-teacher/esposito-antonio/

Project description (*Number of characters*, *including spaces*: 2.000 - 3.000):
AS is the most common valvular heart disease in developed world, affecting 10% of people aged >75 years, and has a poor prognosis especially after symptoms occurrence. Guidelines recommend aortic valve replacement (AVR) for severe AS in symptomatic patients and in asymptomatic patients with ejection fraction (EF) <50%.

For decades, the only definite treatment for AS has been surgical AVR; in 2000s TAVI has been introduced for treatment of high surgical risk patients. Since then, randomized prospective trials have shown the superiority of TAVI over SAVR before in high-risk and, very recently, also in low risk patients[1], increasing the number of TAVI candidates in the years to come.

However, trials have shown that >25% of patients die or have poor quality of life after 1 year from TAVI, with significant HF symptoms. Thus, studies are needed to identify those patients who would not benefit from TAVI to offer them appropriate treatment and to avoid useless expensive procedures.

Besides patients' comorbidities, severe aortic valve calcification and concomitant mitral annulus or left ventricular outflow tract calcification have a negative impact on TAVI outcome[2], but calcifications alone are not enough to select patients that will not benefit from TAVI.

Diffuse interstitial LV fibrosis in AS patients, estimated by cardiac magnetic resonance (CMR) with extracellular volume fraction (ECV) quantification, may also have a strong impact on the capability of recover after TAVI[3], even if more data about the potential association between ECV and TAVI outcome are needed. Moreover, it would be very difficult to include CMR in the examination of all potential candidates to TAVI, because of limited patient's compliance and related costs.

Current guidelines state that CT must be performed in all patients prior to TAVI for assessment of anatomy and dimension of aortic root and aortic valve annulus, and for access routes evaluation. CT also evaluates coronary arteries patency and the degree of aortic valve calcification. However, CT can assess many other aspects of heart structure and function, such as aortic valve area, LV volumes, mass and contractility. Moreover, improvements in technology have made myocardial characterization with CT feasible, and studies suggest that ECV can be calculated from CT with a dedicated approach. We are conducting research on this topic and preliminary data show a good correlation between ECV-CT and ECV-CMR used as non-invasive

standard (Spearman's coefficient = 0.83, p<0.001), with no difference between the methods (Wilcoxon test: Z= -0.83; p=0.40).

Aim of the project is to transform the planning CT examination performed in each TAVI candidate, in a multi-parametric CT, including anatomic, functional and myocardial structure parameters, in order to improve the capability of CT in prognostication of TAVI outcome, in order to achieve a better selection of patients benefit from TAVI procedure.

The PhD student enrolled on this project will design a clinical trial aimed to identify a combination of mpCT features able to define the outcome of AS patients after TAVI. He will take advantage of the huge number of patients undergoing TAVI at IRCCS Ospedale San Raffaele (OSR). A further aim of the project will be to further investigate the relationship between myocardial interstitial fibrosis, AS and the possibility of recover after TAVI. For this last objective, murine models of pressure afterload can be implemented and studied at the Preclinical Imaging Facility of OSR.

Skills to be acquired by the student:

Advanced knowledge about the technical and physical principles of new CT cardiovascular applications. Advanced knowledge about the pharmacology of contrast agents and about the artificial intelligence and deep learning in the post processing of cardiovascular CT and CMR images. Robust knowledge of bioinformatic tools needed to analyse large amount of radiomic data. Advanced knowledge about cardiovascular imaging with CT and CMR. Knowledge of imaging biomarkers affecting TAVI outcomes.

References (max. 3)

1. Mack MJ et al., Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients, N Engl J Med. 2019 May 2;380(18):1695-1705. doi: 10.1056/NEJMoa1814052. Epub 2019 Mar 16.

2. Abramowitz Y, et al. Concomitant mitral annular calcification and severe aortic stenosis: prevalence, characteristics and outcome following transcatheter aortic valve replacement. Eur Heart J. 2017 Apr 21;38(16):1194-1203.

3. Chin CWL et al., Myocardial Fibrosis and Cardiac Decompensation in Aortic Stenosis. JACC Cardiovasc Imaging. 2017 Nov;10(11):1320-1333. doi: 10.1016/j.jcmg.2016.10.007. Epub 2016 Dec 21.