Review

Not peer-reviewed version

Coronary Heart Disease: Implementation of Imaging Modalities to Optimize Cost-Effectiveness

Elisa Milan *, Francesca Dei Rossi , Vittorio Fiore , Stefano Medea , Anna Talin , Laura Vendramin , Raffaele Giubbini

Posted Date: 13 October 2025

doi: 10.20944/preprints202510.0828.v1

Keywords: myocardial SPECT; myocardial PET; cardiac stress-echo; coronary angio-CT; cardiac MRI; cost-effectiveness analysis

doi:10.20944/preprints202510.0828.v1

Review

Coronary Heart Disease: Implementation of Imaging Modalities to Optimize Cost-Effectiveness

Elisa Milan [1,*], Francesca Dei Rossi [1], Vittorio Fiore [1], Stefano Medea [1], Anna Talin [1], Laura Vendramin [1] and Raffaele Giubbini [2]

[1] Ospedale Cà Foncello AULSS2 Marca Trevigiana
[2] International Specialized Hospital of Uganda
* Correspondence: elisa.milan@aulss2.veneto.it

Abstract

Background/Objectives: cardiovascular diseases remain the most significant health and economic challenge in Stable Economy Countries. Myocardial perfusion imaging (MPI) using single-photon emission computed tomography (SPECT) or positron emission tomography (PET) has long been a cornerstone in the diagnosis and management of coronary heart disease (CHD). However, in an era of increasing healthcare costs and emergence of new imaging technologies, the cost-effectiveness of nuclear cardiology has come under critical evaluation and the implementation of different modalities of imaging need to be considerd. **Methods**: this review describe the characteristic of the two principal methods of economic analysis used to measure health benefits and presents an overview of the relevant trials published so far on the cost-effectiveness of different imaging modalities in the evaluation of CHD. **Results**: due to the great variability of data conditioned by facility availability, expertise, setting of patients (inpatients vs outpatients), healthcare systems, reimbursement, systems based on insurance company a definite cost effectiveness analysis cannot be obtain. **Conclusions**: a multimodalities approach seems to offer better performances both in clinical and in the economical analysis.

Keywords: myocardial SPECT; myocardial PET; cardiac stress-echo; coronary angio-CT; cardiac MRI; cost-effectiveness analysis

1. Introduction

According to World Health Organization data published on July 2025, cardiovascular diseases (CVDs) accounted for approximately 19.91 million global deaths in 2022, making them the leading cause of mortality worldwide [1] with a great impact on health systems and economies.

In Europe (EU), CVD remains the most significant contributor to disease burden, causing 1.7 million deaths in 2021: CHD and cerebrovascular diseases account for 34% and 22% of CVD-related deaths, respectively [2].

The incidence and prevalence of CVDs continue to rise due to aging populations, lifestyle factors, and persistent risk factors such as hypertension, smoking, and obesity. In 2019, the age-standardized prevalence of CVD globally was approximately 116.3 cases per 100,000 people, up from 45.5 cases per 100,000 in 1990 [3].

A recent comprehensive study estimated that CVD costs the EU €282 billion annually, representing 2% of the region's GDP and 11% of total health expenditure. This figure reflects both direct and indirect costs, including: health care and long-term care: €155 billion (55% of total CVD costs), Productivity losses: €48 billion (17%) and Informal care: €79 billion (28%) [2].

The average per capita cost of CVD in EU is €630, with significant variation among Countries from €381 in Cyprus to €903 in Germany. The variation in per capita costs among EU Countries reflects differences in healthcare systems, population demographics, and disease prevalence [2].

 doi:10.20944/preprints202510.0828.v1

2. Economic Analysis Aspects

Cost-effective analysis of imaging tests for diagnosis and management of CHD based on available literature is a complex issue.

Economic evaluation of a strategy is commonly performed using a comparative assessment of alternative options based on the analysis of costs and consequences in the utilization of two or more health technologies or therapies.

Two principal methods, focus on different assessment to measure health benefits, are commonly used: cost-effectiveness analysis (CEA) and cost-utility analysis (CUA) [4–6].

CEA: Compares the cost of an intervention with its clinical effectiveness. It is measured in natural units such as life-years gained (LYGs), events prevented, or symptom-free days.

CUA: compares costs, but effectiveness is measured in quality-adjusted life years (QALYs), which incorporate quantity and quality of life.

The main output from both is a ratio: the incremental cost-effectiveness ratio (ICER) for CEA (cost per LYG or other outcome) and the incremental cost-utility ratio (ICUR) for CUA (cost per QALY gained), therefore CEA and CUA can lead to different results.

For example: if a new therapy for chronic heart failure costs € 40,000 and extends life by 2 years compared to standard therapy. The ICER is € 20,000 per life-year gained. The same drug also improves quality of life, resulting in 1.5 QALYs gained. The ICUR is €26,666 per QALY gained.

Both CEA and CUA are essential tools for evaluating medical interventions.

CUA, which incorporates quality of life, is preferred by health technology assessment agencies worldwide. The choice between methods should be guided by the nature of intervention, available data, and local guidelines [7].

A Polish study analyzed 155 submissions to the Agency for Health Technology Assessment between 2007 and 2011 and showed that in 13% of cases, ICER and ICUR led to different reimbursement decisions, highlighting the importance of choosing the right method [8].

3. Cost-Effectiveness Analysis

Studies comparing cost-effectiveness of different tests should be analyze carefully.

A great number of publications on cost-effectiveness of imaging modalities in CHD evaluate only the cost of tests. However, dealing with costs a wider scenario represented by different reimbursement systems, willingness to pay, costs due to layering of additional tests as well as cost of short-term and long-term complications should be consider.

For example, a huge review based on 70 studies tried to evaluate cost-effectiveness of mostly available non-invasive imaging tests and imaging algorithms for the diagnostic workup of patients with stable symptom suspected of having obstructive coronary artery disease (CAD) [9]. Authors suggested that coronary CT angiography (CCTA) is cost-effective for initial imaging in patients with intermediate pre-test probability of disease (PTP), stress echo (SE) or SPECT can be preferred in the same population for functional evaluation and invasive coronary angiography (ICA) can be cost-effective as initial test for patients with high PTP.

Genders et al [10] confront five different initial imaging approaches in a hypothetical 60 year old patient with low to intermediate PTP comparing costs in three different Countries: US, UK and Netherland. The Imaging modalities were CCTA, cardiac stress imaging (CSI) (stress MRI, stress SPECT and SE), CCTA+CSI and ICA. Authors concluded that a multimodality approach was more cost-effective than single modality approach. Moreover, evaluating the impact of strategy guided by different initial imaging modality or optimal medical treatment approach in the three Countries the cost-effective analysis lead to significantly different results.

These two example are useful to understand that several critical elements should be consider in the analysis of data from cost-effectiveness studies. First, the perspective of civil society is rarely taken into account. Frequently, results are derived with a short time frame limited to the time of follow-up but costs should account also for costs of long-term complications and long-term treatments.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 13 October 2025 doi:10.20944/preprints202510.0828.v1

Moreover, costs of tests and therapy can be very different across Countries. There are many studies evaluating the impact of CCTA, while studies evaluating the "no testing" option are underrepresented; the treatment strategy varies between different studies (e.g. optimal medical therapy vs Revascularization). PPT varies greatly among trials. Results of studies do not reflect real-world practice frequently. Finally, in most studies, the performance of noninvasive diagnostic tests is evaluate in relation to their ability to identify or exclude the presence of a coronary lumen alteration compared to the evaluation of invasive coronary angiography.

4. Examples of Trials Evaluating Effectiveness of Tests

Several clinical trials such as PROMISE trial [11], SCOT-HEART trial [12], CE-MARC2 trial [13], PACIFIC trial [14] and EVINCI trial [15] compare different diagnostic strategies in order to evaluate the effectiveness of different imaging procedures or clinical strategies in patients with CHD (Table 1).

Table 1. Comparative Summary of Major CAD Imaging Trials.

Trial	Design & Population	Comparison/Arms	Key Findings	Cost-Effectiveness
PROMISE	RCT, stable chest pain, low–intermediate PTP	CCTA vs functional testing (stress imaging)	CCTA improved diagnostic accuracy, reduced ICA, similar outcomes; ↑ revascularization; low event rates	No significant cost difference at 3 yrs; QoL similar
SCOT-HEART	RCT, suspected CAD; mean FU 1.7 yrs	Standard care vs Standard care + CCTA	CCTA improved CAD diagnosis, optimized therapy, reduced MI; no ↑ ICA/revascularization	No formal CEA; post-hoc: higher 6-month costs in +CCTA arm
CE-MARC2	RCT, intermediate PTP	Stress CMR vs SPECT vs Guideline-directed care	Similar unnecessary ICA for CMR & SPECT; higher unnecessary ICA in guideline arm	Not directly analyzed; guideline less efficient
PACIFIC	Prospective, suspected CAD; invasive FFR reference	CCTA vs SPECT vs PET vs Hybrid	CCTA: highest sensitivity (90%), lowest specificity (60%); SPECT: highest specificity (94%), low sensitivity (57%); PET: best accuracy (85%)	Diagnostic performance only; no cost analysis
EVINCI	Multicenter European trial. ICA reference	CCTA vs functional stress imaging; ICA reference	CCTA superior for stenosis detection; functional better for ischemia/hypoperfusion	CEA: CCTA+ECHO & CCTA+SPECT cost-effective; PET data limited; variability across countries

PROMISE trial and SCOT-HEART trial are two examples of randomized clinical trials that compare one imaging test or strategy with another.

Results from PROMISE trial can be summarized as follow: CCTA-based diagnostic strategy increases diagnostic accuracy by decreasing the need for coronary angiography, showing a similar event rate compared to the strategy that involves the use of functional tests and reducing patient exposure to radiation. However, a more detailed analysis reveal that at a head to head comparison of functional vs anatomical testing CCTA did not improve outcome, ICA showing no obstructive CAD was more frequent after functional evaluation (as greatly demonstrate IHD is not only CAD) and revascularization was more frequent in the CCTA group although without functional evaluation.

In the SCOT-HEART trial the standard care strategy was compared with a standard care + CCTA guided strategy assessing the incidence of major adverse cardiac events (MACE) during a follow-up period of 1.7 years. In the trial CCTA seems to improve diagnosis of CAD, to allow for optimization of therapeutic interventions and reduce the risk of myocardial infarction. However, no increase in the downstream of ICA or of procedures for revascularization was observed in the arm randomized to standard care + CCTA guided strategy and the analysis of a secondary endpoint revealed a similar rate of MACE between randomized arms. Moreover, functional testing and CCTA were perform sequentially in the trial, integrated the management of patients.

Furthermore, overall event rates was low in PROMISE trial as well as in SCOT-HEART trial reflecting the inclusion of a large number of patients without CHD.

CE-MARC 2 trial enrolled intermediate PTP patients to one of three arms. The three arms were guided by the use of: stress MRI, SPECT or a Guideline directed care (including CAC followed by selective CCTA for patients at low PTP, SPECT for patients at intermediate PTP and ICA for patients at high PTP). Primary results from the trial revealed similar 1 year rate of unnecessary ICA for stress MRI and SPECT, but a significant higher rate of unnecessary invasive study for patients assigned to Guideline arm.

Purpose of the PACIFIC trial was to evaluate the accuracy of CCTA, SPECT, PET, and hybrid imaging for detecting significant CAD, using invasive fractional flow reserve (FFR) as the reference standard. As primary findings CCTA showed the highest sensitivity (90%) but the lowest specificity (60%), SPECT showed the higher specificity (94%) but a suboptimal sensitivity (57%) and PET showed the highest diagnostic accuracy (85%).

The Evinci trial compares the performance of CCTA and available non-invasive stress imaging modalities for the diagnosis of coronary artery disease. The gold standard of the study was the presence of stenosis on epicardial vessels depicted by ICA. Being the objective of the study the research of coronary stenoses, the performance of CCTA (anatomical test) resulted higher in comparison to that of functional test; however if the objective had been the detection of hypoperfuse territories, the result could have been change, perhaps in favor of functional tests.

This last aspect is crucial by a clinical point of view because it is widely demonstrated that in chronic coronary syndrome the mechanisms underlying ischemia can be due to epicardial disease, microvascular disease or to the coexistence of both of them. Moreover, ischemia can be correlated to the existence of a structural problem (e.g. atherosclerosis or inward arteriolar remodelling) or to a functional impairment (e.g. epicardial vasospasm or endothelial dysfunction and consequent impaired vasodilation). Finally, not all obstructive stenosis induce ischemia.

These are the major reasons for discordance between anatomical and functional testing approaches

Therefore, due to the peculiar characteristics, diagnostic tests are rarely interchangeable and the definition of the gold standard of what we are looking for and what we need to treat is mandatory (presence of stenosis? Hypoperfuse territories?).

As highlighted in the 2024 European Society of Cardiology guideline for the management of chronic coronary syndromes, the Knowledge of clinical information and the evaluation of clinical likelihood of obstructive coronary artery disease are crucial in order to select the most appropriate first line test for evaluating patients [16]. If clinical likelihood of CAD is ≤ 5 % there is no need for further tests. In patients with low clinical likelihood (5-15%) evaluation by ECG, ECHO, CCS or CCTA is recommend.

Furthermore, the Guide Lines clearly distinguish anatomical from functional tests.

The referring physician should have a clear vision of which is the primary need for the patient in order to choose the most effective investigation, limiting the sequence of tests without losing the necessary information for the optimal management. While in subjects with a clinical likelihood of obstructive CAD ranging from 15% to 50% the selection of anatomical vs functional test can be done based on characteristics of patient, when pre-test likelihood exceeds 50% functional evaluation is always recommended.

The possibility of anatomical-functional discordance is a matter of fact in IHD.

There are several studies reporting the use of non-invasive imaging modality (CCTA) for the quantification of FFR.

Evaluation of FFR provides helpful guidance in the decisional process for selecting the best treatment. However, FFR value is affected by the increase of microvascular resistance therefore hampering the use of this parameter in several clinical scenarios.

PET MPI is the gold standard for the non-invasive evaluation of absolute myocardial blood flow (MBF) and myocardial blood flow reserve (MFR) which reflects the global hemodynamic effect of CAD, including coronary artery stenosis and microvascular disease.

However, there are no randomized multicenter trials that establish the cost-effectiveness of PET flow parameter assessment.

A final aspect, underline also by both PROMISE trial and SCOT-HEART trial, is the use of imaging tests which imply radiation exposure [11,12]. This is a crucial point for ICA, CCTA, SPECT and PET in fact, patients radiation exposure can be significantly different based on technologies used, protocols adopted and presence of dose reduction software.

Moreover, independently from the imaging modality, state of the art technologies should be used in order to reduce radiation exposure.

As far as nuclear cardiology modalities are evaluate, MPI study can be optimize by using radionuclides with short half-life such as Tc-99m and PET tracers, performing stress-only protocol and applying weight-based dosing.

In Nuclear Cardiology, taking into consideration radiation exposure PET/CT studies should be preferred. However, PET facilities are not always available and cardiac testing can be inaccessible or quite expensive in absence of on-site cyclotron. However, optimize technologies such as the use of SPECT/CT scan implemented with Resolution Recovery software or the use of a tomography equipped with Cadmium-Zinc-Telluride (CZT) detectors can minimize patient exposure.

The CZT scanners are much more efficient in comparison to traditional SPECT technology in detecting energy emitted by radiopharmaceuticals therefore allowing images of excellent quality injecting a minimal amount of radiopharmaceutical and offering the possibility of quantitative evaluation of myocardial blood flow both at rest ad during stress testing. Several studies report a significant reduction in radiation exposure of patient undergoing MPI by using CZT cameras [17–19].

5. Cost- Effectiveness Analysis of Trials

Studies reporting cost-effectiveness evaluation of strategies for IHD have increase over the years (9). As notice previously, available data on economic evaluations of diagnostic strategies for CAD are greatly variable due to many afflicting aspects, therefore a definitive economic perspective is still challenging and a clear discrimination between the individual diagnostic strategies is not allowed jet.

In the PROMISE trial symptoms and quality of life did not reveal different improvement in the two strategies. Similarly, the CTTA and functional testing strategies had not significant difference in costs through 3 years of follow-up [20,21].

A real cost-effective analysis was not perform in the SCOT-HEART trial. However, in a post hoc analysis the costs over 6 months for the group of patients assigned to the standard care + CCTA strategy was higher in comparison to costs of group in the standard care strategy [22].

Finally, a very nice cost-effectiveness analysis from the EVINCI trial was publish by Lorenzoni V et al [23]. Authors concluded that combined CCTA-ECHO and CCTA-SPECT strategies were cost-effective for the diagnosis of obstructive CAD and dominated stand-alone stress-testing and other combination. Moreover, taking into consideration early revascularization as measure of effectiveness, only CCTA-SPECT was a cost-effective non-invasive strategy. However, as Authors pointed out, the limited sample size of data of some diagnostic modality (PET) or stategy (CCTA+PET or PET+CCTA) lead to high uncertainty for the extrapolation of generally applicable results. Moreover, results of the

 doi:10.20944/preprints202510.0828.v1

Country-specific cost-effectiveness analysis revealed high variability among European Countries included.

6. Conclusions

In a setting of low-to-intermediate prior probability, there is no simple answer to what the optimal diagnostic imaging strategy is for individuals suspected of having CAD. The reported trials failed to identify a significant difference taking into consideration the effectiveness of the variety of diagnostic test strategies analyzed.

For Patients with an intermediate PTP the referring clinician must define the objective of the require test in order to prescribe the most appropriate one (anatomical vs functional).

For each choice, it is necessary to consider local availability and expertise, timeless of scheduling, ability of the chosen test to give definitive answers that influence prognosis/ therapy and the need of further additional test.

Finally, any imaging modality especially those requiring radiation exposure, need to be optimize in order to offer the maximum clinical benefits while reducing radiation exposure.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

MPI	Myocardial perfusion imaging
SPECT	Single-photon emission computed tomography
PET	Positron emission tomography
CHD	Coronary heart disease
CVD	cardiovascular diseases
EU	Europe
CEA	cost-effectiveness analysis
CUA	cost-utility analysis
LYG	life-years gained
QALY	quality-adjusted life years
ICER	incremental cost-effectiveness ratio
ICUR	incremental cost-utility ratio
CAD	coronary artery disease
CCTA	coronary CT angiography
PTP	pre-test probability of disease
SE	stress echo
ICA	invasive coronary angiography
CSI	cardiac stress imaging
MRI	Magnetic Resonance Imaging
MACE	major adverse cardiac events
FFR	fractional flow reserve
CCS	Coronary calcium scoring
MBF	myocardial blood flow
MFR	myocardial blood flow reserve
CZT	Cadmium-Zinc-Telluride

References

1. Cardiovascular diseases (CVDs). https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)
2. Luengo-Fernandez, R.; Walli-Attaei, M.; Gray, A.; Torbica, A.; Maggioni, A.P.; Huculeci, R.; Bairami, F.; Aboyans, V.; Timmis, A.D.; Vardas, P.; Leal, J. Economic burden of cardiovascular diseases in the European Union: a population-based cost study. Eur Heart Jl 2023; 44: 4752–4767. doi: 10.1093/eurheartj/ehad583

3. Roth, G.A.; Mensah, G.A.; Johnson, C.O.; Addolorato, G.; Ammirati, E.; Baddour, L.M.; Barengo, N.C.; Beaton, A.Z.; Benjamin, E.J.; Benziger, C.P.; Bonny, A; Brauer, M.; Brodmann, M.; Cahill, T.J.; Carapetis, J.; Catapano, A.L.; Chugh, S.S.; Cooper, L.T.; Coresh, J.; Criqui, M.; DeCleene, N.; Eagle, K.A.; Emmons-Bell, S.; Feigin, V.L.; Fernández-Solà, J.; Fowkes, G.; Gakidou, E.; Grundy, S.M.; He, F.J.; Howard, G.; Hu, F.; Inker, L.; Karthikeyan, G.; Kassebaum, N.; Koroshetz, W.; Lavie, C.; Lloyd-Jones, D.; Lu, H.S.; Mirijello, A.; Misganaw Temesgen, A.; Mokdad, A.; Moran, A.E.; Muntner, P.; Narula, J.; Neal, B.; Ntsekhe, M.; Moraes de Oliveira, G.; Otto, C.; Owolabi, M.; Pratt, M.; Rajagopalan, S.; Reitsma, M.; Ribeiro, A.L.P.; Rigotti, N.; Rodgers, A.; Sable, C.; Shakil, S.; Sliwa-Hahnle, K.; Stark, B.; Sundström, J.; Timpel, P.; Tleyjeh, I.M.; Valgimigli, M.; Vos, T.; Whelton, P.K.; Yacoub, M.; Zuhlke, L.; Murray, C.; Fuster, V. for the GBD-NHLBI-JACC Global Burden of Cardiovascular Diseases Writing Group.Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update From the GBD 2019 Study. J Am Coll Cardiol 2020;76: 2982–3021 DOI: 10.1016/j.jacc.2020.11.010
4. Briggs, A.; Sculpher, M.; Claxton, K. Decision Modelling for Health Economic Evaluation. International J Epidemiology 2007; 36: 476–477. DOI: 10.1093/ije/dym062
5. Caro, J.J.; Briggs, A.H.; Siebert, U.; Kuntz, K.M. on Behalf of the ISPOR-SMDM Modeling Good Research Practices Task Force Modeling Good Research Practices—Overview: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-1. VALUE IN HEALTH 15 2012: 796 – 803
6. Abbott, J.H.; Wilson, R.; Pryymachenko, Y.; Sharma, S.; Pathak, A.; Chua, J.Y.Y. Economic evaluation: a reader's guide to studies of cost-effectiveness. Archives of Physiotherapy 2022: 12-28 DOI: 10.1186/s40945-022-00154-1
7. Cylus J.; Papanicolas I.; Smith P.C. editors. Health system efficiency: How to make measurement matter for policy and management European Observatory on Health Systems and Policies 2016
8. Jakubiak-Lasocka, J.; Jakubczyk, M. Cost-effectiveness versus Cost-Utility Analyses: What Are the Motives Behind Using Each and How Do Their Results Differ? A Polish Example. Value in Health Regional Issues 4C 2014: 66 – 74 29702810 DOI: 10.1016/j.vhri.2014.06.008
9. vanWaardhuizen, C.N.; Khanji, M.Y.; Genders, T.S.S.; Ferket, B.S.; Fleischmann, K.E.; Hunink, M.G.M.; Petersen, S.E. Comparative cost-effectiveness of non-invasive imaging tests in patients presenting with chronic stable chest pain with suspected coronary artery disease: a systematic review. European Heart Journal – Quality of Care and Clinical Outcomes 2016; 2: 245–260. doi:10.1093/ehjqcco/qcw029
10. Genders, T.S.S.; Petersen, S.E.; Pugliese, F.; Dastidar, A.G.; Fleischmann, K.E.; Nieman, K.; Hunink. M.G.M. The Optimal Imaging Strategy for Patients With Stable Chest Pain: a cost-effectiveness analysis. Ann Intern Med. 2015; 162:474-84. doi: 10.7326/M14-0027
11. Douglas, P.S.; Hoffmann, U.; Patel, M.R.; Mark, D.B.; Al-Khalidi, H.R.; Cavanaugh, B.; Cole, J.; Dolor, R.J.; Fordyce, C.B.; Huang, M.; Akram Khan, M.; Kosinski, A.S.; Krucoff, M.W.; Malhotra, V.; Picard, M.H.; Udelson, J.E.; Velazquez, E.J.; Yow, E.; Cooper, L.S.; Lee, K.L. for the PROMISE Investigators. Outcomes of Anatomical versus Functional Testing for Coronary Artery Disease. N Engl J Med 2015; 372:1291-300 doi:10.1056/NEJMoa1415516
12. The SCOT-HEART investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. Lancet 2015; 385: 2383–91. doi: 10.1016/S0140-6736(15)60291-4
13. Greenwood, J.P.; Ripley, D.P.; Berry, C.; McCann, G.P.; Plein, S.; Bucciarelli-Ducci, C.; Dall'Armellina, E.; Prasad, A.; Bijsterveld, P.; Foley, J.R.; Mangion, K.; Sculpher, M.; Walker, S.; Everett, C.C.; Cairns, D.A.; Sharples, L.D.; Brown, J.M. for the CE-MARC 2 Investigators 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; 316:1051-60. doi: 10.1001/jama.2016.12680
14. Danad, I.; Raijmakers, P.G.; Driessen, R.S.; Leipsic, J.; Raju, R.; Naoum, C.; Knuuti, J.; Mäki, M.; Underwood, R.S.; Min, J.K.; Elmore, K.; Stuijfzand, W.J.; van Royen, N.; Tulevski, I.I.; Somsen, A.G.; Huisman, M.C.; van Lingen, A.A.; Heymans, M.W.; van de Ven, P.M.; van Kuijk, C.; Lammertsma, A.A.; van Rossum, A.C.; Knaapen P. Comparison of Coronary CT Angiography, SPECT, PET, and Hybrid

Imaging for Diagnosis of Ischemic Heart Disease Determined by Fractional Flow Reserve.. JAMA Cardiol 2017; 2:1100-1107 doi: 10.1001/jamacardio.2017.2471.

15. Neglia, D.; Rovai, D.; Caselli, C.; Pietila, M.; Teresinska, A.; Aguadé-Bruix, S.; Pizzi, M.N.; Todiere, G.; Gimelli, A.; Schroeder, S.; Drosch, T.; Poddighe, R.; Casolo, G.; Anagnostopoulos, C.; Pugliese, F.; Rouzet, F.; Le Guludec, D.; Cappelli, F.; Valente, S.; Gensini, G.F.; Zawaideh, C.; Capitanio, S.; Sambuceti, G.; Marsico, F.; Perrone Filardi, P.; Fernández-Golfín, C.; Rincón, L.M.; Graner, F.P.; de Graaf, M.A.; Fiechter, M.; Stehli, J.; Gaemperli, O.; Reyes, E.; Nkomo, S.; Mäki, M.; Lorenzoni, V.; Turchetti, G.; Carpeggiani, C.; Marinelli, M.; Puzzuoli, S.; Mangione, M,; Marcheschi, P.; Mariani, F.; Giannessi, D.; Nekolla, S.; Lombardi, M.; Sicari, R.; Scholte, A.J.H.A.; Zamorano, J.L.; Kaufmann, P.A.; Underwood, S.R.; Knuuti, J. The EVINCI Study Investigators. Detection of Significant Coronary Artery Disease by Noninvasive Anatomical and Functional Imaging. Circ Cardiovasc Imaging. 2015;8: e002179 doi: 10.1161/CIRCIMAGING.114.002179.
16. 2024 ESC Guidelines for the management of chronic coronary syndromes: Developed by the task force for the management of chronic coronary syndromes of the European Society of Cardiology (ESC) Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart Jl 2024; 45: 3415–3537 doi: 10.1093/eurheartj/ehaf079.
17. Duvall, W.L.; Guma, K.A.; Kamen, J.; Croft, L.B.; Parides, M.; George, T.; Henzlova, M.J. Reduction in Occupational and Patient Radiation Exposure from Myocardial Perfusion Imaging: Impact of Stress-Only Imaging and High-Efficiency SPECT Camera Technology. J Nucl Med 2013, 54: 1251-1257 doi: 10.2967/jnumed.112.112680.
18. Einstein, A.J.; Blankstein, R.; Andrews, H.; Fish, M.; Padgett, R.; Hayes, S.W,; Friedman, J.D.; Qureshi, M.; Rakotoarivelo, H.; Slomka, P.; Nakazato, R.; Bokhari, S.; Di Carli, M.; Berman, D.S. Comparison of image quality, myocardial perfusion, and left ventricular function between standard imaging and single-injection ultralow-dose imaging using a high-efficiency SPECT camera: the MILLI-SIEVERT study. J Nucl Med 2014; 55:1430–7 doi: 10.2967/jnumed.114.138222.
19. Prasad, K.; Adams, C.C.; Quang, E.; Taylor, J.; Stocker. D.J. The effect of body mass index on high versus low administered activity protocol myocardial perfusion imaging scan time and effective dose using a cadmium zinc telluride camera in clinical practice. World J Nucl Med 2021; 20: 247–252 doi: 10.4103/wjnm.WJNM_123_20.
20. Mark, D.B.; Federspiel, J.J.; Cowper, P.A.; Anstrom, K.J.; Hoffmann, U.; Patel, M.R.; Davidson-Ray, L.; Daniels, M.R.; Cooper, L.S.; Knight, J.D.; Lee, K.L.; Douglas, P.S. Economic outcomes with anatomical versus functional diagnostic testing for coronary artery disease. PROMISE Investigators. . Ann Intern Med 2016; 165: 94–102 doi: 10.7326/M15-2639.
21. Mark, D.B.; Anstrom, K.J.; Sheng S.; Baloch, K.N.; Daniels, M.R.; Hoffmann, U.; Patel, M.R.; Cooper, L.S.; Lee, K.L.; Douglas, P.S. on behalf of the PROMISE Investigators. Quality-of-life outcomes with anatomic versus functional diagnostic testing strategies in symptomatic patients with suspected coronary artery disease: results from the PROMISE randomized trial. Circulation 2016: 133: 1995–2007 doi: 10.1161/CIRCULATIONAHA.
22. Williams, M.C.; Hunter, A.; Shah, A.S.V.; Assi, V.; Lewis, S.; Smith, J.; Berry, C.; Boon, N.A.; Clark, E.; Flather, M.; Forbes, J.; McLean, S.; Roditi, G.; van Beek, E.J.R,; Timmis, A.D.; Newby, D.E. SCOT-HEART Investigators. Use of coronary computed tomographic angiography to guide management of patients with coronary disease. J Am Coll Cardiol 2016: 67: 1759–1768 doi: 10.1016/j.jacc.2016.02.026.
23. Lorenzoni, V.; Bellelli, S.; Caselli, C.; Knuuti, J.; Underwood, S.R.; Neglia, D.; Turchetti,· G. For the EVINCI Investigators. Cost-effectiveness analysis of stand-alone or combined non-invasive imaging tests for the diagnosis of stable coronary artery disease: results from the EVINCI study Eur J Health Econ 2019; 20:1437–1449 doi: 10.1007/s10198-019-01096-5.