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COST EFFECTIVENESS OF MULTI DETECTOR CT ANGIOGRAPHY OF THE CORONARY ARTERIES FOR THE DIAGNOSIS OF SUSPECTED NON-ST ELEVATION ACUTE CORONARY SYNDROME (NSTE-ACS) IN THE EMERGENCY DEPARTMENT. MATHEMATICAL ANALYSIS WITH A DECISION MODEL

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The purpose of our study is to model cost-effectiveness of MDCTA for the diagnosis of NSTE-ACS with initially negative enzymes, in the emergency department.
In Belgium, the use of multi-detector computed tomography (MDCTA) is probably cost-effective in the diagnosis of NSTE-ACS in the acute setting A decision tree model was developed and a mathematical study was performed that included two hypothetical strategies: MDCTA and admission with classic clinical follow-up and treatment. Cost-effectiveness for the Belgian situation was simulated with sensitivity analysis using known values for diagnostic performance and known costs for the different strategies or components of strategies.

Key words: Cost-effectiveness – Diagnostic radiology.

Acute chest pain accounts for approximately 6.5 % of all emergency department visits in the US (1, 2) and is considered to lie in the same range in Belgium (oral communication). Failure to diagnose myocardial ischemia as a cause of acute chest pain has serious implications and the triage of patients with possible ischemia is often difficult. To reduce diagnostic error, many patients that present at the emergency department are admitted for observation, even when no initial ECG changes or elevated cardiac enzymes are present. Emergency departments have therefore developed chest pain units and diagnostic protocols commonly including serial cardiac enzyme evaluations and ECG's, supplemented with some form of stress testing with or without imaging (3). Many of these patients are found to have no acute coronary syndrome (ACS) and in the US more than 2 million patients with acute chest pain are admitted to the hospital without developing an ACS (4, 5). Data from Germany reveal that the number of unnecessary hospital days is high, amounting to as much as 839 per 1000 patients admitted for acute chest pain (6).

Non invasive access to coronary anatomy has become available with the emergence of multi-detector computed tomography (MDCTA) of the coronary arteries. Diagnostic performance of MDCTA has been evaluated in many studies (7). Even though appropriate indications for MDCTA remain largely work in progress, the technique has been used as a tool to rule out non ST segment elevation acute coronary syndrome (NSTE-ACS) in the emergency department (8-15). Some of these studies suggest that MDCTA may be an attractive option to reduce costs when evaluating such patients in the emergency room. However, formal cost-effectiveness studies of MDCTA in this situation have not yet been performed.

The purpose of our study was to model cost-effectiveness of MDCTA for the diagnosis of NSTE-ACS with initially negative enzymes, in the emergency department. Since it is know that determination of the exact degree of stenosis on MDCTA is cumbersome (5) we investigated to thresholds for considering MDCTA as positive: a classic approach wherein an obstructive lesion (> 50% diameter) is used a positivity criterion and a more prudent approach, wherein the presence of any degree of plaque is considered positive. A decision tree model was developed and a mathematical study was performed that included two hypothetical strategies: (1) MDCTA (CA), (2) admission with classic clinical follow-up and treatment. Cost-effectiveness for the Belgian situation was simulated with sensitivity analysis using known values for diagnostic performance and known costs for the different strategies or components of strategies.

Methods and materials

Decision model

Cost-effectiveness can be theoretically studied with a model to mathematically project costs for several strategies. In such a model a decision tree is developed that resembles a flow-chart or algorithm and consists of different nodes (16).

To assess potential cost-effectiveness of initial MDCTA we developed such a decision model with two nodes, which compared costs of two model management strategies. The basic decision model used, based on a previous study (17) is displayed in Fig. 1. In the first strategy (MDCTA) the decision whether or not to admit the patient is based on the results of initial MDCTA, performed as fast as possible. Patients with "abnormal" scans are admitted. Patients with "normal" scans are discharged. The model is performed twice, using one out of two practical thresholds for judging a scan result as abnormal: 1/ a less prudent approach: at least one segment with a > 50% diameter stenosis, further referred to as "Obstructive" and 2/ a more conservative approach: at least one segment with plaque of any degree or type, further referred to as "Plaque" In the second strategy (OBSERVATION), all patients are admitted irrespective of their clinical risk assessment score and undergo conventional follow-up and/or treatment. (ECG, Serial enzymes, imaging…).

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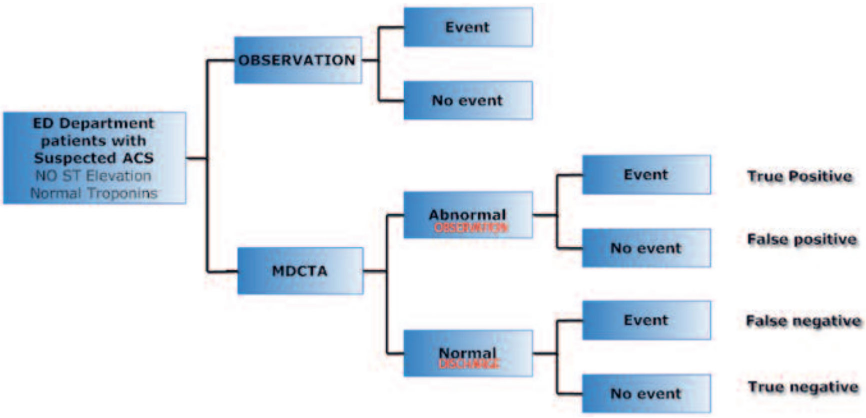

Fig. 1. — Decision tree.

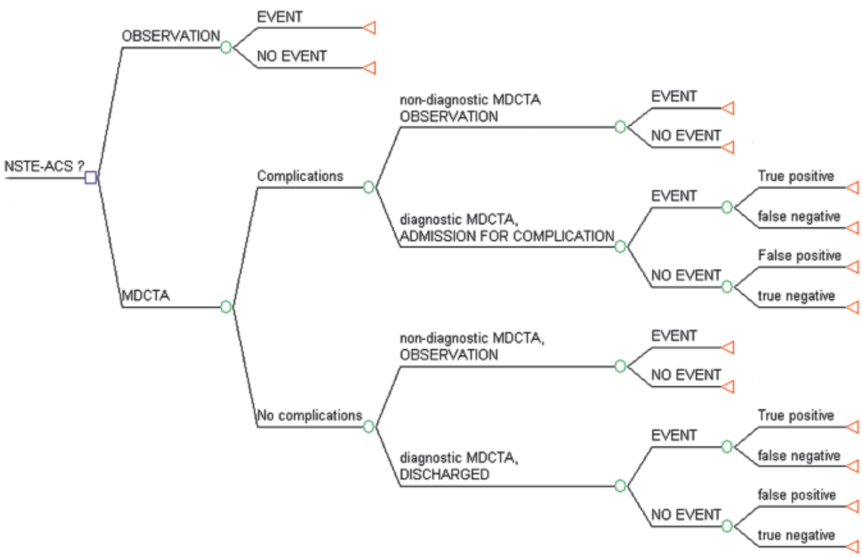

Fig. 2. — Modified decision tree used in the decision analysis software

Table I. — Costs given by APR-DRG values.

	Cost (Euro)	Coding
Cost "Scan procedure" including contrast medium	190.61	N260
"Angina pectoris"	2328.53	APR-DRG 202
"Acute coronary syndrome"	4066.25	APR-DRG 190
"Acute Renal Failure" (typical complication)	5357.80	APR-DRG 410

We choose to include the proportion of non-diagnostic scans and complications, since this may have an influence on the outcome of the model. The final model, used in the software (Tree-age Pro, Healthcare edition 2007) is shown in Fig 2.

In our model the terminal nodes or outcomes were cumulated costs to obtain a diagnosis of ACS (Event). Cost-effectiveness was defined as the ratio of the costs to reach a diagnosis and the number of patients correctly diagnosed as having ACS (18, 19). A decrease in the cost per correct diagnosis indicates improved cost-effectiveness. Correct diagnosis of absence of disease was not considered a direct criterion of cost-effectiveness. We did not assess other utilities such as quality adjusted life years.

Values and ranges for costs

Values for costs and their ranges are tabulated in Table I and consist of data provided by the Belgian state institute for health insurance (RIZIV/INAMI) for all patient related diagnostic groups (APR-DRG) (20). Values used were the following costs (official terminology between quotation marks): (a) cost for "Scan procedure" (b), observation for "angina pectoris" (c), "acute coronary syndrome"(d). As a typical complication of the scanning procedure and its inherent iodine contrast injection, "acute renal insufficiency" and its related costs were used. The estimated cost for a short admission and quick release after a negative scan (excluding the cost for the scan procedure itself) was rated at the cost of a full observation for angina pectoris divided by an estimated arbitrary value of four (e) (local estimation of costs in our hospital).

Except for the additional or altered costs generated by the scan (a), complications(d) or a shorter admission (e), caused by the MDCTA arm, all diagnostic and therapeutic costs for a usual observation or treatment were supposed to be included in the APR-DRG value for "angina pectoris" and "acute coronary syndrome". This may include cumulated costs for ECG, serial enzymes, imaging (invasive/noninvasive), hospital admission and is an average for all patients in Belgium for the year 2004. All monetary values are expressed in Euro.

Probabilities and test characteristics

Values and ranges for probabilities and percentages with 95% confidence intervals (95% CI) are tabulated in Table II.

Sensitivity (SE) and specificity (SP):

For the first threshold -presence of an obstructive lesion- SE and SP and the number of non-diagnostic scans were taken from a previously published meta-analysis (18). In that study a pooled sensitivity/specificity of 0.95 and 0.90 respectively was found. For the second threshold -presence of any degree of plaque- data from a study by Hoffmann (11) were taken. In that study the predictive value an SE/SP of any degree of plaque for ACS was evaluated (SE 1, SP 0.49).

Complications

Complications of MDCTA were rated at 0.004 (22).

Table II. — Proportions and diagnostic performance for sensitivity analysis.
* Values from ref 11, ** from ref 21,*** from reference xx, § no single value was used.

MDCTA Sensitivity using obstructive lesion as threshold	0.95*
MDCTA Specificity using obstructive lesion as threshold	0.90*
MDCTA Sensitivity using presence of any plaque as threshold	1***
MDCTA Specificity using presence of any plaque as threshold	0.49***
Pre-test probability	§
Non-diagnostic scans (ND)	0.03*
Complications of MDCTA	0.004 **
Pre-test probability	§
Non-diagnostic scans (ND)	0.03*
Complications of MDCTA	0.004 **

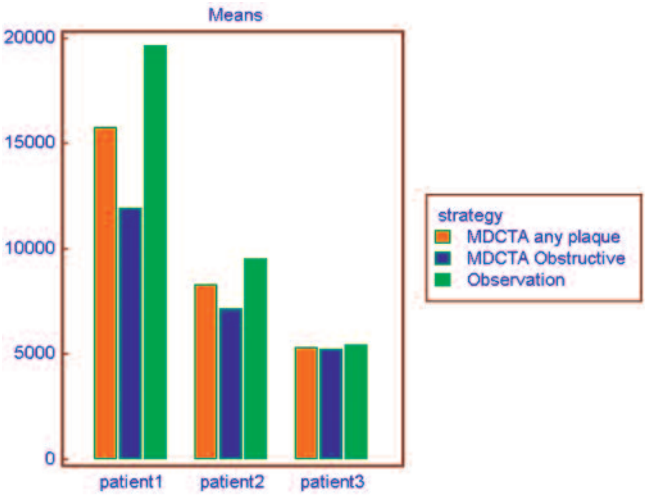

Fig. 3. — Cost-effectiveness for three hypothetical patients with different pre-test probability (patient 1: 0.13; patient 2: 0.30; patient 3: 0.63)

Calculations

Cost-effectiveness

Cost-effectiveness of the two strategies was calculated for three types of patients with varying pre-test probability (PTP): (1) a 40 year-old female smoker with typical angina pectoris (13% PTP) (2) a 35 year-old male patient with typical angina pectoris but without risk factors (30% PTP) (3) a 60-year-old female diabetic patient with typical angina pectoris (63% PTP). Examples came from a study by Dewey (23).

Sensitivity analysis

One-way sensitivity analysis of cost-effectiveness on pre-test probability was performed. This was done by changing the PTP of a positive event in the model. Pre-test probability of NSTE-ACS was used ranging from 0.01 to 0.99 in 100 discrete steps. This was repeated for the two diagnostic thresholds (obstructive and plaque).

Sensitivity analysis investigating the influence of different remuneration or reimbursement of MDCTA on cost-effectiveness was performed, in the three hypothetical patients quoted above, using a range of 190.65 Euro – the actual reimbursement in Belgium – to 1500 Euro. This was done again for the two diagnostic thresholds. Cost-effectiveness was plotted against the cost and break-even analysis with calculation of crossover point of the two lines with equivalence of the two strategies was calculated

A sensitivity analysis and plot of willingness-to-pay per diagnosis (WTP) versus pre-test probability was created for the two diagnostic thresholds, to be able to assess which was the preferred strategy for each combination of WTP and pre-test probability.

Software used was Tree-age Pro 2007, Healthcare, release 1.0

Results

Cost-effectiveness

In Fig 3, a bar graph is displayed that shows the cost per diagnosis of an event for the two strategies in the three hypothetical patients with different pre-test probability.

Three bars are provided per patient type, one displaying the observation strategy, the other two displaying the MDCTA strategy with the use of the two positivity thresholds. Highest cost is in the patient with PTP of 0.13 using the observation strategy (19649.79 Euro). Even when the presence of any plaque is used as positivity criterion, there is an important difference between the MDCTA strategy and the observation strategy, with a savings of 3901.51 Euro. The difference between the strategies becomes much less important when moving to the patients with high pre-test probability. Exact values are given in Table III.

Sensitivity analysis

One-way sensitivity analysis of cost-effectiveness on pre-test probability is displayed in Fig. 4. MDCTA is clearly the most cost-effective strategy in patients that have a pre-test probability that is lower than 0.71 when using as a threshold the presence of an obstructive lesion. For the other threshold MDCTA is most cost-effective in patients that have a pre-test probability below 0.85.

In Fig. 5 A, B graphical examples of sensitivity analysis of cost-effectiveness for remuneration of MDCTA for one of the three hypothetical patients is displayed (low PTP of

Table III. — Cost-effectiveness for three hypothetical patients with varying pre-test probability (PTP), for observation and two thresholds (see also Fig. 3).

Strategy	Patient 1(PTP 0,13)	Patient 2 (PTP 0,30)	Patient 3 (PTP 0,63)
Observation	19649.79	9499.78	5434.1
MDCTA obstructive	11928.51	7148.813	5234.26
MDCTA Plaque	15748.06	8277.53	5305.91

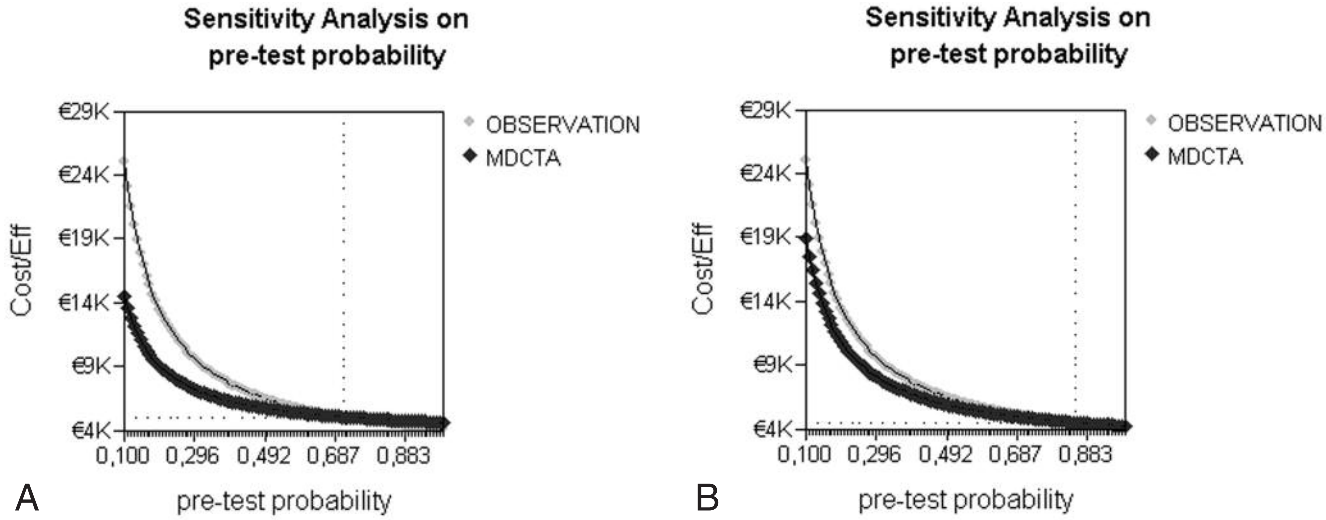

Fig. 4. — Cost effectiveness of the two strategies assuming estimates for SE and SP of 0.93 and 0.90 respectively (threshold = presence of obstructive lesion). MDCTA strategy is cost-effective when pre-test probability is below 0.71(A). Cost effectiveness of the two strategies assuming estimates for SE and SP of 1 and 0.49 (threshold= presence of any plaque) respectively. MDCTA strategy is cost-effective when pre-test probability is below 0.85 (B).

Note that the two curves are lying closer together in B, meaning that the two strategies differ much less in cost-effectiveness.
Cost/eff: Cost-effectiveness.
K: multiplied by 1000

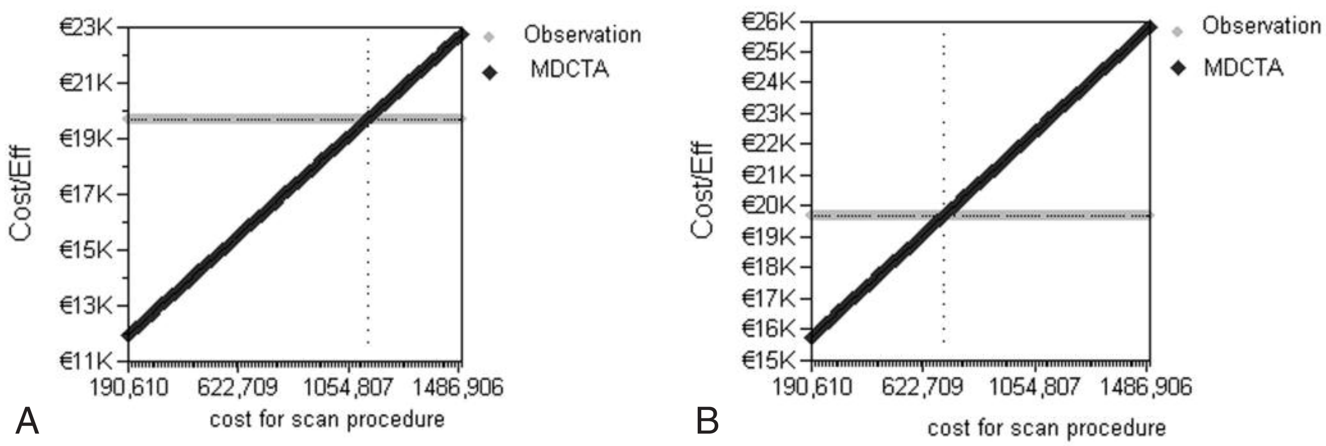

Fig. 5. — Cost-effectiveness for a patient with pre-test probability of 0.13. MDCTA strategy is cost-effective up to 1133.37 Euro (threshold = presence of obstructive lesion (A). Cost-effectiveness for a patient with pre-test probability of 0.13. MDCTA strategy is cost-effective up to 701.72 Euro (threshold = presence of any plaque) (B).

Table IV. — Break-even values for three hypothetical patients with varying pre-test probability (PTP), for two thresholds.

Strategy	Patient 1(PTP 0,13)	Patient 2 (PTP 0,30)	Patient 3 (PTP 0,63)
MDCTA obstructive	1133.71	845.30	308.46
MDCTA Plaque	701.72	557.24	282.26

0.13). MDCTA strategy is most cost-effective up to a cost of 1133.37 (break even point) when using as a threshold the presence of an obstructive lesion. For the other threshold MDCTA is most cost-effective when the cost for the scanning procedure is below 701.72. Exact values for break even values are given in Table IV.

Break even values in the third patient type tend to approach the actual reimbursement value in Belgium (190.65 Euro) with values of 308.46 for the obstructive threshold and 282.26 for the plaque threshold.

In Fig. 6, sensitivity analysis and a plot of willingness-to-pay per diagnosis versus pre-test probability is displayed for the two thresholds. Combinations of willingness-to-pay and pre-test probability that lie to the right of the curve are in favour of the observation strategy whereas the

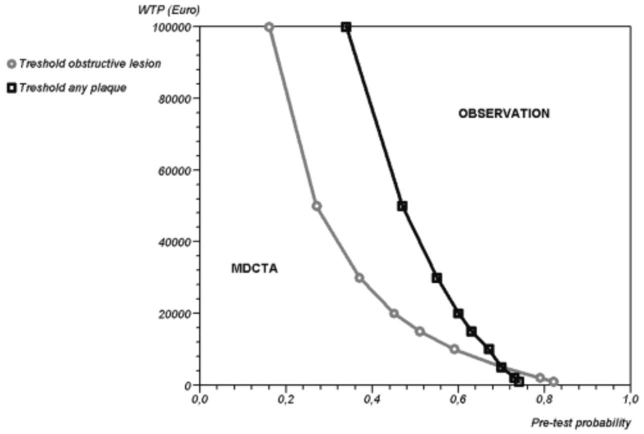

Fig. 6. — Sensitivity analysis on pre-test probability and the willingness-to-pay threshold. The line is the division between the optimal test strategy for the base case. In situations with values of PTP and WTP lying to the right of the curve. observation strategy is more cost-effective.
WTP: Willingness-to-pay threshold.
PTP: Pre-test probability

Table V. — Tabular values for willingness-to pay for the two thresholds and their corresponding pre-test probability (see also Fig. 6).

MDCTA 50%	MDCTA Plaque	WTP
0.16	0.34	100000
0.27	0.47	50000
0.37	0.55	30000
0.45	0.6	20000
0.51	0.63	15000
0.59	0.67	10000
0.7	0.7	5000
0.79	0.73	2000
0.82	0.74	1000

reverse is true if lying to the left of the curve. From this curve we can deduct that below a WTP of 5000 using threshold “obstructive” is cost-effective up to patients with PTP of 0.70 . Above 5000 for WTP, threshold “plaque” is the most cost-effective for higher PTP. Tabular results can be found in Table V.

Discussion

With our decision model, we found that in patients presenting with a possible NSTE-ACS, a strategy that uses MDCTA of the coronary arteries as a quick first imaging step is potentially cost-effective in all patients with a pre-test probability lower than 0.71, using a cut-off value for positivity of MDCTA of 50% diameter stenosis. Depending on the pre-test probability of the patient costs are different for the diagnosis of a positive event, amounting to 19649.79 Euro for a typical low PTP patient (0.13) in the observation strategy. Cost for diagnosis of a positive event is much lower in the MDCTA arm: 11928.51 Euro. Costs for a positive diagnosis go down when considering patients with higher pre-test probability, and the difference between the two strategies diminishes to reach a break even at a PTP of 0.71. With respect to the inherent difficulties to exactly grade a stenosis on MDCTA (5), we also ran the same model with a different threshold or positivity criterion: the presence of any plaque. We observed the same trends. However savings are substantially lower than with the use of the “obstructive” threshold: the cost for a typical low PTP patient was 15748.06 euro. We also found break-even values for the cost of the scanning procedure in the MDCTA strategy, that are substantially higher than the actual reimbursement, at least in low pre-test probability groups.

Irrespective of the threshold used, MDCTA can probably be used as a reliable and cost-effective technique to rule NST-ACS in a acute setting and the test can be done very quickly and does not require complex patient preparation or logistic resources. The scan can be performed in the first hours after the onset of the clinical complaints and when negative, the patient can be discharged from the emergency department immediately. Although the purpose of this study was not to formally study the reliability of MDCTA to exclude all causes of chest pain, it is apparent from the individual data from most studies in this series that alternative diagnoses besides coronary disease can often be ruled out.

These conclusions are important and can probably be an incentive for further randomised trials that should confirm these assumptions in real-life. Only one randomized study using an approach with MDCTA has been published and although the patient sample was rather small, the diagnostic efficacy was equal in the two arms, but the time to patient discharge was much shorter in the MDCTA arm and this approach was probably cheaper than in the conventional arm (14).

It can also be of value to regulatory offices and authorities and insurers.

Cost-effectiveness studies for the diagnosis of coronary disease with non-invasive tests are found throughout the literature, and specifically it has been demonstrated that MDCTA is cost-effective in the diagnosis of stable coronary disease (24-26). In one of these studies (25) a first triage of patients was done with myocardial perfusion scanning but this was only in stable patients. To our knowledge this is the first theoretical decision analysis that also suggests that in the acute setting, MDCTA can be cost-effective. In one other study (14), the patients in the MDCTA arm with equivocal results, or intermediate lesions were subjected to myocardial perfusion scanning, to avoid a simple bifurcated decision based on a simple threshold of 50% diameter stenosis. We tried to circumvent this problem by running the model on a lower threshold: “plaque”, that can be considered more prudent and less aggressive in discharging patients. We choose this threshold because it was the only one available in the literature: further data relating degree of stenosis on MDCTA to prediction of an acute coronary event is lacking.

Other imaging techniques have been used to develop a quick and efficient triage strategy for acute chest pain in the emergency department. Nuclear medicine techniques and to a much lesser degree, echocardiography, have been extensively tested, and there is a large body of literature supporting its use in these circumstances (26). In 2003 a joint task force of the American College of Cardiology, the American Heart Association and the American Society for Nuclear Cardiology published guidelines for the use of Myocardial Perfusion Imaging (MPI) (27). The task force gave a class 1 recommendation to the use of acute rest MPI for the assessment of patients presenting with a possible acute coronary syndrome in whom initial markers and the ECG are non diagnostic. A randomized study (37) showed that MPI improves triage and that unnecessary hospitalization was reduced among patients without acute ischaemia, without reducing appropriate admission for patients with acute ischemia. Wether MDCTA can be recommended as a substitute for MPI needs to be investigated further. Radiation dose may be a matter of debate. A clear disadvantage of MDCTA is the relatively high radiation dose that goes with the examination, with average doses ranging from 10 to 20 mSv (38). How this relates to the dose of MPI now and in the future is a matter that goes beyond this discussion, but it may be anticipated that radiation dose reducing protocols for MDCTA will have an important impact (38).

Some important limitations have to be acknowledged.

The amounts that have been used for the costs are the values that are used in Belgium, which biases the results towards local habits. It was assumed however that relative scaling of these amounts would be similar in other countries and that at least an identical decision tree could be used for different countries. The monetary values used for the APR-DRG categories are only a rough and averaged approximation of all costs incurred and probably prone to inaccuracies.

Although the pooled values for SE, SP and number of non-diagnostic scans were pooled from studies that specifically targeted the emergency situation of suspected NST-ACS with initially negative troponins, it may be that these statistics are not as good in a general population of acute patients that have an irregular rhythm, high age, high body mass index, heavily calcified vessels or otherwise suboptimal patients (27-28).

Third, this study was “theoretical”, meaning that the conclusions were not based on prospective clinical investigations but on a mathematical model. The model only looks at a very simple modification of the classic observation by adding only one test, early in the evaluation.

Last, this simple model took not into account the possible downstream costs induced, due to unexpected cardiac findings. We did not look at the cost of finding or ruling out significant or non significant extra-cardiac findings.

All these limitations can be solved with prospective randomized studies that perform real-life accounting of all included patients.

The conclusion of the study is that, for the Belgian situation, the use of MDCTA is probably cost-effective in the diagnosis of NSTE-ACS in the acute setting. The current reimbursement of MDCTA of the coronary arteries is cost-effective but real life prospective randomized studies have to be performed to confirm this and to investigate subpopulations with clinical characteristics that make them less or more amenable to MDCTA.

An important consideration has to be made about the required level of expertise to accurately evaluate the coronary stenoses. Physicians inexperienced with coronary CT angiography have a clearly lower sensitivity and specificity compared to expert radiologists. Their ability to evaluate significant coronary stenoses can improve after one year of training with approximately 600 cases a year. An increase of sensitivity is seen after one year of training, ranging from 66%-75% (31). Published research about diagnostic performance was almost always carried out by physicians with 3 or more years of experience, resulting in a sensitivity of 90%. One of the suggested theories of this major difference in sensitivity is the approximately 10 years of preparation needed to attain a certain expertise in any domain (32). This period may overlap with normal medical training resulting in a required training period of about 3 years, a seen with expert radiologists.

Conclusion

For the Belgian situation, the use of MDCTA is probably cost-effective in the diagnosis of NSTE-ACS in the acute setting. The current reimbursement of MDCTA of the coronary arteries is cost-effective but real life prospective randomized studies have to be performed. Clinical subgroups with less MDCTA-friendly characteristics have to be investigated.

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