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COST-EFFECTIVENESS ANALYSIS OF CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY AND INVASIVE CORONARY ANGIOGRAPHY FOR DIAGNOSIS OF CORONARY ARTERY DISEASE

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ABSTRACT

Background: The burden of cardiovascular diseases (CVDs) places significant pressure on healthcare economics. Several imaging approaches exist for diagnosing coronary artery disease (CAD), with varying accuracy and cost. A sufficient evidence base to justify the cost of any procedure is necessary.

Materials and Methods: In a prospective study, 58 patients with suspected CAD were recruited to assess the cost-effectiveness of coronary computed tomography angiography (CCTA) compared with invasive coronary angiography (ICA) based on Bayes' theorem. Detailed activity-based cost analyses of the two modalities were carried out.

Results: The costs of ICA (234.23 dollars) were found to be about 4.6 times higher than the cost of CCTA (50.84 dollars). The cost of CCTA per patient increased as a linear function of increasing CAD prevalence. In contrast, the cost per patient for ICA did not increase significantly. Concerning the cost-effectiveness per CAD correct diagnosis, at a CAD prevalence of 55% CCTA and ICA were equally effective with a cost of 448 dollars. CCTA is more cost-effective in patients with a prevalence of up to 54%. In contrast, ICA showed better cost-effectiveness for prevalence above 55%. In terms of quality-adjusted life-years gained (ΔQALY) with cost-effectiveness, the trend was similar, whereby at a CAD prevalence of 55% CCTA and ICA were equally effective (150 dollars).

Discussion: ICA should be considered for patients with clinical characteristics indicating a high prevalence of CAD. CCTA can be useful as a first-line test for risk assessment in patients with mild to intermediate probability of suspected CAD.

Keywords: Computed Tomography Angiography, Coronary Artery Disease, Cost-effectiveness Analysis, Invasive Coronary Angiography.

1. Introduction

Coronary artery disease (CAD) arises when there is an insufficient blood supply to the myocardium due to atherosclerotic accumulation in the coronary arteries. CAD is the leading cause of death worldwide [1]. Consequently, the early diagnosis of patients with suspected CAD can diminish the complications, hence prolong the life of patients [2].

Invasive coronary angiography (ICA) is the most accurate method (the "gold standard") for evaluating and defining CAD. ICA is used to identify the exact location and severity of CAD. However, ICA has obvious limitations. It has a substantial procedural cost, and it is an invasive method associated with serious risks that carry severe long-term consequences. The composite rate of death, stroke or myocardial infarction is 0.1-0.2% in elective procedures [3]. Most importantly, ICA does not directly assess the condition of atherosclerotic disease and change within the vessel wall, but merely allows assumptions on its presence and extent based on lumen obstruction. Images are obtained in only two dimensions, though the use of multiple projections enables a more comprehensive assessment of an individual lesion.

Coronary computed tomography angiography (CCTA) is a diagnostic imaging test that uses multislice computed tomography (MSCT) scanner to non-invasively image the coronary arteries of the heart. CCTA has become an integral imaging modality in the evaluation of CAD, facilitated by dramatic technological advances in the last decade, which has resulted in consistent acquisition of high quality images of the coronary arterial lumen as well as the wall with high accuracy and relatively low radiation doses [4,5]. The accuracy and reliability of CCTA were validated in 2008 with the publication of three landmark controlled clinical trials [6-8]. Since the publication of these landmark trials, we have seen frequent technological progression in the field of coronary imaging. It is generally believed that soon the use of CCTA may replace a substantial proportion of ICA examinations, especially for assessing the degree of stenosis and patency of grafts [9]. Therefore, it is necessary to address these perspectives by creating a model to project clinical outcomes and cost-effectiveness of CCTA as compared with ICA in the evaluation of patients with suspected CAD.

Cost-effectiveness analysis (CEA) provides a framework for different management strategies for maximizing health benefit within the constraint of limited resources [10]. It is an analytical approach that integrates a test's clinical effectiveness with its economic value [11]. The study of CEA provides a rational means to balance health care quality and clinical value in terms of the best outcome at a reasonable price. The economic evaluation suggests that strategies, including CCTA, are likely to be considered cost-effective for imaging patients with CAD while yielding approximately the same amount of quality-adjusted life-years (QALYs) compared to ICA [12].

2. Materials and Methods

2.1 Patients

The researchers prospectively enrolled 58 consecutive patients with symptoms of suspected CAD. We analyzed the total costs for diagnostic coronary imaging at a single diagnostic center. By protocol, the patients who were referred for ICA had undergone CCTA the day before they underwent ICA. Under this protocol, we made sure that all the patients who were selected underwent the CCTA and ICA. Thus, we were able to calculate the accuracy of the CCTA and the cost of the CCTA and ICA for all patients with the same conditions.

2.2 Examination technique of CCTA

The CCTA scan was performed with a Philips Ingenuity 128 CT Scanner. The parameters for the acquisition were a gantry rotation time of 0.33 s, slice thickness 128×0.5 mm, variable pitch and rotation time determined by the cardiac software based on heart rate and adjusted to obtain maximum temporal resolution. Both tube voltage and tube current were tailored to each patient's weight and ranged from 120 kV to 140 kV and 300 mA to 665 mA. Improvement in spatial resolution and dose reduction were accomplished by using an iterative reconstruction.

CCTA scans were performed during the infusion of Iohexol Injection, a high-iodine-concentration contrast agent (OMNIPAQUE 350 contains 755 mg of iohexol equivalent to 350 mg of organic iodine per ml, GE Healthcare). A dose of 80-100 ml of the contrast medium was injected at a flow rate of 6 ml/s followed by a 40-ml bolus of saline at the same flow rate. The contrast medium was injected through an 18-gauge needle cannula placed in an antecubital vein of the right arm. A Stellant dual-head automatic power injector (Medrad, Indianola, IA, USA) was used. Synchronized triggering of the CT scan with the contrast bolus tracking was done with spiral auto start, which involves placing a region of interest (ROI) in the ascending aorta and setting the enhancement threshold at 100 HU above baseline.

Axial images were reconstructed at a slice thickness of 0.5 mm and an increment of 0.5 mm using a B20 kernel and retrospective ECG gating. Images were reconstructed at the multiphase technique of the R-R interval (10 %-100 %). Significant CAD is defined as more than 50% angiographic diameter stenosis in one or more of the epicardial coronary arteries. Based on disease severity, obstructive CAD is classified as single, double, or triple vessel disease [13].

2.3 Examination technique of ICA

In all patients, images of ICA were acquired using Coroskop HIP, Siemens Healthcare. Femoral access was obtained using the Seldinger wire technique with 6F or 7F catheters. Four coronary artery projections were acquired (45° left anterior oblique, a 30° right anterior oblique and a 45° left anterior and 30° cranial projection). Image series were obtained at a high frame rate (15 frames) during the injection of Iohexol Injection (OMNIPAQUE 350, GE Healthcare).

2.4 Cost analysis

The researchers used the Excel program for cost and cost-effectiveness analyses. Concerning the economic evaluation, the costs in dollars of CCTA and ICA were recognized through a detailed analysis of all involved procedures. Total costs of a diagnostic modality included direct costs and induced costs, i.e., expected cost of complications.

2.4.1 Direct cost

Direct costs were classified into three categories: diagnostic-specific equipment costs, materials and supplies costs, and personnel costs. Occupancy costs including heating, air-conditioning, light, cleaning, insurance, furniture, security, secretarial and stationery requirements were considered fixed in both departments, so they were excluded from the cost calculation.

2.4.1.1 Equipment costs

Diagnostic-specific equipment cost included purchasing, repair, and maintenance. Installation contracts provided for a defects' liability period. Equipment purchase costs were obtained from the hospital administration records. The utility of equipment also was taken into account by calculating the equipment lifetime per year divided on all conducted patients. Equipment lifetime, for calculating amortization, was considered to be 10 years, which is the maximum technological lifespan of radiological equipment according to the European Society of Radiology (ESR) [14].

Maintenance and average annual interest payment costs were obtained from the hospital administrative records and purchase contracts awarded to tender equipment. All items of equipment cost have been taken into consideration through the workload of each diagnostic method. Furthermore, we analyzed this cost by determining the total number of patients who received any procedure during the study period. Finally, the cost per patient for each modality was calculated.

2.4.1.2 Cost of materials and supplies

Cost of materials and supplies reflected market prices paid to manufacturers and vendors. We calculated all supplies needed to perform the diagnostic procedure for each patient in the two modalities. The supplies considered as single use for one patient were calculated according to the price list. Supplies used for multiple patients were estimated by a factor for each patient. Contrast media used to visualize the coronary arteries during the diagnostic procedure varies among patients, thus we calculated the cost of the amount used for each patient. We then analyzed the average for all patients for both procedures separately. Blood tests carried out before and after procedures were taken into account because of differences between the two diagnostic strategies. These costs are taken into account regardless of who is responsible for payment - the patient or the hospital. Hospitalization costs after the procedure for the observation and recovery period following diagnostic catheterization were also taken into account.

2.4.1.3 Personnel costs

The salaries of all involved physicians, nurses, and medical imaging specialists were also determined. Thus, personnel costs were calculated according to collective agreements established by the Institutional Civil Service Law. The number of medical staff required for each patient was determined and multiplied by the average income of this staff. This cost was calculated for all patients, and the average was obtained for each patient.

2.4.2 Induced costs

Induced costs included the cost of complications associated with the test false-negative for CAD. In the subgroup of patients with false-negative CCTA, a 15% rate of non-fatal myocardial infarction over 10 years was assumed [15-17]. Induced costs also associated with the complication rates for CCTA (0.004%) and elective ICA (0.05%) were derived from the literature [18-22]. Costs of complications are difficult to estimate. For this purpose, previously published data were combined. It was assumed that the typical complication of both diagnostic tests and untreated CAD would be non-fatal myocardial infarction, requiring hospitalization, rehabilitation, chronic medication and repeated follow-up examinations. On average, conservative cost estimates for a serious complication amounted to 20,000 dollars [15-22].

2.4.3 Total costs

Total costs were calculated as direct and indirect costs (as established by the cost analysis) times the number of patients tested plus the induced costs, as described above. ICA is considered as the gold-standard test in the cost-effectiveness analysis, with a 100% diagnostic accuracy (sensitivity and specificity of ICA=100%) and no non-diagnostic or false results [23].

2.5 Cost-effectiveness analysis

We used the Statistical Package for Social Science (SPSS version 23) program for data entry and analysis and the Origin pro 7.0 program to illustrate the cost-effectiveness analysis. The cost-effectiveness of each strategy was defined as the cost per correct diagnosis. According to this definition, a lower cost value per correct diagnosis translates into better cost-effectiveness. This straightforward approach assumes that the goal of a test is to make a diagnosis.

In the current study, we estimated the costs of the two different strategies relative to their effectiveness, intended to correctly diagnose significant CAD. In particular, the cost-effectiveness of the CCTA and ICA was compared when applied to patient populations with varying CAD pre-test probabilities. Using a mathematical model, we compared the cost-effectiveness for diagnosing the CAD for patient cohorts characterized by the different pretest likelihood (prevalence) of CAD.

2.6 Model characteristics

The model is based on Bayes' theorem and consequently assesses cost-effectiveness ratios of strategies in hypothetical patient cohorts with different prevalence of disease [24]. The mathematical

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model was initially suggested by Paterson and co-workers for a comparison of cost-effectiveness for diagnosis of CAD [15,16] and was later applied by others [17,22,25,26].

2.7 Definitions of the effectiveness of tests

When performing a cost-effectiveness analysis, a wide variety of factors and parameters related to the costs and the performances of the tests have to be considered. The model must be able to take into account the costs associated with false-positive results (i.e., costs of unnecessary diagnostic tests) as well as the costs associated with false negative results (i.e., costs of complications because of inappropriate management of the disease).

The most difficult problem in any assessment of cost-effectiveness is to define the effectiveness of healthcare [27,28]. For our purposes, we defined the effectiveness of diagnostic tests in two ways. The first effectiveness criterion was the ability of a diagnostic test to accurately identify a patient with CAD. This definition represents a straightforward approach, assuming that the single goal of a test is to make a diagnosis [15-17,22].

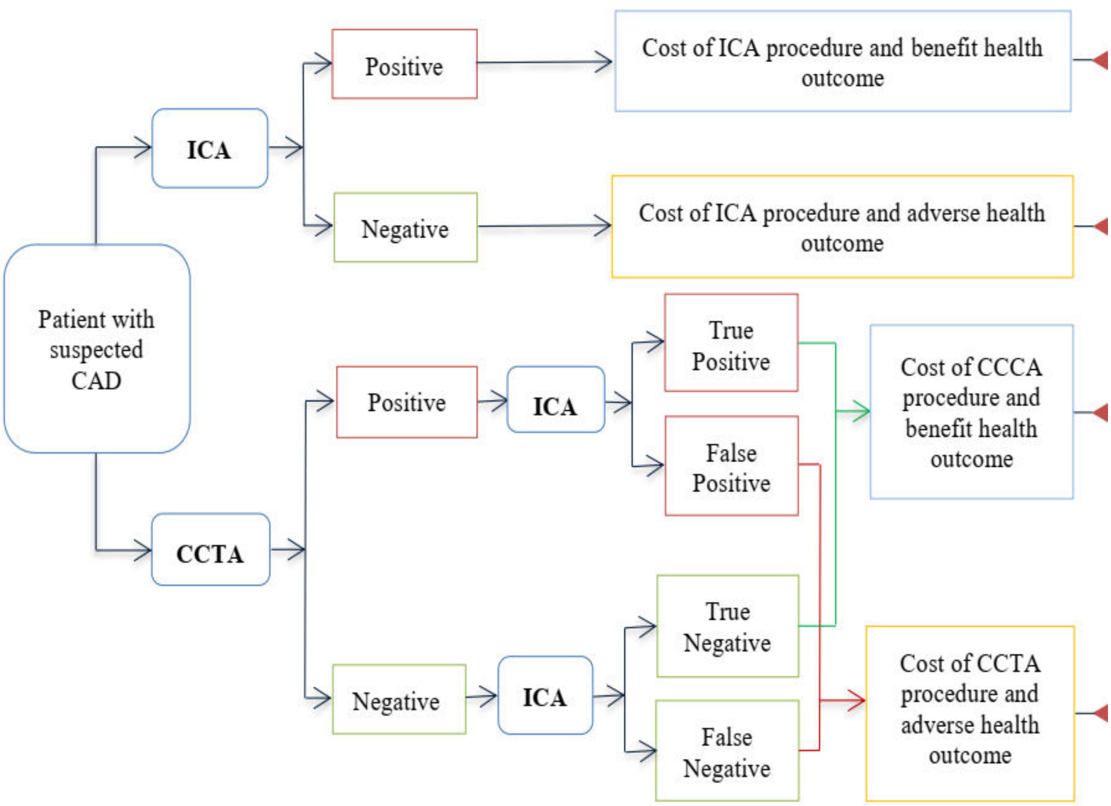
The definition of the second effectiveness criterion was more complex and attempted to account for the future health outcome of patients undergoing the tests [15,16]. It was assumed that a correct diagnosis of CAD would enable patients to receive optimal therapy resulting in improved survival and well-being. Over the follow-up period, the number of life-years gained (Δ) by CAD therapy was adjusted for quality of life, yielding quality-adjusted life years (QALYs). In line with previous cost-effectiveness analyses, an accurate diagnosis of CAD was projected to increase the number of QALYs by 3 years during a 10-year follow-up [16]. Our model describes the patient flow through the two modalities and the diagnostic results and their relationship with the cost and the benefit or adverse health outcome as shown in Figure 1.

Figure 1. Schematic of the decision analytic model patient follow up scenarios for cost analysis and cost-effectiveness

2.8 Cost-effectiveness equations

Calculations of cost-effectiveness and utility for CCTA and ICA are illustrated in Table 1 and in the equations below, which defines the parameters and rates required for the cost-effectiveness equations.

Direct Costs + Induced Costs



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Effectiveness

Cost-effectiveness analysis of CCTA
1. **Costs** = NCCTA × (DCCTA + RCCTA × C) + NICA × (DICA+RICA × C) + FNCCTA × (RFN × C) **Whereas:** NICA = NCCTA × (1- FPCCTA) × [P × SnCCTA + (1-P) × (1-SpCCTA)] + NCCTA × FPCCTA FNCCTA = NCCTA × (1- FPCCTA) × P × (1-SnCCTA)
2. **Effectiveness =** NCCTA × (1- FPCCTA) × P × SnCCTA + NCCTA × P × FPCCTA
3. **ΔQALY** = (CADDx) × (ΔQALY) - 10 × (NCCTA × MCCTA + NICA × MICA) - 5 × (FNCCTA × MFNCCTA) - 10 × (0.1) × (NCCTA × RCCTA + NICA × RICA + FNCCTA × RFN)

Cost-effectiveness analysis of ICA
1. **Costs** = NICA × (DICA+RICA × C) **Whereas:** NICA = 1
2. **Effectiveness** = NICA × P
3. **ΔQALY** = NICA × (ΔQALY) × P – 10 × NICA × MICA- NICA × RICA

Table 1. Parameters and Rates required for Cost-effectiveness equations

Parameters	Definitions
NCCTA	Number of patients having CCTA
DCCTA	Direct costs for CCTA
RCCTA	Rate of complications with CCTA
C	Average costs of a complication (assumed to be non-fatal myocardial infarction)
NICA	Number of patients having ICA
DICA	Direct and indirect costs for ICA
RICA	Rate of complications with ICA
FNCCTA	Rate of patients with false-negative CCTA
RFN	Rate of complications per 10-year follow-up period for patients with CAD and false-negative tests
FPCCTA	Rate of false positive CCTA
P	Prevalence of CAD in patient cohort
SnCCTA	Sensitivity of CCTA
SpCCTA	Specificity of CCTA
CADDx	Effectiveness
ΔQALY	Quality-adjusted life years extended by therapy after making diagnosis of CAD (per 10 years of follow-up)
MCCTA	Mortality rate due to CCTA
MICA	Mortality rate due to ICA
MFNCCTA	Mortality per 10 years for patients with CAD but false negative CCTA

2.9 Sensitivity analysis of variables influencing cost-effectiveness

A sensitivity analysis was performed to evaluate whether some key parameters used in the mathematical model are robust within a certain range of uncertainty. Thus, cost-effectiveness calculations were repeated after:

1. Increasing and decreasing the rates of complications associated with invasive coronary angiography (RICA= 0.1% and 0.01%) [15-17,25].
2. Taking into account the high and lower costs of complications (C=25000 dollars and 10000 dollars) [15-17,25].
3. Increasing and decreasing CCTA sensitivity (SnCCTA= 85.84 and 99.93) and specificity (SpCCTA= 69.62 and 98.83) concerning to our accuracy calculations.

3. Results

3.1 Diagnostic accuracy of CCTA

We tested the diagnostic accuracy of CCTA by performing ICA on 58 patients who were first assessed by CCTA. The ICA revealed that 36 patients were true positive (significant CAD ≥50% stenosis), and two patients false positive (non-significant CAD). Nineteen patients were true negative (non-significant CAD), and one patient was false negative (significant CAD ≥50% stenosis). The overall sensitivity and specificity of the CCTA technique was 97.3% (95% CI: 85.84% to 99.93%) and 90.48% (95% CI: 69.62% to 98.83%), respectively. The positive predictive value was 94.74% (95% CI: 82.79% to 98.54%), and the negative predictive value was 95% (95% CI: 73.23% to 99.25%).

3.2 Cost analysis

A cost analysis is an important first step before engaging in a cost-effectiveness analysis of economic evaluation and to determine the suitability or feasibility of a potential procedure. The costs of both diagnostic methods were identified through a detailed analysis of all involved procedures. In our cost analysis, the following general considerations were taken into account:

1. Operational hours

Operational hours for MSCT and cardiac catheterization systems were 7 hours/day, 250 days/year according to the Ministry of Health regulations based on the Institutional Civil Service Law, which regulating working hours and official holidays.

2. Equipment lifetime

Equipment lifetime of MSCT equipment and cardiac catheterization was set at 10 years, which was determined according to categories established by the European Society of Radiology (ESR) [14].

3. Procedure time period

Independent samples t-test shows that there was a significant difference between the means of the procedure duration for CCTA and ICA at the 0.05 level of significance (P-value <0.001). The mean procedure time of CCTA was 10.24 minutes, while the mean procedure time of ICA was 37.00 minutes.

4. Reporting time period

Independent samples t-test shows that there was a significant difference between the means of the reporting time for the diagnostic modalities at 0.05 level of significance (P-value <0.001). The mean reporting time of CCTA result is 42.02 minutes, while the mean reporting time of ICA result is 12.32 minutes.

5. Cost of contrast medium

Independent samples t-test shows that there was a significant difference between the means of the cost of contrast medium per patient for the diagnostic modalities at 0.05 level of significance (P-value <0.001). The mean cost of contrast medium of CCTA procedure per patient was 17.47 dollars, while the mean cost of contrast medium of ICA procedure per patient was 11.68 dollars.

3.2.1 Cost analysis of CCTA procedure

Direct costs for CCTA are defined as the sum of the equipment costs, personnel costs and medical supplies cost of CCTA procedures.

3.2.1.1 Equipment costs

Equipment or unit costs of equipment were the sum of purchasing and warranty costs, which include service contracts and maintenance. Equipment lifetime for MSCT equipment was set at 10 years. Operational hours for MSCT equipment was 7 working hours, 250 working days. The cost calculation steps revealed that the cost per minute equals 1.12 dollars. The total equipment cost per CCTA procedure was 11.43 dollars, which results from multiplying the cost per minute (1.12 dollars) by the average CCTA procedure time (10.24 minutes).

3.2.1.2 Personnel salaries cost

Personnel salaries were determined based on the need for highly experienced employees with established experience. Thus, there is a salary in accordance with the years of experience and level of professional certification. The salary of the most experienced employee was calculated according to the Institutional Civil Service law.

Personnel cost is the total of the salaries of medical imaging specialists, consultant radiologists, and nursing and was estimated on the basis of the procedure time, which includes for each patient also the time of reporting. Regarding specific time requirements for CCTA, medical imaging specialists and nursing spend only the time of the procedure (10.24 min), but the radiologist's time includes the procedure and time of reporting (10.24 min plus 42.02 min). The total salary cost per CCTA procedure was 13.95 dollars, which results from multiplying the salary cost per minute by the CCTA procedure time.

3.2.1.3 Medical supplies and blood tests cost

The cost of medical supplies is the total cost of materials used during the CCTA procedure, cost of contrast medium used to visualize the coronary arteries, and cost of preparation. Supplies and preparation costs were calculated for each patient. Contrast medium was calculated as an average of contrast cost for all patients. The total medical supplies cost per CCTA procedure was 25.46 dollars.

3.2.1.4 Direct cost of CCTA

Direct cost of CCTA per procedure is equal to the sum of total equipment cost per procedure (11.43 dollars), total personnel cost per procedure (13.95 dollars) and total medical supplies cost per procedure (25.46 dollars). The total direct cost per CCTA procedure was 50.84 dollars.

3.2.2 Cost analysis of the ICA procedure

Direct costs for ICA are defined as the sum of the costs for equipment, medical supplies, recovery periods and personnel associated with the procedure.

3.2.2.1 Equipment costs

Unit costs of equipment were the sum of the purchasing and warranty costs, which include the service contract and maintenance. The total equipment cost per ICA procedure was 40.44 dollars. The calculation steps of catheterization equipment cost per ICA procedure are similar to previous steps in the CCTA.

3.2.2.2 Personnel salaries cost

Personnel salaries cost of medical imaging specialists, a consultant cardiologist, and nursing were determined. Personnel cost was estimated on the basis of the procedure time, which for each patient includes the time of reporting and recovery. With respect to the specific time requirements for ICA, medical imaging specialists and nursing spend only the duration of the procedure (37 min), other nursing is required only during the recovery (11.40 min), and the cardiologist is involved during the procedure and reporting (37 min plus 12.32 min). The total direct cost of personnel salaries per ICA procedure was 32.91 dollars. The indirect cost of the salary of a recovery nurse per ICA procedure was calculated as the annual salary divided by the average number of cases conducted per year. This was then multiplied by the number of nurses who serviced all patients during the recovery period. The indirect cost of the salary for recovery nursing per ICA procedure was 11.40 dollars. The total personnel cost per ICA procedure was estimated from the sum of direct and indirect costs to be 44.31 dollars.

3.2.2.3 Medical supplies and blood test cost

Medical procedure supplies cost included the materials used during the ICA procedure and the cost of contrast medium and its preparation. Supplies and preparation costs were calculated for each patient. Contrast medium was calculated as an average of contrast cost for all patients. Supplies used during the recovery period were also calculated. The total medical supplies cost per ICA procedure was 149.48 dollars.

3.2.2.4 Total cost per ICA procedure

Finally, the total cost of ICA per procedure is equal to the sum of equipment cost (40.44 dollars), total personnel cost per examination (44.31 dollars), and the total medical supplies cost (149.48 dollars), yielding a total cost per ICA procedure of 234.23 dollars.

3.2.3 Cost comparison CCTA versus ICA

Cost categories for both diagnostic approaches are summarized in Table 2.

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Table 2. Cost comparison CCTA versus ICA

Cost category	CCTA (in dollar)	ICA (in dollar)
Equipment	11.43	40.44
Materials and supplies	13.95	149.48
Personnel	25.46	44.31
Total	50.84	234.23

3.3 Cost per patient tested

The cost per patient tested in relation to different prevalence of CAD is shown in Figure 2. These results indicate that the cost of both CCTA and ICA are equal at a prevalence of 57%. The cost of CCTA increased as a linear function of the CAD prevalence (direct relation between false diagnosis and prevalence). In contrast, the cost for ICA did not increase significantly (no false diagnosis, both sensitivity and specificity are 100%). Cost increases with the CAD prevalence for CCTA but not significantly for ICA. CCTA showed a lower cost than ICA with CAD prevalence <57% but higher costs with CAD prevalence >57%.

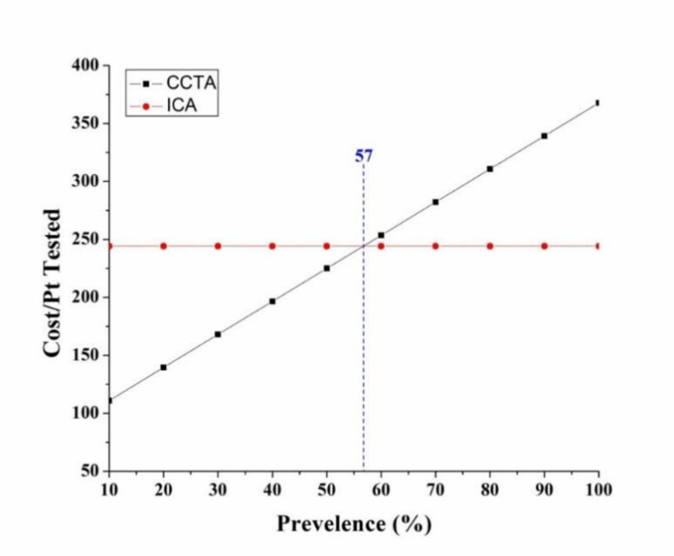

Figure 2. Effects of disease prevalence on cost

3.4 Impact of CAD prevalence on cost-effectiveness in terms of cost per effect

As cost per effect is the inverse of cost-effectiveness, the hyperbolic decrease in cost per effect indicates increased cost-effectiveness. Despite the increase in total cost with increasing prevalence of CAD, especially in CCTA, cost-effectiveness improved with different CAD prevalence for both diagnostic tests. Cost and prevalence are inversely proportional in both CCTA and ICA as shown in Table 3. Moreover, cost per effect (cost per patient with CAD diagnosed accurately) versus increasing prevalence of CAD is illustrated in Figure 3.

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Table 3. Cost-effectiveness of CCTA and ICA at different levels of CAD prevalence in terms of cost per effect

Prevalence	CCTA	ICA
10%	1139.1	2442.3
20%	716	1221.2
30%	575	814.1
40%	504.5	610.6
50%	462	488.5
54%	449.7	452.3
55%	448	448
56%	443.9	436.13
60%	434	407.1
70%	413.9	384.9
80%	398.8	305.3
90%	387	271.4
100%	377.6	244.23

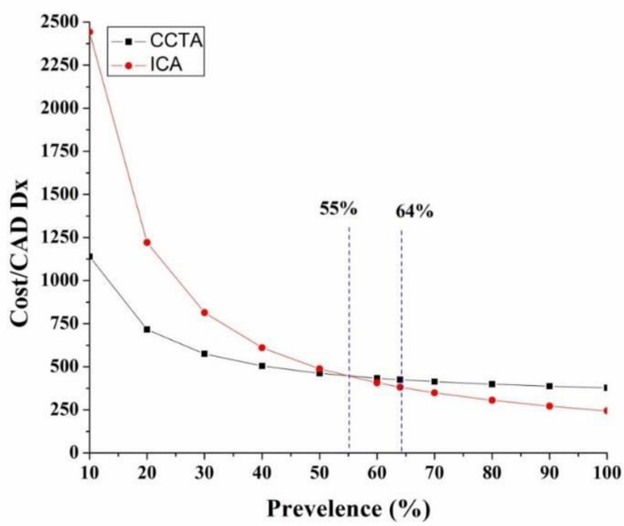

Figure 3. Effects of disease prevalence on cost-effectiveness in terms of cost per effect

3.5 Impact of CAD prevalence on cost-effectiveness in terms of ΔQALY

The cost per cost-effectiveness in terms of ΔQALY versus increasing prevalence of CAD is shown in Figure 4. The decrease in cost per ΔQALY indicates increased cost-effectiveness. Regardless of the increase in cost with increasing prevalence of CAD, especially in CCTA, ΔQALY improved with different CAD prevalence for both diagnostic tests.

At a CAD prevalence of 55%, CCTA and ICA were equally effective in terms of ΔQALY with costs of 150 dollars. CCTA was more cost-effective in terms of ΔQALY up to a CAD prevalence of 54%, ranging from 399.21 dollars (10% prevalence) to 128.06 dollars (54% prevalence). By contrast, ICA shows better cost-effectiveness for a prevalence of 56%–100%, with a cost in terms of

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ΔQALY of CAD between 146.55 dollars (56% prevalence) and 81.79 dollars (100% prevalence) as shown in Table 4.

Table 4. Cost-effectiveness of CCTA and ICA at different levels of CAD prevalence in terms of ΔQALY

Prevalence	CCTA	ICA
10%	399.21	852.46
20%	245.84	416.42
30%	196.42	275.5
40%	171.89	205.84
50%	157.24	164.3
54%	128.06	152.03
55%	150	150
56%	150.92	146.55
60%	147.49	136.71
70%	140.55	117.05
80%	135.34	102.34
90%	131.30	90.91
100%	128.06	81.79

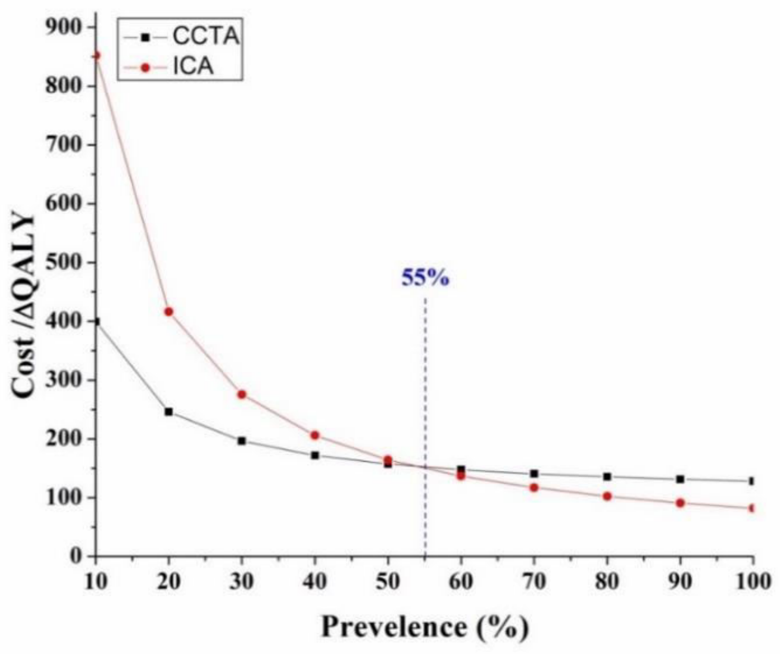

Figure 4. Effects of disease prevalence on cost-effectiveness in terms of ΔQALY

4. Discussion

Regarding the overall sensitivity and specificity of the CCTA, the current results are close to a recent study conducted by Mansour et al. [29] revealed sensitivity and specificity of the CCTA technique was 94.74% and 94.23%, respectively.

The overall direct costs of ICA were found to be about 4.6 times the cost of CCTA, mainly due to higher materials and supplies costs (5.9 times), equipment costs (3.5 times), and personnel costs (3 times). This ratio is markedly lower than those reported in previous studies, which have found that the cost of ICA exceeds that of CCTA up to a factor of nine [20,22,30]. However, the latter studies have, at least partly, applied inconsistent cost-accounting practices, and thus, the results might not be directly comparable. However, the main factor that contributes to the low-cost ratio between CCTA and ICA is the relatively low direct costs of machines, reflecting increasingly different equipment manufactures specifications costs. In contrast, the current results are comparable to those reported by Dorenkamp et al. [17], which revealed that the overall direct costs of ICA were approximately three times the cost of CCTA, mainly as a result of similar MSCT equipment specifications.

Regarding the correct diagnosis, CCTA was more cost-effective up to a CAD prevalence of 54%. The cost for one patient correctly diagnosed as having CAD was 449.7 dollars with CCTA and 452.3 dollars with ICA. Given the 64% CAD prevalence of the investigated patient cohort in the current study, the cost for one patient correctly diagnosed as having CAD was 425.2 dollars with CCTA and 381.6 dollars with ICA. At a CAD prevalence of 55%, CCTA and ICA were equally effective with costs of 448 dollars. With higher disease prevalence (>55%), ICA became more cost-effective. In particular, the data demonstrate that CCTA is more cost-effective in patients with a prevalence up to 54%, with a cost per correct diagnosis of CAD ranging from 1139.1dollars (10% prevalence) to 449.7 dollars (54% prevalence). By contrast, ICA shows better cost-effectiveness for a prevalence of 56%–100%, with a cost per correct diagnosis of CAD between 436.13 dollars (56% prevalence) and 244.23 dollars (100% prevalence).

From a cost-effective point of view, our results indicate that the range of patients eligible for CCTA is smaller than previously believed and that ICA becomes the more cost-effective diagnostic approach at a disease prevalence > 55%. These findings are supported by guidelines for the assessment and diagnosis of recent onset chest pain issued by the NICE [31]. According to NICE guidelines, CCTA is recommended if a patient has a 10-29% prevalence for CAD. The guideline further recommends ICA as the most cost-effective first test if the prevalence of CAD is >61% [31]. In agreement with our results, a study conducted by Dorenkamp et al. [17] that revealed above a threshold value of disease prevalence of 55%, proceeding directly to the ICA was more cost-effective than CCTA. In contrast to our results, two previous studies applied different cost-accounting practices and largely overestimated the costs of ICA or the rate of severe complications associated with the ICA. One of these previous studies demonstrated that CCTA is cost-effective in patients up to 60-70% prevalence for CAD, whereas ICA is the most cost-effective preferred approach in patients with a higher prevalence [20]. The second study found CCTA to be more cost-effective than ICA even up to a prevalence for CAD of 86% [22].

We systematically changed the numerical values of various, key parameters in the equations. Increasing (0.1%) or decreasing (0.01%) the rates of complications associated with ICA changed the cost-effectiveness threshold of CCTA marginally (56% and 53% CAD prevalence, respectively). With higher (25,000 dollars) costs of complications, the cost-effectiveness of CCTA decreased marginally up to a CAD prevalence of 51%, but with lower (10,000 dollars) costs of complications, the cost-effectiveness of CCTA was significantly increased up to a CAD prevalence of 62%. The most substantial changes occurred at maximally decreased and increased diagnostic accuracies. However, CCTA remained significantly more cost-effective than ICA up to a disease prevalence of 77%. In contrast, with maximum decreased diagnostic accuracies, the cost-effectiveness decreased dramatically to 14%.

Finally, one of the key requirements of cost-effectiveness analysis is the identification of cost per effect, which means that decreased cost with high benefit indicates increased cost-effectiveness. Likewise, as the prevalence of CAD increased, there were decreased costs per utility unit in terms of QALYs gained, indicating increased cost-utility at higher disease prevalence. Thus, despite the fact that total costs increased with the increasing prevalence of CAD, cost per effect and cost per utility improved. The hyperbolic relationship between CAD prevalence and cost per effect or cost per utility implies very high costs per effect or utility unit at low disease prevalence. At a low prevalence of CAD, the rank order of cost per utility unit was principally the same as that of cost per effect in CCTA. Again, the rank order of tests changed at high disease prevalence, and performing ICA as the first and only test was the most cost-effective diagnostic approach at high disease prevalence. Our analysis shows cost-effectiveness of CCTA for diagnosing CAD in patients suspected as having mild to intermediate CAD. Thus, the most important step for physicians in selecting the appropriate diagnostic approach is based on a clinical estimation of disease prevalence. The score by Morris et al. [32] provides an easy, memorable, and accurate method for categorizing and subcategorizing patients with suspected CAD into probability groups upon which decisions concerning diagnostic testing could be based. Although ICA remains the gold standard for diagnosing CAD, carefully performed CCTA may be an economically efficient alternative to ICA, especially in ruling out CAD in patients with an intermediate pretest likelihood.

5. Conclusion

Our results suggest a more rational approach to avoid unnecessary testing and to optimize the utilization of diagnostic testing. It is important to ensure that patients with CAD are referred to ICA for diagnosis and that patients who do not have CAD avoid unnecessary invasive testing. Although ICA has been the gold standard for evaluating CAD, it should not be routinely performed as an initial test to assess patients with suspected CAD due to cost, invasiveness, and measurable risk. CCTA might be reasonable for patients with a low to intermediate pretest probability of CAD. Diagnostic options should be made through a clear policy of shared decision-making, including information about risks, benefits, and costs to the patient.

Abbreviations

CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CEA, cost-effectiveness analysis; ICA, invasive coronary angiography; MSCT, multislice computed tomography; QALYs, quality-adjusted life-years

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