Hybrid anatomo-functional imaging of coronary artery disease: Beneficial irrespective of its core components

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Coronary artery disease (CAD) is the most common and important cause of ischemic heart disease, with major implications on global morbidity and mortality. Non-invasive testing is crucial in the diagnostic and prognostic work-up of patients with or at risk of CAD, and also to guide decision making in terms of pharmacologic and revascularization therapy. The traditional paradigm is to view anatomic (i.e., coronary computed tomography) and functional imaging (e.g., myocardial perfusion scintigraphy) tests as opposing alternatives. Such approach is too reductionist and does not capitalize on the strengths of each type of test while risking to overlook the inherent limitations. The combination of anatomic and functional tests in a logic of hybrid imaging holds the promise of overcoming the limitations inherent to anatomic and functional testing, enabling more accurate diagnosis, prognosis, and guidance for revascularization in patients with CAD. (J Nucl Cardiol 2019;26:752–62.)

Key Words: Coronary artery disease • computed tomography • hybrid imaging • single-photon emission computed tomography

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Abbreviations and acronyms	
CAD	Coronary artery disease
CMR	Cardiac magnetic resonance
CT	Computed tomography
CTA	Computed tomography angiography
CTP	Computed tomography perfusion
CZT	Cadmium-zinc-telluride
CT-FFR	Computed tomography fractional flow reserve
PET	Positron emission tomography
SPECT	Single-photon emission computed tomography
SYNTAX	Synergy between PCI with Taxus and Cardiac Surgery

Man, a hybrid of plant and ghost.
Friedrich Nietzsche.

See related editorial, pp. 693–695

INTRODUCTION

Coronary artery disease (CAD) is the most common and important cause of ischemic heart disease, with major implications on global morbidity and mortality.[1] It is particularly important to identify subjects at risk of sudden death as, for instance, cardiac arrest among competitive athletes aged 35 years or more is often due to CAD.[2] Notably, CAD represents a continuum with unfavorable evolution of plaque paralleling stenosis severity.[3] However, even if less significant lesions are at lower risk of instability than more significant ones, their much larger prevalence means that many major adverse cardiac events occur even in the absence of angiographically significant lesions.[4]

ANATOMIC VERSUS FUNCTIONAL IMAGING

Imaging can provide important insights for patients with CAD, providing diagnostic clues, prognostic insights, and guiding operational strategy.[5–7] For these purposes, several alternative tests have been developed and applied successfully in clinical practice over several decades, which can be broadly distinguished in functional tests aiming at appraising ischemia, and anatomical tests aiming at estimating atherosclerotic burden and coronary anatomy.[8] ECG stress testing, stress echocardiography, positron emission tomography (PET), and single-photon emission computed tomography (SPECT) are all functional tests, whereas computed tomography angiography (CTA) is the key non-invasive anatomical test.[9] Notably, recent developments in computed tomography (CT) can also provide functional results by means of computed tomography perfusion (CTP) and non-invasive fractional flow reserve (CT-FFR).[10] Cardiac magnetic resonance (CMR) has both functional and anatomic capabilities, but given size and motion of coronary arteries, its main role in patients with CAD is functional.[11]

In general terms, CMR, ECG stress testing, and stress echocardiography appear more appealing than other non-invasive imaging tests as they are not associated with any radiation exposure, which instead is the rule for CT-based tests, PET, and SPECT. Yet, we should gauge radiation exposure also in its indirect form, which depends on the ability of a given test to identify which patient to refer for coronary angiography or percutaneous revascularization, both much more burdensome in terms of radiation exposure in comparison to non-invasive tests, and whose clinical inappropriateness may be missed by imprecise or inaccurate preliminary tests.[12] Accordingly, we should seek to reduce total radiation exposure (the sum of direct and indirect ones) by using the test which best maximizes the appropriateness of invasive tests requiring much higher radiation exposure.[13] Moreover, the burden of major adverse cardiac events is much more significant than the burden of stochastic risk due to radiation exposure (e.g., cardiovascular death is much more likely in patients with suspected CAD not undergoing any radiation exposure-associated test than cancer death in similar subjects undergoing such tests).[14]

After careful appraisal of clinical history, which should always encompass symptoms and signs, risk factors, and history of prior revascularization (including evidence of myocardial ischemia if previously assessed), the typical framework for most imaging tests has rested until recently on a one step-one test paradigm, whereby a patient undergoes one or more tests, but only sequentially, and only if the prior tests have been inconclusive or require further corroboration (Figure 1). Whereas this approach may save resources, at least initially, and reduce radiation exposure, especially if early tests are not leading to any such exposure, misclassifications are common, and timeliness of diagnosis and risk prognostication may be impaired. Yet, rather than focusing on the subtleties of a given test, it is important to appraise its role to accurately define patient diagnosis, prognosis, and guide subsequent management. In addition, one of the most important drawbacks of any non-invasive diagnostic test for CAD is operator and institutional variability.[15] Indeed, operator experience and skill, case mix, and overall volume of a given test impact significantly on its diagnostic and prognostic accuracy. The more the tests performed by a center, the better its overall performance. Unfortunately, focusing on operator experience and skill, case mix, and overall volume as

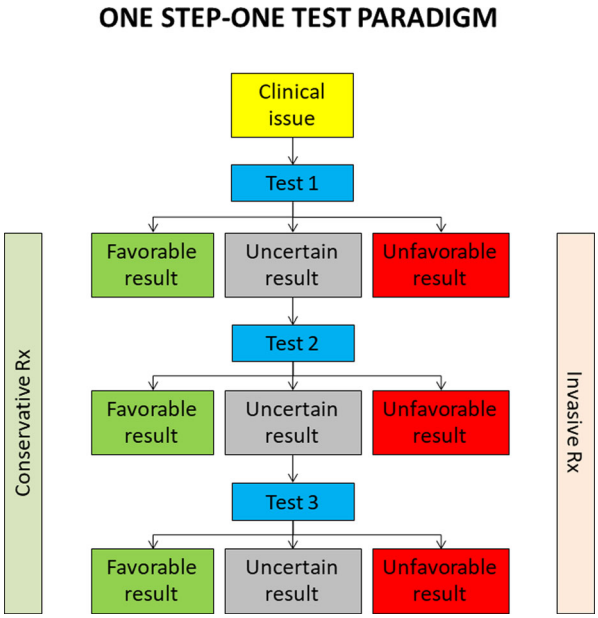

Figure 1. Algorithm of the one step-one test approach for the diagnostic, prognostic, and procedural appraisal of a clinical issue in patients who are not at very low nor very high risk, based on subsequent testing of patients, depending on results of prior tests.

sanctionable issues may be futile, unfeasible, or destructive of other competence or effectiveness dimensions. Accordingly, focusing on data processing, analysis, and reporting of a single study is likely to provide only marginally incremental benefits for accuracy.

Notwithstanding these subtleties, nuclear cardiology has been historically and continues to be the most robust and used non-invasive imaging modality for CAD, with SPECT largely toppling PET at least in terms of volume of procedures.[16,17] Advantages of nuclear imaging include the possibility of using exercise as stressor and the accrual of several diagnostic features such as myocardial perfusion, viability, geometry (e.g., stress and rest end-diastolic diameter), regional wall motion (after stress and at rest), and global systolic function (ejection fraction and end-systolic volume, and contractile reserve).[16–20] The advent of Alcyone technology-based solid-state cadmium-zinc-telluride (CZT) detectors, thanks to heightened spatial and energy resolution, increases sensitivity and specificity as well as acquisition time (< 3 minutes) and effective radiation dose (< 3 mSv).[21] This new-generation camera has many advantages in comparison to Anger cameras: increased specificity, more precise quantification of ischemia severity, quantitative appraisal of coronary flow reserve (CFR), heightened sensitivity in recognizing patients with multivessel disease, easier identification of the culprit lesion, more accurate measurement of ventricular geometry (end-diastolic and mass) and function (stress/rest), dual isotope imaging (e.g., Tl and MIBG), and integrated SPECT/CTA imaging.

HYBRID IMAGING

Improvements in technology, such as availability of imaging suites with multimodality capabilities, decreased radiation exposure, and fusion processing software, have recently enabled clinicians to combine one or more tests according to a hybrid anatomo-functional paradigm, suitable for more timely and precise evaluation of patients at low to high risk (Figures 2, 3).[7,9,10,22–25] This novel algorithm capitalizes on clinical assessment and profiling, and by combining the results of two potent and complementary tests provides detailed multidimensional insights on patient diagnosis, risk, warranty period, and optimal management. In particular, risk is very high in subjects with both tests yielding clearly unfavorable results, and very low in patients with both tests yielding clearly favorable results. Yet, the vast majority of patients will have some discrepancies between tests. The careful appraisal of anatomic detail in light of functional data yields the promise of accurate definition of diagnosis, risk, warranty period, and management. Notably, such algorithm is best applied using the Maximal Ischemia Score (MIS) strategy previously outlined by our group given its greater accuracy and clinical relevancy for risk prognostication.[16] Moreover, on top of ischemia appraisal, the role of functional imaging, especially when embodied in state-of-the art SPECT suites, is strengthened by the possibility to provide additional details on cardiac viability, function, geometry, and desynchronization.

Despite its ingeniousness and the fact that such fusion imaging can be obtained in real time or even at post-processing, with substantial flexibility, the hybrid approach faces important challenges, including specialist turfs, radiation exposure, cost, and, most importantly, a limited yet expanding evidence base. In addition, it remains unclear whether only doubly abnormal tests should be considered indicative of disease (for instance a patient with an anatomically and functionally significant stenosis at CT-FFR/CTA), or instead any abnormality should be viewed as posing the patient at risk, with a hierarchy in severity depending on the specific results of each test. Yet, the appeal of a combined imaging strategy is self-evident if one considers that 50% or even less of lesions which are significant at CTA or invasive coronary angiography are associated with myocardial ischemia, as atherosclerosis may lead to positive remodeling and flow regulation mechanisms which may increase rest flow substantially

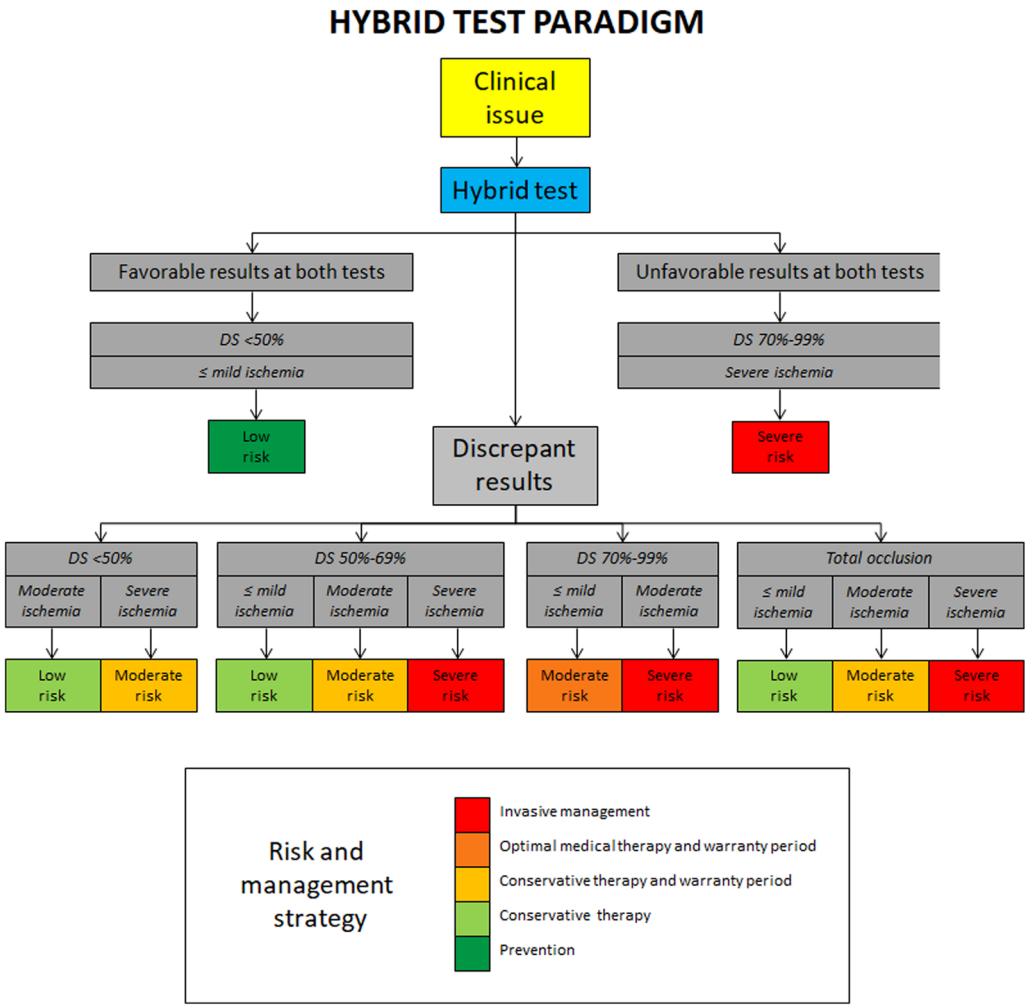

Figure 2. Algorithm for hybrid anatomo-functional testing, based on the combination of two tests for the definition of the prognosis, risk, warranty period, and management. Italics show different results from the combined appraisal of myocardial perfusion scintigraphy and computed tomography angiography, whereas colored boxes provide details on ensuing risk and guidance for management.

and thus minimize the pathophysiologic impact of angiographically mild, moderate, and also severely significant lesions, in particular in case of coronary occlusion.[26] Indeed, the main goal of hybrid imaging rests on the capability of identifying among patients with angiographically (> 50% diameter stenosis) significant lesions those who also have accompanying myocardial ischemia, expliciting its extent and degree, as revascularization has evidence-based benefits only in subjects with extensive or severe ischemia. In addition, identification of the culprit coronary lesion is easily accomplished with hybrid imaging. On the other hand, recognizing CAD due to moderate or significant angiographic disease, even in the absence of myocardial ischemia, is also clinically important, as it prompts and guides optimal medical management.

In the landmark Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) study, invasive anatomic (based on quantitative coronary angiography) and functional testing (based on fractional flow reserve [FFR]) showed low agreement for moderately severe stenoses.[27] Indeed, functional significance occurred only in 35% of stenoses with 50 to 70% luminal narrowing, in 80% of stenoses with 71 to 90% luminal narrowing, and in 95% of stenoses with > 90% luminal narrowing. On top of this and most importantly, functional details better predict prognosis and thus can more accurately guide decision making. Several non-

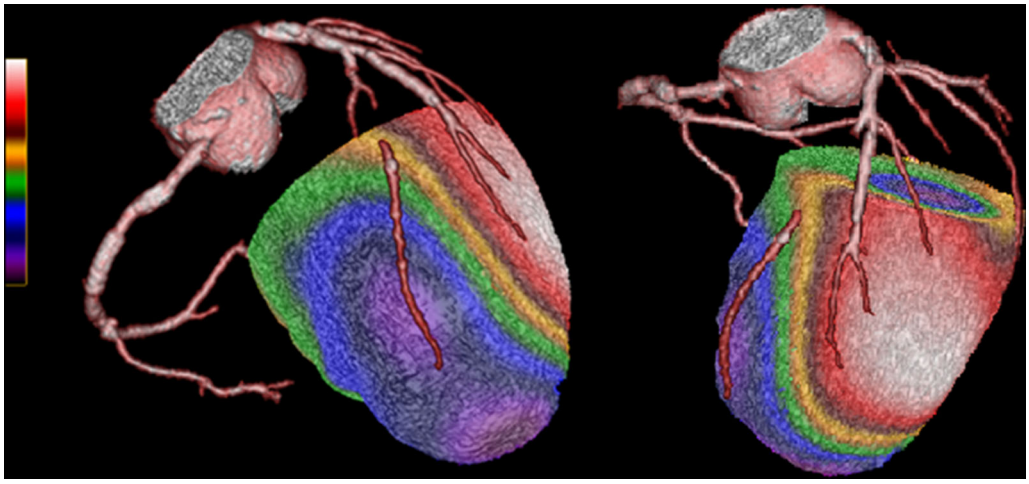

Figure 3. Prototypical case of hybrid anatomo-functional non-invasive imaging based on the combination of computed tomography angiography (CTA) of coronary arteries and myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) in a 68-year-old gentleman with multiple cardiovascular risk factors and clinical history of effort angina. The left anterior descending is chronically occluded in the mid-segment, and there is concomitant severe ischemia in the corresponding myocardial regions. Accordingly, and in keeping with the algorithm outlined in Figure 2, invasive management is recommended. Left panel: right anterior oblique-caudal projection. Right panel: left anterior oblique-cranial projection.

invasive alternatives to FFR are available, including parameters which are more closely related to flow such as myocardial perfusion, but other features can also be exploited for this purpose, such as wall motion, despite its less indirect association with flow. Overall, and in light of the strong agreement between non-invasive and invasive tests with a similar scope, the key advantage of non-invasive imaging rests on providing a result which precedes invasive coronary angiography and may establish its indication, making it clearly cost-effective.

Several studies have compared SPECT with invasive coronary angiography, focusing on prognostic accuracy, which remains the real benchmark to guide the choice of any imaging test. In a landmark study, it was shown that the incidence of major adverse cardiac events in patients with angiographically significant CAD but normal SPECT was $< 1\%$.[28] In similar studies, the prognosis of patients with CAD but normal SPECT appeared similar to that of subjects without normal coronary arteries ($< 1\%$ incidence of major adverse cardiac events).[29,30]

Prognostic accuracy and the validity in guiding decision making for each test of choice cannot be overemphasized, and they are both in keeping with diagnostic accuracy and cost-effectiveness. Accordingly, the information yield of an imaging test such as SPECT is best used in an integrative framework, which sees the interpretation of each test not banalized in a positive/negative or abnormal/normal dichotomy, but instead exploited for an accurate evaluation and stratification of the risk of the patient, for instance using the concept of vessel-related ischemia (VRI).[16,17]

We hereby briefly highlight the main alternatives for hybrid anatomo-functional imaging of CAD, emphasizing their potential benefits and drawbacks in light of the chosen combination (Tables 1, 2). Of course, despite their many differences, all functional tests share a common core of diagnostic and prognostic role, and the key is combining a functional test with CTA, rather than picking and sticking to a single functional or anatomic test.

Exercise ECG can be viewed as ECG imaging and thus also be considered as a non-invasive functional imaging test, given the multiple derivations used with ECG and the combination with exercise testing. However, its limitations in terms of diagnostic and prognostic accuracy are well known, and to date no combination approach with CTA has been proposed.

Transthoracic echocardiography has been often used together with exercise or, more commonly, pharmacologic stress to monitor segmental wall motion as a marker of ischemia and necrosis in patients with CAD. Recent scholarly evidence suggest estimates for sensitivity of 86% and specificity of 74% for the detection of anatomically significant CAD (defined as angiographic evidence of $\geq 50\%$ diameter stenosis at invasive coronary angiography [ICA]), whereas these figures go to 77% and 75% when using as reference standard

Table 1. Key features of alternative approaches for hybrid anatomo-functional imaging for coronary artery disease

Approach	Main components	Pros	Cons
CMR/CTA	Pharmacologic stress required; gadolinium-chelate contrast; perfusion and wall contractility assessment	Comprehensive assessment of viability and perfusion; no additional radiation exposure	Lack of exercise stress; prone to artifacts
CT-FFR/CTA	Imaging processing from CTA data	No additional radiation exposure; no stressor needed	Lack of exercise stress; prone to artifacts
CTP/CTA	Pharmacologic stress optional; perfusion and wall contractility assessment	No additional radiation exposure	Lack of exercise stress; prone to artifacts
Echo/CTA	Exercise or pharmacologic stress required; echocardiographic contrast; wall contractility assessment	No additional radiation exposure	Between and within-operator variability; dependance on echographic image quality
PET/CTA	Pharmacologic or exercise stress required; several radionuclides; perfusion, viability, blood flow, and wall contractility assessment	Comprehensive assessment of viability and perfusion	Additional radiation exposure
SPECT/CTA	Exercise or pharmacologic stress; several radionuclides; perfusion, viability, blood flow, and wall contractility assessment	Comprehensive assessment of viability and perfusion	Additional radiation exposure

CMR, cardiac magnetic resonance; *CTA*, coronary computed tomography angiography; *CT-FFR*, computed tomography fractional flow reserve; *CTP*, computed tomography perfusion; *Echo*, echocardiography; *PET*, positron emission tomography; *SPECT*, single-photon emission computed tomography

functional significance (defined as fractional flow reserve [FFR] $\leq$ 0.80).[8,31] Despite these favorable results, stress echocardiography is used only by selected institutions for the diagnosis of CAD given issues related to reproducibility and reimbursement. Recent developments in fusion technology have enabled physicians to perform hybrid anatomo-functional imaging with stress echocardiography or similar echocardiographic techniques and CTA.[32–34] Unfortunately, no study has yet reported on the incremental comparative accuracy of such hybrid imaging in comparison to invasive assessments, even if reports using CT-FFR as gold standard are already available.[35]

Cardiac magnetic resonance has gained significant ground in the comprehensive anatomic and functional assessment of cardiovascular disease. In the diagnosis of CAD, CMR, incorporating the administration of a pharmacologic stressor and gadolinium-chelate contrast, has proven as a valuable non-invasive alternative to ICA and FFR, with sensitivity and specificity of 90% and 77%, and of 90% and 85%, respectively.[35] Several studies have appraised the benefit of combined imaging with CMR and CTA, finding that CMR/CTA has in comparison to ICA a sensitivity ranging between 88% and 99% and a specificity ranging between 87% and 100%.[10,36,37] Similarly favorable results have been reported in comparison to FFR, with sensitivity of 85% and specificity of 94%.[10,38]

Positron emission tomography continues to play an important role in the diagnosis and management of CAD, thanks to the availability of several radionuclides with enhanced pathophysiologic relevance.[39] It can be used to appraise in absolute quantitative terms myocardial perfusion, viability, wall motion, inflammation, and apoptosis. Indeed, it has been clarified that, on top of perfusion, details on hyperemic myocardial blood flow and coronary flow reserve may improve diagnostic and prognostic accuracy of PET.[40] Given the ongoing improvements in technology, procedures, and protocols, PET has reached favorable results in terms of sensitivity and specificity in comparison to ICA, with figures, respectively, of 84% and 81%. Similar results were

Table 2. Key studies on alternative approaches for hybrid anatomo-functional imaging for coronary artery disease

Approach	Study (first author, PubMed ID)	Patients	Main findings
CMR/CTA	Groothuis,[38] 23475530	192	Combination of CMR and CTA increases specificity in comparison to CTA only and thus overall diagnostic accuracy
CT-FFR/CTA	Coenen,[60] 25322342	106	CT-FFR improves the diagnostic accuracy of CTA by boosting mainly specificity but also marginally sensitivity
CTP/CTA	Osawa,[52] 26894686	53	Hybrid imaging with CTP and CTA has good diagnostic accuracy in comparison to FFR
Echo/CTA	Mor-Avi,[33] 29576220	78	Hybrid imaging with rest CTA and 3D echo is feasible and shows good diagnostic accuracy in comparison to ICA and FFR
PET/CTA	Danad,[8] 23232274	120	Hybrid imaging has superior diagnostic accuracy in comparison to CTA alone or PET alone
SPECT/CTA	Pazhenkottil,[22] 21804107	335	Hybrid imaging improves prognostic stratification of patients with CAD

CAD, coronary artery disease; *CMR*, cardiac magnetic resonance; *CTA*, coronary computed tomography angiography; *CT-FFR*, computed tomography fractional flow reserve; *CTP*, computed tomography perfusion; Echo, echocardiography; *FFR*, invasive fractional flow reserve; *ICA*, invasive coronary angiography; *PET*, positron emission tomography; *SPECT*, single-photon emission computed tomography

found for FFR, with sensitivity reaching 86% and specificity 88%. Several studies have provided evidence on the feasibility and value of hybrid PET/CTA imaging.[10] In comparison to ICA, PET/CTA appears to have sensitivity ranging between 91% and 96% and specificity of 100%.[41,42] When using FFR as gold standard, PET/CTA yields instead sensitivity ranging between 76% and 95%, and specificity ranging between 92% and 100%.[8,43]

Myocardial perfusion imaging with SPECT remains a mainstay in the diagnosis of CAD, with recent developments such as the introduction of CZT suites further expanding its potential by providing details on absolute myocardial blood flow and coronary flow reserve. Pooled estimates for SPECT in comparison to ICA are of 88% for sensitivity and 61% for specificity.[44] When using FFR as reference standard, sensitivity appears to decrease to 70% and specificity to increase to 78%.[8] Analyses limited to CZT suites only versus ICA suggest for sensitivity estimates ranging between 56% and 95%, and for specificity between 25% and 88%.[5] According to Mouden et al., comparative analysis for CZT SPECT vs FFR suggests instead sensitivity of 60% and specificity of 76%.[45] Several studies have provided details on the added benefits of combining SPECT and CTA in patients with suspected CAD.[10] In comparison to ICA, SPECT/CTA reaches sensitivity ranging between 86% and 99%, and specificity between and 67% and 87%.[46] Notably, Schaap and colleagues have compared SPECT/CTA to FFR, reporting 96% sensitivity and 95% specificity.[47]

Thanks to momentous developments in CT suites, myocardial perfusion can be appraised with CT on top of coronary anatomy.[48] Static CTP uses a single acquisition, which can also be employed for CTA. Otherwise, dynamic CTP requires both stress and rest acquisitions, leading to improved accuracy, but leading to higher contrast volume and radiation exposure when compared to CTA.[49] In terms of diagnostic accuracy, CTP has a sensitivity of 77 to 82% and a specificity of 78% to 89% in comparison to ICA.[50] Moving to FFR as reference standards, these estimates move to 94% and 77%, respectively.[51] The combination of CTP and CTA has been already tested in several centers, yielding promising estimates for diagnostic accuracy. In particular, the sensitivity of CTP/CTA in comparison to ICA is 94% whereas specificity is 93%.[47] Corresponding figures for FFR are 91% and 72%.[52]

Innovations in image processing have enabled the development of algorithms to infer non-invasively FFR stemming from CTA, with a technique aptly named CT-FFR. This approach can be best considered another example of functional ischemia test. Data for CT-FFR are still accruing, and the comparative accuracy of the two competing systems for CT-FFR has not been quantified formally yet. However, CT-FFR appears to

have a sensitivity of 90% and a specificity of 72% in comparison to FFR.[51] Estimates for other comparative analyses have not been reported.

While this overview of different embodiments of anatomo-functional imaging may guide physician, institution, and patient choice, we prefer to disregard explicit head-to-head comparisons between functional tests, leaving thus ample room to choose individually the specific functional test, based on expertise, availability, evidence, experience, cost, and so forth.

CASE STUDIES IN HYBRID IMAGING

The real potential of hybrid anatomo-functional imaging is all too evident when examining its impact in real clinical practice (Figure 3). In particular, the combination of anatomic appraisal of CAD (detailing number, location, extent, and complexity of coronary lesions) and of functional evaluation (detailing number, location, extent, and severity of ischemia, plus insights on myocardial necrosis, as well as ventricular function and geometry) represents a paradigm shift for individualized patient management. Most importantly, hybrid imaging is not simply the algebraic sum of two reasonably accurate tests, but exponentially improves overall test results, by focusing on agreements and highlighting discrepancies, which may be crucial for decision making (e.g., by shifting the management strategy from revascularization to medical therapy only, or vice versa).

Moreover, combination of anatomic and functional non-invasive imaging may provide additional diagnostic and prognostic clues for patients with CAD by enabling the computation of the anatomic Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) score.[53] Indeed, this score of CAD extent and complexity, originally designed for invasive angiography, has been later successfully applied to CTA.[54,55] Concomitantly, the application of invasive FFR has enabled the computation of the functional SYNTAX score, by discounting anatomically significant lesions which were not significant at FFR (or instantaneous wave-free ratio [iFR]).[26,55] This was most recently extended to non-invasive assessment of CAD with CT-FFR.[56] Accordingly, we hereby propose in general terms for the first time that anatomic and functional SYNTAX scores can be computed non-invasively with the combination of CTA and any non-invasive functional test (Figure 4). The importance of jointly appraising anatomic and functional significance of a coronary lesion is all too evident when, for instance, comparing the clinical impact of a proximal LAD lesion with complex angiographic features and causing extensive and severe myocardial ischemia versus that of a distal lesion of a

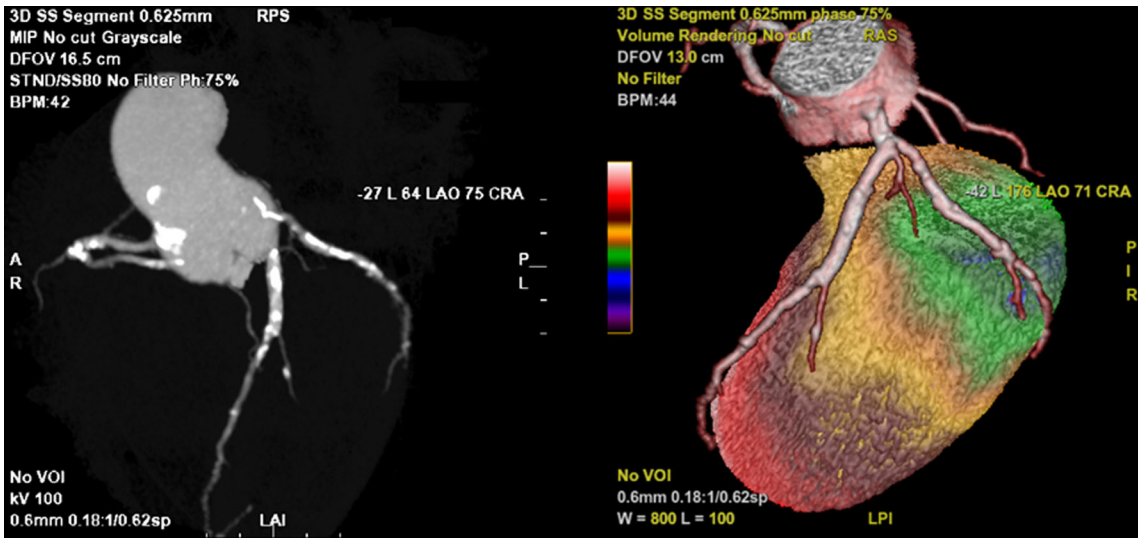

Figure 4. Exploiting hybrid non-invasive anatomo-functional imaging to compute anatomic and functional Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) score in a 75-year-old gentleman with multiple atherosclerotic risk factors and chronic stable angina. There are diffuse and severe coronary calcifications thus leading to a high calcium score. Anatomic evidence of moderately severe lesions in the three main coronary vessels, with concomitant moderate ischemia only in the regions fed by the left circumflex, thus qualifying the patient at moderate risk. Accordingly, the non-invasive anatomic SYNTAX score was 22, whereas the non-invasive functional SYNTAX score was reduced to 6. Left panel: anatomic imaging. Right panel: hybrid anatomo-functional imaging.

minor diagonal branch with simple angiographic features and causing minimal subsegmental ischemia.

IMPLICATIONS AND CONCLUSIONS

The possibility of combining functional imaging tests with an anatomic test such as CTA has created novel and important opportunities for refined diagnosis, prognosis, and treatment of CAD. In addition, hybrid imaging may be exploited to appraise coronary plaque pathophysiology,[23] atherothrombotic burden,[57] and risk of instability,[58] as well as myocardial inflammation, apoptosis, and dysinnervation.[21]

Indeed, several key elements for successful implementation and use hybrid imaging should be borne in mind. First, when appraising stenoses of similar angiographic severity (e.g., 70% diameter stenosis), it is paramount to be able to distinguish lesions which have impaired coronary reserve and thus impact unfavorably on prognosis in comparison to those which have preserved coronary reverse and thus do not confer a prognostic disadvantage, and hybrid imaging is ideally equipped to do it. Indeed, a negative CT in as much a positive CT is insufficient to precisely guide decision making. Second, patients without evidence of ischemia at functional testing (e.g., normal SPECT) include subjects with very different features, and thus very heterogeneous (e.g., a patient may have angiographically normal coronary arteries, another may have atherosclerotic disease without angiographically significant lesions, and another still may have an angiographically significant or even occlusive lesion). Accordingly, even MPI or other functional tests if viewed alone are insufficient to establish diagnosis and prognosis. Third, stressor presence and type is key, with exercise ECG testing being indeed already a rudimentary imaging test, whereas exercise is the most valid stressor, and surely better than any pharmacologic stress.[59] Accordingly, use of a functional test encompassing exercise as stressor is particularly appealing in a logic of hybrid imaging. Fourth, another important aspect requiring attentive analysis is the assessment of viability in myocardial regions with angiographically significant coronary lesions.[19] Only hybrid imaging can provide such detail and integrate it with coronary anatomy and evidence of ischemia. On top of these benefits, hybrid imaging including MPI can quantify the severity of ventricular dyssynchrony thus informing the indication to cardiac resynchronization therapy, whereas hybrid imaging with MIBG can also inform on dysinnervation/denervation, thus improving the clinical appropriateness of implantable cardioverter-defibrillator therapy.[21]

In conclusion, hybrid anatomo-functional imaging holds the promise of overcoming the limitations inherent to anatomic and functional testing, enabling more accurate diagnosis, prognosis, and guidance for revascularization in patients with CAD.

Disclosure

Prof. Biondi-Zoccai has consulted for Abbott Vascular and Bayer. Dr. F. Nudi, Prof. Romagnoli, Prof. Schillaci, Dr. A. Nudi, and Prof. Versaci have nothing to disclose.

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