EDITORIAL

Non-invasive work-up of suspected obstructive CAD in Romania – quo vadis?

Ali Yilmaz[1]

Editorial comment to

Miftode et al., „SPECT versus ECG/echocardiography in the evaluation of ischemic heart disease – preliminary results in northeastern Romania"

Cardiovascular disease (CVD) – including coronary artery disease (CAD) – is the leading cause of death (not only) in Europe: According to the latest available European data[1], 45% of all deaths are caused by CVD – with an even higher percentage in „middle income" European countries compared to „high income" ones. Hence, prevention, early diagnosis and successful therapy of CAD are of paramount importance – particularly in countries with a promising future, however, middle income such as Romania.

Hemodynamically relevant coronary artery stenoses may cause chest pain and/or dyspnea, but also be present without any symptoms. And vice versa, angina pectoris may also occur in patients without obstructive CAD due to different other reasons[2]. Therefore, a physician taking care of patients with cardiovascular risk factors and/or presence of chest pain symptoms is in need of appropriate diagnostic tools in order to safely rule-in or rule-out obstructive CAD in such patients[3]. The chosen diagnostic approach should be straightforward and minimise use of both personal and financial resources while allowing a conclusive and clinically helpful diagnosis.

Current European guidelines suggest to first assess the individual pre-test probability (PTP) of CAD and thereafter, to choose the appropriate non-invasive diagnostic modality based on the respective PTP value[4]. Possible non-invasive methods for further work-up of suspected CAD comprise exercise-ECG, stress-echocardiography, single-photon emission computed tomography (SPECT), cardiovascular magnetic resonance (CMR), positron emission tomography (PET) and coronary computed tomography angiography (CCTA). Each method has its individual strengths and limitations, and one has to consider both patient specific as well as technical/local factors before choosing the most appropriate non-invasive imaging modality[3].

In this context, Miftode et al. performed a small-sized study in northeastern Romania comprising 17 stable patients who underwent (exercise) ECG, echocardiography and exercise-SPECT for non-invasive work-up of suspected or known CAD5. Due to the fact that this study was performed in a Romanian hospital without a cath lab and that the authors are presenting their preliminary results, data from invasive coronary angiography were unfortunately not available (or not yet included into their analyses). Rather broad (and somewhat imprecise) inclusion criteria defined as presence of either symptoms, resting ECG abnormalities or known CAD were used. In 13 out of 17 (76%) patients, exercise-SPECT demonstrated the presence of ischemic perfusion defects whereas ischemic ECG changes were only observed in 9 out of 17 (53%) patients. Noteworthy, there were two female patients with ischemic ECG changes but without any perfusion defects at SPECT. Moreover, there were some correlations detected between scintigraphic findings and echocardiographic parameters such as left ventricular wall thickness or end-diastolic diameter. Unfortunately, study limitations such as the small sample size, the authors' approach in patient selection and the missing gold- or reference-standard regarding the presence of obstructive CAD (e.g. data from invasive coronary angiography) do not really allow to draw any substantial conclusions. Nevertheless, the additional use of non-invasive SPECT imaging will hopefully allow to better identify those patients that suffer from relevant myocardial ischemia (and will therefore benefit from sub-

[1] Department of Cardiology and Angiology University Hospital Münster, Germany

Contact address:
Ali Yilmaz, University Hospital Münster, Albert-Schweitzer-Campus 1, Building A1. 48149 Münster, Germany.
E-mail: ali.yilmaz@ukmuenster.de

sequent invasive coronary angiography) while sparing patients without obstructive CAD unnecessary cardiac catheterizations. Considering available data that implicates the number of interventional cardiologists (only 4.4 per million people in Romania compared to e.g. 31.0 per million in Austria) are so far rather low in Romania[1], accurate non-invasive work-up of suspected obstructive CAD is of paramount importance.

There is no doubt that exercise-SPECT will improve the diagnostic yield regarding non-invasive detection of obstructive CAD when compared to (exercise) ECG or resting echocardiography – as was done in the study of Miftode et al. From a clinical point-of-view, it will be more appropriate to compare the diagnostic accuracy of exercise-SPECT to other non-invasive stress methods - that are also available in northeastern Romania - such as stress-echocardiography. Which of those methods (at least of those that are locally available) shows the best diagnostic performance to rule-in and rule-out obstructive CAD? While the aforementioned European guidelines clearly state that exercise-ECG should only be performed in patients with a PTP of 15-65% whereas stress-echocardiography, SPECT, CMR and PET can be performed in those with a PTP of 15-85%[4], these guidelines do not suggest any algorithm regarding the appropriate or individual choice of the respective non-invasive method.

Fortunately, Knuuti et al. as well as Danad et al. recently addressed exactly this question and performed well reasoned and comprehensive meta-analyses6, 7. When looking only at those studies that used invasive fractional flow reserve (FFR) measurements for the diagnosis of obstructive CAD, Knuuti et al. detected some important findings[7]: In total, 4.131 patients from 23 studies were included into this analysis; the best performance in ruling-in obstructive CAD was documented for stress-CMR, followed by PET and SPECT whereas the best performance for ruling-out obstructive CAD was documented for stress-CMR, PET and CCTA (with similar likelihood ratios). In general, both stress-CMR and PET demonstrated the best performance within a broad range of PTP values whereas stress-echocardiography and SPECT showed a poorer performance, and exercise-ECG the poorest performance (being actually without a relevant additional value in ruling-in or -out obstructive CAD). It will not be a surprise if the present recommendation to perform exercise-ECG in patients with a PTP of 15-65% will completely be removed in the upcoming revision of the respective European guidelines.

Taken together, the efforts of Miftode et al. to use SPECT imaging in northeastern Romania in order to improve the non-invasive diagnosis of obstructive CAD deserve attention and will certainly increase the diagnostic accuracy in identifying those patients that will benefit from subsequent cardiac catheterization. Moreover, including SPECT (similar to stress-CMR) into the diagnostic algorithm of CAD work-up may also be cost-effective from a general point-of-view8. However, in consideration of local resources and expertise, not only SPECT imaging but also novel methods such as stress-CMR that promises an even higher diagnostic yield without any radiation burden should also be pursued in Romania - in the interest of the Romanian people.

Conflict of interest: none declared.

References

1. Timmis A, Townsend N, Gale C, Grobbee R, Maniadakis N, Flather M, Wilkins E, Wright L, Vos R, Bax J, Blum M, Pinto F, Vardas P. European Society of Cardiology: Cardiovascular Disease Statistics 2017. Eur Heart J 2018 February 14;39(7):508-79.
2. Yilmaz A, Sechtem U. Angina pectoris in patients with normal coronary angiograms: current pathophysiological concepts and therapeutic options. Heart 2012 July;98(13):1020-9.
3. Yilmaz A, Sechtem U. Ischaemia testing in patients with stable angina: which test for whom? Heart 2014 December;100(23):1886-96.
4. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di MC, Ferreira JR, Gersh BJ, Gitt AK, Hulot JS, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabate M, Senior R, Taggart DP, van der Wall EE, Vrints CJ, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hamilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Ryden L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirir A, Zamorano JL. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J 2013 October;34(38):2949-3003.
5. Miftode R. SPECT versus ECG/Echocardiography in the evaluation of ischemic heart disease - preliminary results in northeastern Romania. 2019.
6. Danad I, Szymonifka J, Twisk JWR, Norgaard BL, Zarins CK, Knaapen P, Min JK. Diagnostic performance of cardiac imaging methods to diagnose ischaemia-causing coronary artery disease when directly compared with fractional flow reserve as a reference standard: a meta-analysis. Eur Heart J 2017 April 1;38(13):991-8.
7. Knuuti J, Ballo H, Juarez-Orozco LE, Saraste A, Kolh P, Rutjes AWS, Juni P, Windecker S, Bax JJ, Wijns W. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. Eur Heart J 2018 September 14;39(35):3322-30.
8. Greenwood JP, Ripley DP, Berry C, McCann GP, Plein S, Bucciarelli-Ducci C, Dall'Armellina E, Prasad A, Bijsterveld P, Foley JR, Mangion K, Sculpher M, Walker S, Everett CC, Cairns DA, Sharples LD, Brown JM. Effect of Care Guided by Cardiovascular Magnetic Resonance, Myocardial Perfusion Scintigraphy, or NICE Guidelines on Subsequent Unnecessary Angiography Rates: The CE-MARC 2 Randomized Clinical Trial. JAMA 2016 September 13;316(10):1051-60.