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ORIGINAL RESEARCH

Cost-Effectiveness of Computed Tomography Angiography in the Diagnosis of Ischemic Heart Disease in Patients with Intermediate Probability of Coronary Artery Disease

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ABSTRACT

Introduction: Ischemic heart disease remains a leading cause of morbidity and mortality worldwide. Coronary computed tomography angiography (CCTA) is recommended by current European guidelines as a first-line test for suspected obstructive coronary artery disease, but data on its economic impact in Romania remain limited. We evaluated a CCTA-first diagnostic strategy compared with a hypothetical strategy of invasive coronary angiography (ICA) in all patients with intermediate pretest probability. **Material and methods:** We conducted a retrospective cohort study of 248 patients with intermediate pretest probability (15–50%; RF-CL model) who underwent CCTA as a first-line test. CCTA findings were classified according to CAD-RADS 2.0, and patients with obstructive stenoses or non-diagnostic examinations were referred for ICA. Diagnostic performance, ICA avoidance, and costs were evaluated and compared with a hypothetical ICA-for-all strategy. **Results:** The mean age was 58.5 ± 9.1 years, 41.9% of patients were women, and the mean pretest probability was 31.0 ± 9.8%. Confirmed obstructive coronary artery disease was present in 63 patients (25.4%). CCTA had a sensitivity of 95.2%, specificity of 82.7%, negative predictive value of 98.1%, and overall accuracy of 85.9%. The CCTA-first strategy avoided ICA in 151 patients (60.9%) and reduced the average cost per patient from 4,249 to 2,525 RON, representing a 40.6% reduction and total savings of 427,600 RON. The cost per correct diagnosis was 2,940 RON with the CCTA-first strategy. **Conclusions:** In patients with intermediate pretest probability, a CCTA-first diagnostic strategy substantially reduced costs and the need for invasive testing while providing high sensitivity and negative predictive value. These findings support the use of CCTA as a diagnostic gatekeeper in cardiology practice in Romania.

Keywords: coronary computed tomography angiography, coronary artery disease, cost-effectiveness, pretest probability, CAD-RADS

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INTRODUCTION

Ischemic heart disease remains the leading cause of morbidity and mortality globally. According to the most recent update of the Global Burden of Disease study, more than 19 million deaths attributable to cardiovascular disease were recorded worldwide in 2023, and ischemic heart disease remained the single leading cause of cardiovascular burden, with important regional variations in age-standardized mortality.[1] Eastern Europe, including Romania, is among the regions with the highest cardiovascular mortality worldwide, underscoring the particular relevance to optimizing diagnostic algorithms for coronary artery disease in this context.[1,2]

The diagnosis of coronary artery disease in symptomatic patients without a known history of coronary artery disease is based on estimating the pretest probability (PTP) of obstructive disease, followed by selection of the most appropriate imaging or functional test. The 2024 European Society of Cardiology (ESC) Guidelines for the management of chronic coronary syndromes introduced the Risk Factor-weighted Clinical Likelihood (RF-CL) model, which includes age, sex, symptom type, and the number of cardiovascular risk factors, thereby improving the prediction of obstructive disease compared with the previous ESC pretest probability model, which was based exclusively on age, sex, and symptom type.[3] This model reclassifies a significantly larger proportion of patients into the very low or low probability categories, in whom further testing may be deferred; however, for patients remaining within the intermediate probability range (approximately 15–50%), the choice of the optimal diagnostic strategy continues to represent a relevant clinical and economic decision.[3,4]

Coronary computed tomography angiography (CCTA) has become the recommended first-line test for excluding obstructive coronary artery disease in patients with low or intermediate probability, owing to its high negative predictive value and its ability to characterize both luminal stenoses and non-obstructive atherosclerotic plaque.[3,5] The 2024 ESC Guidelines assign CCTA a Class I, Level of Evidence A recommendation for the diagnosis of obstructive coronary artery disease in patients with low or moderate clinical probability, with functional testing used primarily to assess the ischemic significance of lesions or in patients with moderate-to-high clinical probability.[3]

The randomized SCOT-HEART trial provided strong evidence for the clinical impact of CCTA in patients with stable chest pain, demonstrating that adding CCTA to standard care resulted in a 41% relative reduction in the risk of coronary heart disease death or non-fatal myocardial infarction at 5 years, through better targeting of preventive therapy and revascularization.[5,6] The recently published 10-year results confirmed the persistence of this long-term clinical benefit, supporting the role of CCTA as a first-line test rather than merely a triage tool.[6] By contrast, the PROMISE trial, which compared an anatomical strategy (CCTA) with a functional strategy (stress testing) in patients with intermediate probability, did not show a significant difference in major cardiovascular events at 2 years. However, the associated economic analysis suggested comparable costs between the two strategies in the short term, with a long-term economic advantage for the anatomical strategy, subsequently demonstrated through Markov modeling based on individual patient data from PROMISE.[7,8]

Beyond diagnostic accuracy, evaluating the cost-effectiveness of various diagnostic strategies has become a central objective of research in cardiovascular imaging, particularly in the context of limited healthcare resources in Central and Eastern European health systems. Decision analyses based on Markov models and microsimulation have repeatedly shown that, in patients with low-to-intermediate pretest probability, a strategy based on CCTA as the initial test is less costly and at least as effective, with a favorable incremental cost-effectiveness ratio (ICER), generally below commonly accepted willingness-to-pay thresholds per quality-adjusted life year (QALY).[9,10] In an analysis conducted in a middle-income country, with healthcare system characteristics broadly similar to those of Romania, the CCTA-based strategy remained the most cost-effective option among the available anatomical and functional tests, with a cost per diagnosis substantially lower than that of other diagnostic modalities.[10,11]

An additional aspect relevant to the cost-effectiveness of CCTA is the substantial reduction in radiation dose associated with the technique over the past decade, achieved through the adoption of prospective ECG gating, low-tube-voltage protocols, and iterative reconstruction. These advances have reduced the average effective dose by up to 80% compared with previously used retrospective gating techniques, without compromising diagnostic quality.[12] These technical advances have strengthened the safety profile of CCTA and supported the expansion of its clinical indications, including repeated use in the same patient for monitoring the progression of coronary atherosclerosis.

In Romania, although coronary CCTA is available at an increasing number of centers, its use as a first-line test in patients with intermediate probability remains inconsistent, and invasive coronary angiography continues to be frequently used as the initial diagnostic test, with im-

plications both for healthcare system costs and for the procedural risk to which patients without significant obstructive disease may be exposed. The absence of local economic data based on Romanian tariffs and institutional practice limits the ability of decision-makers to support the expansion of CCTA as a first-line diagnostic option on the basis of cost-effectiveness.

Building on these premises, the main objective of the present study was to evaluate the cost-effectiveness of a diagnostic strategy based on CCTA as a first-line test compared with a hypothetical strategy of invasive coronary angiography performed in all patients, in a cohort of patients with intermediate pretest probability of coronary artery disease. Secondary objectives included assessing the diagnostic accuracy of CCTA using invasive coronary angiography as the reference standard, quantifying the proportion of invasive coronary angiography procedures avoided through the use of CCTA as the initial test, and estimating the cost per correct diagnosis for each of the two strategies.

The choice of the CardioMed Cardiology Clinic in Târgu Mureș as the study site and source of the analyzed data is relevant for several reasons. First, the substantial volume of invasive coronary angiography procedures performed annually at this center allows the estimation of procedural costs representative of current practice in Romania, including both imaging-related costs and those associated with hospitalization. Second, the availability of state-of-the-art CCTA equipment, with radiation dose-reduction protocols aligned with international standards, allows a realistic evaluation of the current diagnostic performance of CCTA, avoiding the limitations associated with older equipment with lower temporal and spatial resolution that was used in much of the historical literature on CCTA diagnostic accuracy. In this context, the present study aims to contribute to the currently limited local evidence base needed to support resource-allocation decisions in cardiovascular imaging in Romania.

MATERIAL AND METHODS

STUDY POPULATION

We conducted a retrospective cohort study with an economic analysis component at the CardioMed National Center of Excellence in Interventional Cardiology in Târgu Mureș. The analysis included 248 consecutive patients who underwent coronary CCTA for suspected stable coronary artery disease and had an intermediate clinical pretest probability, estimated according to the RF-CL model recommended by the 2024 ESC Guidelines for the management of chronic coronary syndromes.[3] For the purposes of the present analysis, the intermediate probability range was defined as 15–50%, in accordance with the thresholds used in the reference cost-effectiveness literature.[3,9,10] The study was approved by the institution's Ethics Committee (approval no. 3/11.02.2026.)

INCLUSION AND EXCLUSION CRITERIA

The study included symptomatic adult patients with typical or atypical chest pain or anginal equivalents, with no known history of angiographically documented coronary artery disease or myocardial revascularization, for whom imaging was indicated by the attending cardiologist during outpatient evaluation or admission for diagnostic assessment. Patients with contraindications to iodinated contrast administration, uncontrolled arrhythmias that could compromise image quality, or severe renal impairment (estimated glomerular filtration rate <30 ml/min/1.73 m^2) were excluded. Patients who underwent CCTA in an emergency setting (suspected acute coronary syndrome) or for non-coronary indications (e.g., preoperative valvular assessment), were also excluded.

CCTA PROTOCOL AND IMAGE INTERPRETATION

Examinations were performed using multidetector computed tomography scanners with at least 64 detector rows, with prospective step-and-shoot ECG gating used whenever permitted by the patient's heart rate and rhythm, in accordance with current radiation dose-reduction recommendations.[12] CCTA findings were interpreted by physicians experienced in cardiovascular imaging and classified according to CAD-RADS 2.0 (Coronary Artery Disease Reporting and Data System), a standardized reporting system that classifies the severity of coronary stenosis from CAD-RADS 0 (absence of plaque or stenosis) to CAD-RADS 5 (total occlusion) and includes the CAD-RADS N category for non-diagnostic examinations due to artifacts or insufficient technical quality.[13] For the purposes of the analysis, obstructive coronary artery disease was defined as luminal stenosis ≥50% in at least one major epicardial vessel, corresponding to CAD-RADS categories 3–5, consistent with the threshold used by most diagnostic accuracy and cost-effectiveness studies cited in the literature.[9,13,14]

DIAGNOSTIC ALGORITHM AND PATIENT PATHWAY

According to institutional protocol, patients with a CAD-RADS 3–5 result on CCTA, as well as those with a non-

diagnostic examination (CAD-RADS N), were referred for invasive coronary angiography (ICA) for confirmation and, where applicable, interventional treatment of significant lesions. Patients with a CAD-RADS 0–2 result were considered negative for significant obstructive disease and continued to receive conservative medical management, with no indication for further invasive testing, except in cases of persistent or worsening symptoms during subsequent clinical follow-up of at least 12 months. The diagnostic accuracy of CCTA was evaluated by comparing the CAD-RADS result with ICA findings in patients who underwent both investigations and, for patients who did not undergo invasive testing, by clinical evaluation during follow-up, which was used as a surrogate reference standard for the absence of obstructive disease—a methodological approach used in studies of non-invasive test accuracy when invasive testing is not available for all participants.[9,13]

ECONOMIC MODEL

The cost-effectiveness analysis compared two hypothetical diagnostic strategies applied to the same cohort of 248 patients: 1) the 'CCTA first-line' strategy, representing the actual pathway followed by the patients included in the study, in which all patients initially underwent CCTA, and invasive coronary angiography was reserved for those with a positive or non-diagnostic result; and 2) the comparative 'invasive coronary angiography for all patients' strategy, which assumed invasive coronary angiography as the initial test for the entire cohort, without a prior non-invasive triage step. The costs used in the model were estimated based on institutional tariffs and reference costs from the Romanian social health insurance system, updated for 2024, and included the following: the cost of a coronary CCTA examination with CAD-RADS reporting (850 RON), the cost of an invasive coronary angiography, including the associated day hospitalization (4,200 RON), the cost of functional testing with stress echocardiography, used for patients with a non-diagnostic CCTA examination in whom invasive coronary angiography was not considered appropriate (380 RON), and the average additional cost associated with a major vascular access complication after invasive coronary angiography (6,100 RON), with a major complication rate of 1.2% applied in accordance with the reference literature on the procedural risks of invasive coronary angiography.[15]

STATISTICAL ANALYSIS AND GENERATION OF RESULTS

Statistical analyses were performed using GraphPad Prism 8 (GraphPad Software). Continuous variables were expressed as means ± standard deviations and compared using Student's t-test for independent samples; categorical variables were expressed as absolute frequencies and percentages and compared using the chi-square test. Statistical significance was defined as $p < 0.05$. The sensitivity, specificity, and positive and negative predictive values of CCTA were calculated using invasive coronary angiography for patients who underwent invasive testing and clinical follow-up for those who did not, together constituting the reference standard used in the analysis. The cost-effectiveness analysis was reported in terms of the average cost per patient, total cost across the cohort, percentage cost reduction, and cost per correct diagnosis for each strategy, following the general principles of cost-effectiveness analyses in cardiovascular imaging described in the literature.[9,10,16]

RESULTS

BASELINE CHARACTERISTICS OF THE STUDY POPULATION

The cohort included 248 patients, with a mean age of 58.5 ± 9.1 years, of whom 104 (41.9%) were women. The mean pretest probability, estimated according to the RF-CL model, was 31.0 ± 9.8%, with all patients falling within the intermediate probability range (15–50%). Cardiovascular risk factors were distributed as follows: arterial hypertension in 169 patients (68.1%), dyslipidemia in 144 patients (58.1%), diabetes mellitus in 62 patients (25.0%), active smoking in 71 patients (28.6%), and a family history of premature coronary artery disease in 84 patients (33.9%). In terms of clinical presentation, 46 patients (18.5%) had typical angina pectoris, 141 patients (56.9%) had atypical angina, and the remainder had anginal equivalents or nonspecific symptoms. The detailed characteristics of the cohort, stratified by the presence of confirmed obstructive coronary artery disease, are presented in Table 1.

Patients with confirmed obstructive coronary artery disease had a significantly higher pretest probability than those without obstructive disease ($p < 0.001$), with no statistically significant differences between the two groups in mean age ($p = 0.68$), prevalence of diabetes mellitus ($p = 0.93$), arterial hypertension ($p = 0.89$), or active smoking ($p = 0.07$), consistent with the relatively uniform distribution of individual risk factors within the intermediate probability band, where the severity of coronary artery disease is determined by a combination of factors rather than by a single dominant predictor.

TABLE 1. Demographic and clinical characteristics of the cohort, stratified by the presence of obstructive coronary artery disease

Parameter	Total (n = 248)	Obstructive CAD (n = 63)	No obstructive CAD (n = 185)	p value
Age (years), mean ± s.d.	58.5 ± 9.2	58.1 ± 9.0	58.7 ± 9.2	0.67
Female sex, n (%)	104 (41.9)	30 (47.6)	74 (40.0)	0.29
Diabetes mellitus, n (%)	62 (25.0)	15 (23.8)	47 (25.4)	0.93
Arterial hypertension, n (%)	169 (68.1)	42 (66.7)	127 (68.6)	0.89
Dyslipidemia, n (%)	144 (58.1)	39 (61.9)	105 (56.8)	0.47
Active smoking, n (%)	71 (28.6)	12 (19.0)	59 (31.9)	0.07
Family history of premature CAD, n (%)	84 (33.9)	22 (34.9)	62 (33.5)	0.83
Typical angina, n (%)	46 (18.5)	18 (28.6)	28 (15.1)	0.02
Atypical angina, n (%)	141 (56.9)	36 (57.1)	105 (56.8)	0.96
Pretest probability (%), mean ± s.d.	31.0 ± 9.8	34.8 ± 10.2	29.7 ± 9.3	<0.001

CAD, coronary artery disease

CCTA RESULTS AND CAD-RADS DISTRIBUTION

The distribution of CCTA results according to the CAD-RADS 2.0 system is presented in Table 2. A total of 151 patients (60.9%) had a CAD-RADS 0–2 result and were considered negative for obstructive coronary artery disease and continued to receive conservative management without further invasive testing. A total of 92 patients (37.1%) had a CAD-RADS 3–5 result, suggestive of obstructive stenosis, and 5 patients (2.0%) had a non-diagnostic examination (CAD-RADS N) and were referred for further evaluation. Overall, 97 patients (39.1% of the cohort) were referred for invasive coronary angiography based on the CCTA findings.

COST-EFFECTIVENESS ANALYSIS

The average cost per patient was 2,525 RON for the 'CCTA first-line' strategy and 4,249 RON for the comparative 'invasive coronary angiography for all patients' strategy, representing a difference of 1,724 RON per patient (a relative reduction of 40.6%). Across the entire cohort, the total cost of the 'CCTA first-line' strategy was 626,200 RON, compared with 1,053,800 RON for the comparative strategy, resulting in total savings of 427,600 RON (Table 3, Figure 1). The CCTA-based strategy allowed invasive coronary angiography to be avoided in 151 of the 248 patients (60.9%), without an associated increase in the risk of undiagnosed obstructive disease, with a reported negative predictive value of 98.1%.

The cost per correct diagnosis was 2,940 RON for the 'CCTA first-line' strategy (calculated as the ratio between the total cost of the strategy and the number of correct diagnoses (213 of 248 patients, representing the sum of true-positives and true-negative results), compared with 4,249 RON for the comparative strategy, which assumed complete diagnostic accuracy of invasive coronary angi-

TABLE 2. Distribution of CCTA results according to the CAD-RADS 2.0 system

CAD-RADS category	n	%
0 (no plaque)	44	17.7
1 (1–24% stenosis)	49	19.8
2 (25–49% stenosis)	58	23.4
3 (50–69% stenosis)	53	21.4
4 (70–99% stenosis)	28	11.3
5 (total occlusion)	11	4.4
N (non-diagnostic)	5	2.0

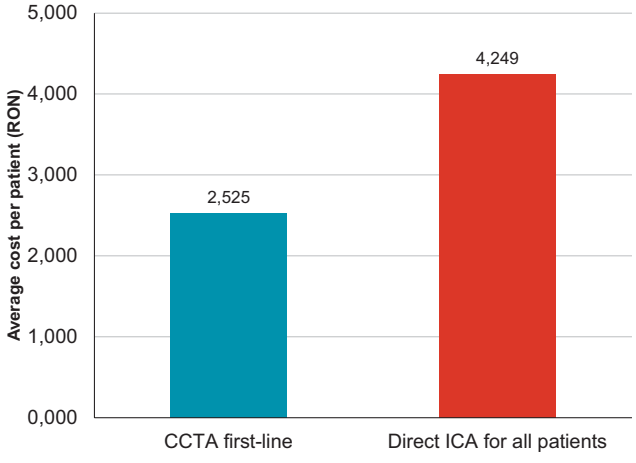

FIGURE 1. Average cost per patient by diagnostic strategy used

TABLE 3. Comparison of the two diagnostic strategies from a cost perspective (RON, 2024 prices)

Indicator	CCTA first-line	ICA for all patients	Difference
Average cost per patient (RON)	2,525	4,249	1,724 (40.6%)
Total cohort cost (RON)	626,200	1,053,800	427,600
Patients in whom ICA was avoided, n (%)	151 (60.9)	0 (0.0)	–
Cost per correct diagnosis (RON)	2,940	4,249	1,309
ICA major complication rate (%)	1.0	1.2*	–

*Complication rate applied to all 248 procedures in the comparative strategy

ography as the reference standard. Although the CCTA-based strategy was associated with 32 false-positive results, leading to potentially avoidable invasive coronary angiographies in the absence of obstructive disease, the cost per correct diagnosis remained substantially lower than that of the 'invasive coronary angiography for all patients' strategy.

The rate of major vascular access complications associated with invasive coronary angiography was estimated at 1.2% of the procedures performed. The reduction in the number of invasive coronary angiographies performed through the use of CCTA as a triage test resulted, according to the model, in approximately one fewer major complication across the studied cohort, illustrating, beyond the economic benefit, the potential procedural safety benefit of a diagnostic strategy that limits the exposure of patients without obstructive disease to the risks of an invasive procedure.

DISCUSSION

The present study evaluated the cost-effectiveness of a diagnostic strategy based on coronary CT angiography as a first-line test, compared with a strategy of routine invasive coronary angiography in all patients, in a cohort of patients with intermediate pretest probability of coronary artery disease evaluated at a tertiary cardiology center in Romania. The main results showed a reduction of more than 40% in the average cost per patient, with invasive coronary angiography avoided in nearly two-thirds of patients. These results are consistent with a substantial body of international literature, while also extending the available evidence to an Eastern European economic context that remains underrepresented in the literature.

In a meta-analysis of 14 studies comprising 2,533 patients referred for transcatheter aortic valve replacement and evaluated for obstructive coronary artery disease, Gatti *et al.* reported a sensitivity of 97% and a specificity of 68% for CT angiography, with a summary ROC area under the curve of 0.96.[13] Although the reference population of that study differs from the present cohort in terms of clinical context (preoperative valvular evaluation, with a higher prevalence of severe coronary calcification), the general pattern of high sensitivity accompanied by moderate specificity, partly explained by the overestimation of stenosis severity in the presence of extensive calcification, is consistent with findings reported in other populations undergoing CCTA.[14] A more recent meta-analysis comparing the diagnostic accuracy of CT angiography and CT-derived fractional flow reserve (FFR-CT) across different levels of coronary calcium score confirmed that the specificity of CT angiography progressively decreases with increasing calcium burden, a finding that may partly explain relatively modest positive predictive value (65.2%) observed in our cohort.[11]

From an economic perspective, the results of the present study are consistent with the international cost-effectiveness literature, which has shown that, in patients with low-to-intermediate pretest probability, strategies based on CT angiography as the initial test may be economically favorable compared with alternative diagnostic strategies, with reported ICERs below commonly accepted willingness-to-pay thresholds per QALY gained.[9,10] The Markov microsimulation analysis based on individual data from the 10,003 patients in the PROMISE study showed that anatomical strategies, including CT angiography, were associated with a gain of approximately 6 months of perfect health over a lifetime compared with functional testing, with an incremental cost-effectiveness ratio of approximately 2,743 USD per QALY gained for the CT angiography-based strategy, well below the willingness-to-pay thresholds used in most Western healthcare systems.[8] An earlier economic analysis of the PROMISE data, based directly on costs observed during the trial, reported comparable costs between the anatomical and functional strategies in the short term, with more substantial economic

differences emerging in subsequent long-term modeling.[17] Likewise, the 5-year results of the SCOT-HEART trial confirmed the persistence of the clinical benefit of the CT angiography-guided strategy without an increase in the revascularization rate, providing additional support for the clinical value of this diagnostic approach.[18] In a decision analysis conducted in a middle-income country with healthcare system characteristics broadly similar to those of Romania, the CT angiography-based strategy remained the most cost-effective option among the available anatomical and functional tests, with a substantially lower cost per correct diagnosis than the alternatives,[10,19] consistent with findings from the North American context regarding the long-term cost-effectiveness of CT angiography in patients with suspected acute coronary syndrome at low to intermediate risk.[20] Although the economic model of the present study compared CT angiography with routine invasive coronary angiography in all patients rather than with functional testing, the overall finding that CCTA-based non-invasive triage may substantially reduce diagnostic costs and the need for invasive testing is broadly consistent with the existing literature.

The observed reduction in the number of invasive coronary angiography procedures has implications that extend beyond the economic domain. Invasive coronary angiography, although considered the reference standard for the diagnosis of coronary artery disease, is associated with procedural risks, including complications at the vascular access site, arterial dissection, cholesterol embolism, and, rarely, major complications such as periprocedural myocardial infarction or stroke.[15] By limiting the use of ICA in patients without significant obstructive disease, a strategy based on CT angiography as a first-line test may reduce the overall procedural risk in the investigated population, a potential safety benefit that complements the economic advantages of this approach. The present analysis estimated approximately one fewer major complication at the cohort level, a modest figure in absolute terms, but potentially more relevant when extrapolated to larger numbers of patients investigated annually across the healthcare system.

Another aspect relevant to the interpretation of the results is the role of the CAD-RADS 2.0 reporting system in standardizing management decisions following CT angiography. The system was updated in 2022 to incorporate FFR-CT and plaque burden and aims to facilitate standardized interpretation and communication of CCTA findings, with management recommendations associated with each category, building on the framework introduced by the original 2016 version of CAD-RADS.[21,22] The current American guidelines for the management of chronic coronary disease are broadly consistent with European recommendations regarding the important role of CT angiography in the evaluation of patients with suspected coronary artery disease, reflecting increasing international support for this diagnostic approach.[23]

The role of additional functional assessment with FFR-CT in patients with stenoses of uncertain significance on CT angiography represents a potential means of further optimizing the diagnostic strategy, although real-world economic data remain limited. A recent multicenter audit across several centers in the United Kingdom reported a low rate of major cardiovascular events in patients with normal FFR-CT, supporting the prognostic value of this complementary technology. However, its additional cost may currently limit widespread adoption in resource-limited healthcare systems, including Romania.[24]

The relevance of the results to the Romanian context must also be interpreted in light of the cost-effectiveness thresholds applicable to middle-income healthcare systems. The World Health Organization recommends, as an orientative benchmark, willingness-to-pay thresholds ranging between 0.5 and 1.5 times the gross domestic product per capita per QALY gained, although more recent analyses suggest effective thresholds that are often lower than this range in most countries, including in the upper-middle-income economies of Central and Eastern Europe.[25,26] Regardless of the exact applicable threshold, the absolute reduction in cost per patient documented in the present study suggests that a CT angiography-based strategy may offer an economically favorable approach in a resource-constrained healthcare setting.

It is worth noting that the international cost-effectiveness literature reports heterogeneous results when CT angiography is compared with functional strategies, such as stress echocardiography or myocardial perfusion scintigraphy, rather than directly with invasive coronary angiography. The FORECAST trial, which evaluated the addition of FFR-CT to CT angiography in patients with stable chest pain and low risk of coronary artery disease, did not demonstrate a significant reduction in total costs within the UK National Health Service, although it showed a significant reduction in the rate of invasive coronary angiography (19% vs. 25%, $p = 0.01$) in the experimental arm.[27] This finding is broadly consistent with the reduction in invasive testing observed in the present study and suggests that an important potential economic benefit of advanced non-invasive testing may arise from reducing subsequent invasive procedures rather than from the direct cost of the initial test itself. This observation is consistent with the finding in the present analysis that the economic ad-

vantage of the 'CT angiography first-line' strategy was largely determined by the proportion of invasive coronary angiography procedures avoided rather than by the difference in the unit costs of the two diagnostic tests.

An additional aspect worth mentioning is the relationship between the severity of coronary calcification and the diagnostic accuracy of CT angiography, as extensive calcification can cause blooming artifacts, resulting in overestimation of stenosis severity and, consequently, an increased rate of false-positive results leading to potentially avoidable invasive coronary angiography procedures. Recent studies comparing the performance of conventional CT angiography with photon-counting detector CT angiography, an emerging technology with substantially higher spatial resolution, suggest that this new generation of CT systems may reduce the false-positive rate in patients with high coronary calcium scores, potentially providing an additional economic benefit beyond that observed in the present study, which used conventional CT equipment.[11]

STUDY LIMITATIONS

The present study has several limitations that must be taken into account when interpreting the results. The cost model included the direct costs of imaging and invasive procedures, without incorporating indirect costs such as additional hospitalization days, work absenteeism associated with invasive procedures, or the long-term costs of differences in pharmacological treatment between the two strategies, which could modify the magnitude, and potentially the direction, of the observed cost difference. The comparison was performed between the 'CT angiography first-line' strategy, which was applied to the studied cohort, and a strategy of routine invasive coronary angiography in all patients. No parallel contemporary cohort of patients undergoing invasive coronary angiography as the initial diagnostic test was available, which limits the ability to control for potential systematic differences that may have influenced the choice of initial diagnostic test. In addition, the reference standard for patients with negative CT angiography was, in part, clinical follow-up rather than invasive coronary angiography performed in all participants. This represents an inherent methodological limitation when invasive testing is not performed in patients with a negative non-invasive test and may result in underestimation of the true false-negative rate. Finally, the analysis did not include a long-term perspective on clinical outcomes (including major cardiovascular events and mortality). Therefore, the economic conclusions are limited to the initial diagnostic episode and do not allow calculation of an incremental cost-effectiveness ratio expressed as cost per QALY gained, as reported in international studies using long-term Markov modeling.[8,9]

RESEARCH PERSPECTIVES

The results of the present study open several directions for future research. A first direction would involve the prospective validation of the cost-effectiveness model in a contemporary cohort, with randomization or pragmatic allocation between the CT angiography-based strategy and direct invasive coronary angiography, allowing a direct comparison of costs and clinical outcomes in the short and medium term. A second relevant direction would concern extending the time horizon of the economic analysis, through longitudinal follow-up of major cardiovascular events, reinterventions, and costs associated with long-term pharmacological treatment, allowing the calculation of an incremental cost-effectiveness ratio expressed as cost per QALY gained, comparable to international standards for reporting cost-effectiveness analyses in healthcare. A third direction of interest would be to evaluate the economic impact of integrating artificial intelligence tools into CT angiography interpretation on the false-positive rate and, consequently, on the cost per correct diagnosis, given the favorable preliminary data reported by recent meta-analyses on the diagnostic performance of these tools.16 Finally, a multicenter, national-level analysis would be useful, integrating data from several centers with different activity volumes and variable technical capabilities, to assess the generalizability of the conclusions of the present study to the entire Romanian healthcare system, including centers with limited access to newer-generation coronary CT angiography systems.

From the perspective of patient experience, a CT angiography-based diagnostic strategy offers additional advantages over direct invasive coronary angiography, including the outpatient nature of the procedure, the absence of vascular access and associated local anesthesia, and a significantly shorter recovery time. These aspects, although not monetarily quantified in the present economic model, may contribute to greater acceptability of this strategy among patients and treating physicians. Exposure to ionizing radiation remains a relative disadvantage of CT angiography compared with radiation-free functional testing, such as stress echocardiography. However, compared with invasive coronary angiography, which involves prolonged fluoroscopy, especially in cases with complex anatomy or associated therapeutic inter-

ventions, the effective dose associated with CT angiography using modern prospective ECG-gating protocols generally remains comparable to, or even lower than, that associated with invasive coronary angiography.[12]

CONCLUSIONS

In patients with intermediate pretest probability of coronary artery disease, a diagnostic strategy based on coronary CT angiography as a first-line test reduced the average cost per patient by 40.6% compared with a hypothetical strategy of routine invasive coronary angiography in all patients, allowing invasive coronary angiography to be avoided in 60.9% of patients, with a sensitivity of 95.2% and a negative predictive value of 98.1%. The cost per correct diagnosis was substantially lower for the CT angiography-based strategy, supporting its economic advantage in the studied cohort.

These results support the expanded use of coronary CT angiography as a first-line test, in accordance with the current recommendations of the 2024 ESC Guidelines for the management of chronic coronary syndromes, in patients with intermediate pretest probability evaluated at cardiology centers in Romania. Beyond the direct economic benefit, the reduction in the number of invasive coronary angiography procedures may contribute to reducing the exposure of patients without significant obstructive disease to the procedural risks associated with invasive testing, providing a potential safety benefit in addition to the economic benefit.

Prospective validation of these findings in contemporary cohorts, with follow-up extended to include long-term clinical events and costs, remains necessary to strengthen the local evidence base for the efficient allocation of resources within the Romanian healthcare system and to further evaluate the cost-effectiveness of diagnostic strategies for stable coronary artery disease.

CONFLICTS OF INTEREST

There are no conflicts of interest related to the present work.

AUTHOR CONTRIBUTIONS

V.-D.B. and T.B. conceptualized the study. V.-D.B., I.T., and T.B. developed the methodology. V.-D.B. and D.P. contributed to software development. I.T., I.B., and T.B. validated the study. V.-D.B., I.T., and D.P. performed the formal analysis. V.-D.B., D.P., and I.H. conducted the investigation. I.B. and T.B. provided resources. D.P., I.H., and I.T. curated the data. V.-D.B. and I.T. prepared the original draft. D.P., I.H., I.B., and T.B. reviewed and edited the manuscript. V.-D.B. and D.P. contributed to visualization. I.B. and T.B. supervised the study. T.B. administered the project. All authors have read and agreed to the published version of the manuscript.

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