Non-Invasive Diagnostic Testing for Coronary Artery Disease in the Hypertensive Patient: Potential Advantages of a Risk Estimation-Based Algorithm

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Coronary artery disease (CAD) continues to be a leading cause of death1 and arterial hypertension is one of the major risk factors for CAD development and progression.2 The Prospective Studies Collaboration showed consistent relationship between increases in both systolic and diastolic blood pressure (BP) and the risk of CAD, such that for each 20 mmHg increase of systolic BP or a 10 mmHg in diastolic BP, a twofold increase in the risk of CAD events is estimated.3 Approximately 72 million adults in the general population of the United States have hypertension4 and the estimated prevalence in European adult population ranges between 20 and 25%.5 This high prevalence of hypertension is a critical factor in determining preventive strategies for CAD, in order to early identify and properly treat high-risk patients.6

In this article, we review the strengths and limitations of current diagnostic methods used to properly identifying coronary artery disease in hypertensive patients. Furthermore, we analyze the usefulness of adopting preliminary and comprehensive cardiovascular risk stratification, together with the evaluation of markers of organ damage, in order to improve the diagnostic efficacy.

Hypertension is a major risk factor for cardiovascular disease, including coronary atherosclerosis and its clinical manifestations. Non-invasive diagnosis of coronary artery disease in hypertension, however, remains a major clinical challenge. Chest pain frequently occurs in hypertensive patients with and without impairment of coronary blood flow supply. Electrocardiographic abnormalities are also common in these patients, thereby leading to further diagnostic difficulty. On the other hand, international guidelines are rather elusive on the recommended diagnostic pathway for coronary artery disease detection in hypertensive patients.

In this article, we review the strengths and limitations of current diagnostic methods used to properly identifying coronary artery disease in hypertensive patients. Furthermore, we analyze the usefulness of adopting preliminary and comprehensive cardiovascular risk stratification, together with the evaluation of markers of organ damage, in order to improve the diagnostic efficacy.

Despite the high prevalence of arterial hypertension, we still lack a strategy which would lead to validated and cost-effective clinical decision-making processes in hypertensive patients, which help clinicians to minimize useless, ineffective and expensive diagnostic steps. For this purpose, future guidelines should address the issue of diagnostic strategies for an early identification of hypertensive patients at risk of coronary artery disease. This may facilitate appropriate therapeutic choices to optimize the clinical management of coronary disease in hypertension.

Keywords: arterial hypertension; blood pressure; cardiovascular prevention; cardiovascular risk stratification; coronary artery disease; global cardiovascular risk; hypertension

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Recent randomized clinical trials in high cardiovascular (CV) risk patients, such as hypertensive and diabetic patients have consistently reported an increased risk of CAD, particularly myocardial infarction, when very low BP levels are achieved.10 This observation suggests caution in aggressive BP lowering in patients with clinical suspicion of CAD and, thus, highlights the importance of a closer scrutiny for CAD in high-risk patients.

In this article, by analysing the available medical literature, we critically discuss diagnostic methods currently used for identifying CAD in hypertensive patients. The potential usefulness of the use of a comprehensive CV risk stratification, based on the assessment of concomitant CV risk factors associated with organ damage markers is also discussed.
A large and unselected use of non-invasive diagnostic tests for “CAD screening” in hypertensive patients may often result in a high proportion of false positive and less frequently in false negative results, leading to avoidable hospitalizations and raised expenses for healthcare systems. Such an approach may also expose individual patients to unnecessary invasive, even potentially life-threatening, procedures.11

When evaluating a possible CAD in a hypertensive patient, the first step is to define his/her added CV relative risk, in order to choose the appropriate diagnostic strategy. The 2007 ESH-ESC Guidelines emphasize that the management of hypertension should be related to the quantification of global CV risk. The coexistence of more CV risk factors causes an exponential increase of CV risk.12 Indeed, hypertensive subjects with previous CAD or affected by diabetes mellitus, chronic kidney disease, or with BP levels >180/110 or with >3 traditional CV risk factor have a high/very high added relative risk.12

Several methods have been developed for estimating total CV risk, which is usually defined as the chance of suffering from an acute CV event for a CV event over 10 years. The most widely known ones are the Framingham risk score, derived by an American cohort13 and the SCORE charts, available for high and low risk countries in Europe.14 These charts take into account the presence of traditional CV risk factors (dyslipidemia, hypertension, diabetes mellitus, smoking, age, and sex) to define the “global risk score”, categorizing patients in broad terms as “low risk,” “intermediate risk,” and “high risk.” In general, patients are deemed to be high risk if they are found to have a global risk estimate for major cardiac events of at least 20% for Framingham risk score or 5% for SCORE over 10 years. The threshold for separating low risk from intermediate risk is 10% for Framingham risk score and 1% for SCORE.13–15

Recently, the relevance to identify the presence of target organ damage in hypertensive patients has been raised, since hypertension-related subclinical alterations in several organs markedly increase the risk beyond the presence of traditional risk factors.16 Left ventricular hypertrophy (LVH),17,18 ultrasound presence of atherosclerotic carotid plaque or intima/media thickness >0.9 mm,19 increased arterial stiffness,20 reduced estimated glomerular filtration rate,21–24 microalbuminuria,25,26 and ankle-brachial BP index <0.927 are the best known indexes of target organ damage and their association is presented with an important increase in CV risk,12 beyond that calculated by SCORE charts.28 Some of the indexes of target organ damage could be detected with widely available tests at reasonable costs, like electrocardiographic (ECG)-LVH, estimated glomerular filtration rate, and microalbuminuria, whereas others, like ultrasound intima/media thickness or ankle-brachial index measurement, coronary artery calcium score or pulse wave velocity,12 despite the growing evidence of their prognostic usefulness, especially in asymptomatic patients at intermediate CV risk are less easily available and are more expensive.12,20,29–38 In general, screening for microalbuminuria and ECG-LVH should now be considered routine procedures to be done in all hypertensive patients whereas the other above-mentioned tests can be considered as recommendations based on a thorough clinical evaluation.12

NON-INVASIVE SCREENING TESTS
In this section of the article we discuss the role of the available tests currently proposed to detect CAD in hypertensive population (Table 1).

Exercise electrocardiographic stress test
The exercise ECG stress test has been considered as a potential useful modality for CAD screening since it is simple to administer, relatively cheap, and safe.39 However, its relatively poor accuracy for diagnosing CAD, even in symptomatic subjects, has led to recommendations that discourage the use of exercise testing as a screening tool. This test has poor value in low-risk subjects and there is insufficient evidence for or against testing in subjects at higher risk. Indeed, it must be realized that false-positive tests are common among asymptomatic adults, especially women, and may lead to unnecessary further investigations and overtreatment.40

Using exercise ST-depression >0.1 mV or 1 mm to define a positive test, the reported sensitivity and specificity for the detection of significant CAD ranges between 23–100% and 17–100%, respectively. Excluding patients with prior CAD, the mean sensitivity was 67% and specificity 72%. However, interpretation of exercise ECG findings requires a Bayesian approach to achieve the diagnosis, whereby pre-test estimates of the disease, influenced by age, gender, and nature of symptoms, along with the results of diagnostic tests generate individualized post-test disease probabilities for a given patient. In population with a low prevalence of CAD, the proportion of false-positive tests will be high when compared with a population with a high pre-test probability of disease. Conversely, in male patients with severe exertional angina, with clear ECG changes during pain, the pre-test probability of CAD is high (>90%), and in such cases, the exercise test will not offer additional information for the diagnosis. Indeed, the usefulness of exercise testing has been restricted to those patients at intermediate pre-test risk for CAD.39 A significant proportion of patients with hypertension present with chest pain or thoracic discomfort, more frequently during exercise, but the specificity of exercise stress test in determining the probability of obstructive CAD is very low in hypertensive patients, especially in those with LVH and/or presence of baseline ECG alterations.41,42 For this reason, it has been suggested that
Exercise ECG stress test can be used to screen patients with negative maximal test (those achieving 85% of maximum predicted heart rate based on age and sex during exercise without developing symptoms or ECG changes) due to its high negative predictive value, which is comparable both in normotensive and hypertensive populations. On the other hand, patients with an intermediate pre-test risk, presenting with an uninterpretable ECG, inability to exercise or with an exercise-ECG stress test that is either uninterpretable or ambiguous, an imaging stress echo test is warranted for a reliable identification of significant epicardial CAD. In fact, ST segment depression is frequently found in patients with angiographically normal coronary arteries associated with LVH and/or microvascular disease.12,43–45

This test is not recommended in women, young patients, patients unable to exercise because of physical limitations (e.g., arthritis, amputations, severe peripheral vascular disease, severe chronic obstructive pulmonary disease, general debility), abnormal resting ECG due to left bundle branch block, preexcitation syndrome, LVH, digoxin therapy, or those demonstrating major (>1 mm) ST-segment depression or elevation.46

Stress echocardiography. The use of stress imaging tests also presents limitations in making an accurate diagnosis of CAD in hypertensive subjects, due to its false positive results.41,47

Stress echocardiography is not indicated for CV risk assessment in low- or intermediate-risk asymptomatic adults. Stress echocardiography is primarily used for its role in cardiac disease evaluation in hypertensive subjects.1

### Table 1 | Comparison of non-invasive diagnostic tests for detection of coronary artery disease in hypertensive subjects

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Cost</th>
<th>Biological impact</th>
<th>Indications</th>
<th>Not recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>EET</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>0</td>
<td>Pts at intermediate risk of CAD</td>
<td>In women, young pts, or unable to exercise, or with resting ECG abnormalities</td>
</tr>
<tr>
<td>Dipyridamole echocardiography</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++</td>
<td>+</td>
<td>Pts at intermediate risk of CAD unable to exercise/ with positive EET (especially women and &gt;75 aal) with interfering abnormalities ECG (LVH, LBBB)</td>
<td>In pts with poor acoustic window, or with resting abnormal wall motion; or with contraindication to pharmacologic stressor agents</td>
</tr>
<tr>
<td>Dobutamine echocardiography</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++</td>
<td>+</td>
<td>Pts at intermediate risk of CAD unable to exercise/ with positive EET (especially women and &gt;75 aal) with interfering abnormalities ECG (LVH, LBBB)</td>
<td>In pts with poor acoustic window, or with resting abnormal wall motion; or with contraindication to pharmacologic stressor agents</td>
</tr>
<tr>
<td>Exercise echocardiography</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++</td>
<td>0</td>
<td>Pts at intermediate risk of CAD unable to exercise/ with positive EET (especially women and &gt;75 aal) with interfering abnormalities ECG (LVH, LBBB)</td>
<td>In pts with contraindication to pharmacologic stressor agents</td>
</tr>
<tr>
<td>MPS</td>
<td>++++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>++++</td>
<td>Pts at intermediate risk of CAD unable to exercise/ with positive EET (especially women and &gt;75 aal) with interfering abnormalities ECG (LVH, LBBB); asymptomatic pts at high risk of CAD or with a strong familiarity for CAD</td>
<td>Women or young pts or with serum creatinine &gt;1,5 mg/dl</td>
</tr>
<tr>
<td>CCT</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>Pts at intermediate risk of CAD with positive EET pts and low/intermediate risk unable to exercise/ with interfering abnormalities ECG (LVH, LBBB); asymptomatic pts at high risk of CAD or with a strong familiarity for CAD</td>
<td>In claustrophobic pts, or with ferromagnetic objects, or with creatinine clearance &lt;30 ml/min; in pts with contraindication to pharmacologic stressor agents</td>
</tr>
<tr>
<td>CMR</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>++++</td>
<td>+</td>
<td>Pts at intermediate risk of CAD unable to exercise/ with positive EET/ with interfering abnormalities ECG (LVH, LBBB); asymptomatic pts at high risk of CAD</td>
<td>In claustrophobic pts, or with ferromagnetic objects, or with creatinine clearance &lt;30 ml/min; in pts with contraindication to pharmacologic stressor agents</td>
</tr>
</tbody>
</table>

Specificity, sensitivity, positive and negative predictive values, cost, biological impact and field of application for different non-invasive tests in the diagnosis of coronary artery disease in the hypertensive population. Bold text represent most relevant data.

CAD, coronary artery disease; CCT, coronary computed tomography; CMR, cardiac magnetic resonance; ECG, electrocardiography; EET, electrocardiographic exercise test; LBBB, left bundle branch block; LVH, left ventricular hypertrophy; MPS, myocardial perfusion scintigraphy; n.a., not available; NPV, negative predictive value; PPV, positive predicted value; pts, patients.

0, 0; +, 1–25%; ++, 26–50%; ++++, 51–75%; ++++, 76–100%.

Source: 51; 58; 81; 88; 89; 90.
evaluation of symptoms suspected of representing CAD, especially in women and older men (>75 years), for whom the predictive power of exercise ECG is uncertain. Depending on the meta-analysis, the overall sensitivity and specificity of exercise echocardiography are reported to be as 80–85% and 84–86%, respectively; whereas those of dobutamine stress echocardiography range from 40–100% to 62–100%, respectively, and 56–92% to 87–100% for vasodilator stress.

In hypertensive patients, stress echocardiography has provided particularly interesting results. Comparison of dipyridamole stress echocardiography and exercise ECG in a series of patients with chest pain of unknown origin, revealed a similar sensitivity, but a higher specificity for the imaging technique. Similar results have been reported with dobutamine. Moreover, exercise echocardiography showed better sensitivity, specificity, and diagnostic accuracy than exercise ECG in hypertensive patients, both on or off treatment. Therefore, stress echocardiography may add value to the diagnostic accuracy of the exercise ECG test, without being affected by the presence of LVH and allowing at the same time both a structural and a functional evaluation of the heart. A recent study by Lu and colleagues suggested that dobutamine echocardiography can be a useful first-line imaging test in hypertensive women. However, the specificity of dobutamine stress echocardiography may be impaired in patients with marked LVH.

The test is not recommended in patients with poor acoustic windows (e.g., obese, obstructive lung disease) or with resting wall motion abnormalities (e.g., prior infarction, severe LV dysfunction, right ventricular pacing, and prior cardiac surgery).

Dobutamine is contraindicated in unstable ventricular arrhythmias, hypertrophic cardiomyopathy, and not recommended in hypovolemia or atrial fibrillation. Dipyridamole is not recommended in patients with hepatic impairment. Adenosine is contraindicated in obstructive lung disease, atrio-ventricular block or sinus node dysfunction.

Nuclear medicine imaging test
The development of quantitative methods in the attempt to diagnose CAD by nuclear imaging test, has provided a more objective measure, thus reducing operator bias compared with traditional diagnostic approaches in the hypertensive population. Nuclear stress imaging tests, using exercise or dipyridamole as stimulating factors, are largely used in the diagnosis of CAD in high-risk patients or in those symptomatic with abnormal baseline ECG or as a further investigation in risk assessment after an ECG stress test. They appear to add little prognostic/diagnostic information to exercise ECG in middle-aged men, but may be useful for risk assessment in women and old men (>75 years). They may also be considered for advanced CV risk assessment in asymptomatic adults at high risk (such as those with diabetes or with a coronary artery calcium score >400) or with a strong family history of CAD. Single photon emission computed tomography (SPECT) and myocardial perfusion scintigraphy are known to involve exposure to ionizing radiation, so the use of these modalities should be limited to patients in whom the expected clinical benefit exceeds the risk of radiation exposure. Such diagnostic techniques, especially after the introduction of the “gated” SPECT, enable a simultaneous assessment of the functional status and the perfusion rate of the myocardium.

Myocardial perfusion scintigraphy has high sensitivity for detecting CAD in hypertensive patients. There are no differences between normotensive and hypertensive patients in terms of sensitivity (77% vs. 75%), specificity (74% vs. 72%), and accuracy (77% vs. 74%) of exercise SPECT. In the presence of LVH, the diagnostic accuracy of myocardial perfusion imaging is subjected to controversy, with some studies indicating a low specificity, frequently yielding false-positive results possibly due to microvascular abnormalities and others demonstrating preserved specificity. The risk of radiation exposure in young subjects and women represents a limitation for application of myocardial perfusion scintigraphy as well as the general recommendations for the pharmacological stressor agents applied already mentioned for stress echocardiography.

Cardiac magnetic resonance and computed tomography angiography
Cardiac magnetic resonance (CMR) and coronary computed tomography (CCT) have high diagnostic accuracy and negative predictive value since both enable a direct visual assessment of the coronary anatomy. CMR is one of the emerging imaging techniques used in the non-invasive diagnosis of CAD. This is achieved both via the direct visualization of coronary arteries (magnetic resonance angiography) and via the functional and perfusional assessment of reduced coronary reserve during provocative stress tests. Its multiple-plane scanning views, its high spatial resolution, and the lack of ionizing radiation make this an attractive diagnostic test. However, the clear visualization of the coronary arteries using magnetic resonance angiography still remains challenging, due to confounding factors such as the small dimensions and tortuous nature of the vessels, and the continuous heart and lung movements. Current guidelines limit the usefulness of CMR in diagnosing CAD to subjects at intermediate pre-test CV risk, with uninterpretable ECG, inability to exercise, or to subjects with equivocal stress tests (exercise ECG, stress SPECT, or stress echo). At present, there are no published prospective population data to evaluate the role of CMR findings in the risk assessment of asymptomatic adults.
In clinical studies for the detection of CAD, the results of CMR are very good in comparison with X-ray CA and SPECT. A meta-analysis including patients with intermediate likelihood of disease demonstrated a sensitivity of 90% and a specificity of 81% for adenosine stress perfusion CMR, whereas another meta-analysis, including 14 studies with a high prevalence of CAD, demonstrated a sensitivity of 83% and specificity of 86% for dobutamine stress CMR. The diagnostic performance of dobutamine stress CMR has been found to have superior diagnostic accuracy compared with dobutamine stress echo (86% vs. 73%). The application of dobutamine stress CMR is particularly advantageous in patients with poor acoustic windows and also in women who regularly have false-positive or negative stress nuclear scans.

An international multicenter study assessing the diagnostic accuracy of coronary magnetic resonance angiography revealed a high sensitivity (92%) and a low specificity (59%) for the detection of CAD. Other studies reported higher specificity.

It has been proposed that if coronary magnetic resonance angiography could be used to screen low-risk patients currently referred for catheterization, substantial cost savings may be achieved among the patients with normal catheterization (current rate in United States ~35%). In one report, the total cost savings was expected to exceed $1,000 per patient (or >60% cost reduction).

Despite the lack of specific data about the hypertensive population, almost all the cohorts from different trials included a large proportion of hypertensive patients. This test cannot be performed in patients who are claustrophobic or have implanted ferromagnetic objects (e.g., pacemaker, clips). Due to the rare but potentially life-threatening complication of nephrogenic systemic fibrosis, administration of gadolinium is contraindicated in patients with creatinine clearance ≤30 ml/min/1.73 m²54; contraindications to stressor agents are limitations as well.

Although CMR shows great promises as iodinated contrast-free and radiation-free diagnostic test, it currently still lags behind the more commonly used CCT. CCT is much more widely implemented in clinical practice and if correctly applied, it can be potentially a readily available non-invasive test for the diagnosis of CAD. CCT is useful as an advanced tool for risk assessment in the detection of CAD of symptomatic patients without known heart disease at intermediate pre-test probability of CAD, if the ECG is interpretable and they are able to exercise; or in patients at low/intermediate pre-test probability of CAD, if ECG results are uninterpretable or if patients are unable to exercise. CCT is not recommended for symptomatic patients with high probability of CAD because these patients are likely to need CA given the fact that CCT currently cannot be combined with percutaneous coronary revascularization.

A recent review of 45 studies noted that for a significant epicardial coronary artery stenosis of ≥50% 64-slice CCT had sensitivities of ≥90% in patient-based evaluations (the presence of CAD somewhere in the coronary tree of a given patient), named vessels (the presence of disease somewhere in a particular coronary artery), segments (the presence of disease in a particular segment of a particular coronary artery), and coronary artery bypass grafts, except the left circumflex (88%), distal segments (80%), and stents (88%), specificities of 88% in patients based analysis and >90% in all individual sites, variable positive predictive values ranging from 91 to 93% for patient-based evaluations, left main coronary artery, whereas ranging from 69 to 84% elsewhere (due to the low prevalence of disease in any particular segment or vessel), negative predictive values from 96 to 100%. Across studies, the negative predictive value for 64-slice CCT angiography was very high (median 100%). 64-slice CT is almost as good as CA in terms of detecting true positives. However, it is somewhat poorer in its rate of false positives. It seems likely that diagnostic strategies involving 64-slice CT will still require invasive CA for CT test positives. The consistently low false-negative rate makes this exam particularly attractive for excluding the presence of CAD in patients with intermediate risk. A recent study by Meijboom et al. showed that the patients most likely to benefit from the CCT are those with inconclusive ischemia testing or those with a positive test, but in whom the probability based on clinical assessment suggests that it is probably a false positive.

A CCT is particularly useful in hypertensive patients for assessing the risk of subsequent cardiac events and for defining a patient group with particular high risk. With respect to hypertensive patients suffering from chest pain, it has been shown that the sensitivity and specificity for Dual-Source CT to detect significant CAD was 100 and 90%, respectively with a negative predictive value of 100%.

CCT has a higher sensitivity and specificity and a higher negative predictive value for detecting coronary stenosis than other non-invasive tests, including CMR. Furthermore, CCT enables the direct visualization of the vessel wall, therefore allowing an indirect assessment of the plaque burden, which is not otherwise possible by CMR. The size and the presence of calcifications of the plaque may also be of additional value. However, the long-term risk due to the ionizing radiation of this test still limits its use as a “screening” tool for CAD. Moreover, the need for a relatively low heart rate (<70 bpm) and a regular heart rhythm represent other potential limitations.

The risk of radiation exposure in young subjects and women is a possible limitation. Finally, this test not recommended if serum creatinine <1.5 mg/dl and in case of allergy to iodine.
INVASIVE SCREENING TESTS
Selective coronary angiography
Nowadays, CA still represents the “gold standard” to diagnose CAD in clinical practice. More than 2.5 million CA are performed every year in Europe and in the United States. Patel and colleagues recently analyzed the American College of Cardiology, National Cardiovascular Data Registry and found that only 40% of patients undergoing CA electively had obstructive CAD and were then treated by revascularization. Therefore, in the vast proportion of patients without known CAD undergoing invasive CA, the diagnostic yield is relatively low. This is a great limitation of this diagnostic test in populations with low prevalence of CAD.

A number of CV risk factors, such as male sex, use of tobacco, diabetes, dyslipidemia, peripheral vascular disease, cerebrovascular disease, and hypertension were each independent predictors of obstructive CAD. There was also a significant and independent association between the positivity of a non-invasive test and a diagnosis of CAD as compared with no testing. This suggests that a more thorough CV risk assessment can help improving the clinical decision making process. The choice for the most appropriate non-invasive tests should be based on an approach characterized by multiple comparisons among different diagnostic tests applied to the daily clinical management of CV disease for each individual. Given the widespread diffusion of hypertension in the general population, the use of CA in all eligible patients in the attempt to diagnose CAD cannot be pursued, as it would actually produce a detrimental impact for the healthcare system, especially, in terms of cost and hospitalization burden.

DEVELOPING ALGORITHMS FOR IMPROVING CAD DIAGNOSIS IN HYPERTENSION
The use of any single diagnostic tool is often inadequate for the accurate detection of CAD in hypertensive patients. Moreover, routine performance of CA in unselected hypertensive patients should not be recommended as a first choice, not only because the test is invasive, but also because of the low diagnostic yield.

A diagnostic algorithm based on global risk assessment, such as the Framingham risk score or SCORE charts (Figure 1) to stratify the CV risk level, may represent a viable strategy to increase the diagnostic yield of CA. This approach might become even more effective when implemented with markers of target organ damage (LVH, microalbuminuria, etc.). Indeed, the above mentioned markers can significantly increase the discriminatory power of CV risk estimation tools, particularly in intermediate risk patients, and hence help to identify hypertensive patients, which would benefit from a more accurate non-invasive diagnostic technique for the identification of CAD.

The second step of the diagnostic algorithm is represented by the selection of the most appropriate non-invasive test. The wide range of readily available diagnostic tests in clinical

**Figure 1** | Proposed algorithm of the clinical tests for the diagnosis of coronary artery disease in the hypertensive population. CCT, Coronary Computed Tomography; CMR, Cardiac Magnetic Resonance; ECG, electrocardiography; FRS, Framingham risk score; LVH, left ventricular hypertrophy; RNI, radionuclide imaging.
practice and their interpretation does appear “friendly” for physicians. Stress ECG is generally recommended as the first diagnostic step also in hypertensive patients, in view of its high negative predictive value. Its appropriateness, however should be carefully evaluated in each individual. When it is not recommended, imaging techniques represent a reasonable alternative. As discussed above, the choice of the most appropriate imaging test should consider not only the performance characteristics of each diagnostic tool, which are generally very high, but also its biologic impact and costs.

Finally, the choice of CA should be limited to those patients with a high or very high risk profile, to those with low threshold responses to positive provocative tests or to those with high threshold positive test, but high risk profile.

CONCLUSIONS AND FUTURE PERSPECTIVE FOR CAD DIAGNOSIS IN HYPERTENSION

Hypertension is the most important CV risk factor for CAD. Hypertensive patients have double the risk of CAD compared with the normotensive population. Early and effective identification and treatment of CAD in hypertensive patients are recommended.12 In this paper, we highlight the potential additional value of an accurate CV risk stratification, with the aim to effectively implement the clinical decision-making process that leads to the current diagnostic use of CA. An accurate CV risk stratification applied to the choice of diagnostic test for CA screening may help clinicians to overcome the hurdles of this diagnosis, so that the costs of ineffective testing could be substantially minimized. In addition, diagnosis of CAD in hypertension could help to define targets of treatment, reducing the risk related to an excessive blood pressure lowering.85,86

Despite the growing evidence over the last decades, further research is still needed for the development of more accurate strategies in the diagnosis of coronary disease in hypertension. Probably, in future new items will become part of this panorama. The recent development of 256-slice and 320-detector CT row scanners will reduce radiation exposure, and minimize motion artifacts. Lower contrast doses will also help to reduce potential nephrotoxicity. It is likely that these new advances in CCT technology will successfully compete with existing stress imaging methods at least in patients with an intermediate risk of CAD.87 Moreover, in the next few years, thanks to new developing biomarkers, it will become possible to characterize atherosclerotic lesions at the molecular level during their preclinical state. This will enable the assessment of the stability of the atherosclerotic plaque and the identification at an even earlier stage of patients at high risk of developing CAD, therefore allowing physicians to adopt a more aggressive treatment strategy.88

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Diagnosis of Coronary Disease in Hypertension


