

Cardiac Multidetector CT:

Technical and Diagnostic Evaluation with Evidence-based Practice Techniques¹

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The “bottom-up” model of evidence-based practice (EBP) emphasizes the principles of integrating best research evidence with clinical expertise and patient values. It is derived from multidisciplinary sources, including clinical medicine, epidemiology, and adult learning theory, and has been applied to many medical disciplines, including radiology. Central to its implementation in everyday busy radiology practice is its emphasis on accurate, rapid modern informatics/internet to get the best current research evidence into everyday practice. In this article, the authors apply the principles of EBP to the topic of cardiac computed tomography. EBP is ideally suited to asking, searching, appraising, applying, and evaluating the literature on this rapidly developing technology.

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You are a busy attending radiologist approached by a newly appointed cardiologist in your tertiary referral center. She recently examined a patient with chest pain. The patient is a middle-aged man with a history of smoking who describes atypical chest pain. There is no family history of coronary artery disease (CAD) and he does not have diabetes. Nevertheless, the cardiologist is bothered by some T-wave changes at electrocardiography (ECG), and the cholesterol-to-high-density lipoprotein (HDL) ratio is elevated. The tertiary referral center you practice in has recently installed a 64-section computed tomographic (CT) scanner, and the cardiologist is considering referring the patient for cardiac multidetector CT but is unfamiliar with its technique and unsure of its effectiveness.

She ponders the problem, thinking, "CAD is one of the leading causes of morbidity and mortality in most developed countries. In Ireland, CAD is re-

sponsible for 20.6% of all deaths (1). In the United States, CAD is the largest single cause of death in men and women, resulting in 653 000 deaths in 2002 (2). Conventional invasive coronary angiography currently remains the standard for the evaluation of the coronary arteries in patients known to have or suspected of having CAD (3). Limitations of the modality include its invasiveness, expense, and time consumption, with a small but substantial complication rate (stroke, coronary artery dissection, cardiac arrhythmias, hemorrhage at the arteriotomy site, and pseudoaneurysm formation). The overall complication rate is around 1.8% (4). The mortality rate from the procedure is low (0.1%) but may be up to 0.55% in high-risk populations (5)."

The cardiologist also considers, "Several clinical risk-stratification scores (Framingham Risk Score [6] and European Systematic Coronary Risk Evaluation [7]) have been devised to allocate patients into low-, intermediate-, and high-risk groups. Such pretest stratification attempts to avoid over-investigating patients with low and intermediate pretest probabilities for hemodynamically significant CAD while directing invasive angiography toward those with a high pretest probability. Such scores provide some index prediction of who will have CAD and who will not, but overall they perform poorly (8). As a result, many patients with low and intermediate pretest probabilities for hemodynamically significant CAD undergo unnecessary coronary angiography. A noninvasive test such as coronary multidetector CT would be of immense benefit to patients in these clinical pretest categories."

You also consider the problem, thinking, "The heart has traditionally been difficult to evaluate in detail with non-ECG-gated CT of the chest because of cardiac motion and resultant inherent motion artifacts. The rapid technology evolution has yielded dramatic improvements in temporal and spatial resolution. As a result, there is an expanding interest in using cardiac multidetector CT for evaluation of the heart for many conditions (9). There have

been many recent studies on the use of multidetector CT in the diagnosis of coronary artery stenosis as a potential alternative to invasive coronary angiography."

You raise the topic at your weekly radiology teaching rounds—your current resident is unfamiliar with cardiac multidetector CT. You decide this would be an appropriate time for him to read up on the subject and suggest he discusses it at the next week's meeting. At the meeting he explains, "Several technologic advancements have made multidetector CT a realistic replacement for conventional coronary angiography in selected patients: The latest scanners have gantry rotation times of 330 msec. The technique of partial scanning by using a half-scan algorithm means data from only 180° of gantry rotation are used for image reconstruction, which improves temporal resolution to 165 msec. During data acquisition, the patient's ECG data are recorded so that image reconstruction can be performed with ECG gating. In general, the highest quality, motion-free images of the coronary arteries are produced when data obtained during mid-to-end diastole are used for reconstruction. To increase the relative proportion of the cardiac cycle spent in diastole, oral and/or intravenous β -blockers are administered to reduce the heart rate to around 60 beats per minute."

Your resident describes his search of the literature initially using the Google search engine with the terms "coronary artery disease" and "CT." This yielded 1 420 000 hits—only one result on the first page was from the medical literature. He then searched PubMed, a Web

Essentials

- Evidence-based practice (EBP) involves a structured approach to searching the literature, evaluating the retrieved published material, reaching and applying conclusions, and evaluating performance; a recent series published in *Radiology* has highlighted many aspects of applying EBP to the discipline of radiology.
- EBP principles are particularly suited to rapidly evolving technologies such as cardiac multidetector CT; specifics of such innovative techniques are often absent from contemporary textbooks.
- EBP principles applied to the literature involving cardiac multidetector CT show the current generation of cardiac CT to have a high sensitivity and specificity with satisfactorily narrow confidence intervals for the detection of hemodynamically significant coronary stenosis in patients with low and intermediate pretest probabilities for hemodynamically significant coronary artery disease.

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Abbreviations:

CAD = coronary artery disease
 CI = confidence interval
 EBP = evidence-based practice
 ECG = electrocardiography
 GCP = graph of conditional probabilities
 HDL = high-density lipoprotein

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site developed by the National Center for Biotechnology Information that is designed to provide access to citations from the biomedical literature (10). By using the same search terms as for the Google search, the resident retrieved articles that included one diagnostic study on dual-source coronary artery CT, one diagnostic study comparing 16-section cardiac CT to conventional angiography, two diagnostic studies comparing cardiac CT to myocardial perfusion single photon emission computed tomography, two review articles evaluating the cost-effectiveness of cardiac CT, a cardiac CT review article in French, a study evaluating CT of the cardiac veins, and a review of atherosclerosis in mice. Your resident realizes that using Google for this topic and not using a good search strategy with the PubMed site may result in a low hit rate of useful articles.

Your radiology group expresses great interest in introducing cardiac multidetector CT to the practice but first wants an assessment of its technical and diagnostic capabilities. You have previously used evidence-based practice (EBP) and applied it to new or difficult problems in radiology. You decide that such EBP is highly suited to evaluating this rapidly developing technology. You suggest to the cardiologist and to your radiology group that you will undertake an EBP evaluation of cardiac multidetector CT and discuss your findings when completed.

EBP is a stepwise process. There are five steps in applying the “evidence-based” approach (11): Ask, search, appraise, apply, and evaluate. For this article, these steps were completed in December 2006.

Step 1: Ask

Asking a focused clinical question involves four components by using the “PICO” format (12): (a) patient, (b) investigation, (c) comparison, and (d) outcome of interest. This format is used to construct a single, focused question—for example, “In patients with disease X, how does test A compare with test B for outcome Y.” Components are most useful if they are used as PubMed MeSH (ie, “medical sub-

ject heading”) terms. A search for suitable MeSH terms for any topic can be found by using the Preview/Index tab on the PubMed home page (10).

For asking a focused question on cardiac multidetector CT, in text format the question would read, “In patients suspected of having hemodynamically significant coronary artery stenosis, how does cardiac multidetector CT compare with invasive coronary angiography for diagnosis?”

Step 2: Search

There is a hierarchy of evidence in the literature, which can be divided into primary and secondary levels (Fig 1) (13). The primary literature consists of original studies and is the lowest level on the “evidence pyramid.” At the top of the evidence pyramid are evidence-based guidelines that summarize important and relevant topics in clinical medicine; one such system is Clinical Evidence from the British Medical Journal Publishing Group (14). Between these two levels are evidence-based journals, such as the *American College of Physicians Journal Club* (15) and evidence-based reviews, guidelines, and databases—for example, the Cochrane Collaboration (16). We find that the best results when searching a level in the pyramid are obtained by using the PICO format, which allows us to link concepts in a search strategy. Boolean operator terms (first derived by George Boole, an English mathematician) provide a logical way to search complex databases through concept variables such as AND, OR, NOT, and NEAR. For medical database searching, terms inserted into the search bar allow us to link similar concept terms by using OR and different concept terms by using AND. Each level was searched by using a combination of MeSH terms (Fig 2). Studies without abstracts were excluded.

Results from searching the literature for the purposes of this article can be seen in Figure 3. A search of evidence-based Web sites revealed that there were no articles on the evaluation of cardiac multidetector CT. For evidence-based journals, the author did

not subscribe to the *American College of Physicians Journal Club*, and there were no free symposia on cardiac multidetector CT. A search of the Cochrane Library, Guidelines Finder, and the Scottish Intercollegiate Guidelines Network revealed no reviews on cardiac multidetector CT. An evaluation of SUMSearch (a search engine that combines meta-searching and contingency searching) by using a combination of MeSH terms (Fig 2) and limited to diagnostic studies yielded 25 possible systematic reviews and 104 possible diagnostic studies in PubMed. Each article for which the title and abstract seemed relevant to the topic was appraised further by two authors (E.J.H., J.D.D.) independently by assigning a level of evidence. Discrepancies were resolved by consensus. To avoid missing potentially useful articles, a separate search of PubMed was also performed by using a combination of MeSH terms (Fig 2).

Step 3: Appraise

Appraising the Diagnostic Radiology Literature: Applying Levels of Evidence

One of the key problems with searching the radiology literature on a given topic is the time required to read and appraise retrieved articles. The purpose

Figure 1

Level/Websites	
1 – Evidence-based guidelines	http://www.guidelines.gov http://www.rcr.ac.uk/index.asp?PageID=667 http://www.sign.ac.uk/index.html
2 – Evidence-based journals	http://ebm.bmj.com/ http://www.elsevier.com (evidence-based cardiovascular medicine) http://www.jr2.ox.ac.uk/Bandolier/index.html
3 – Evidence-based reviews/databases	http://www.cochrane.org http://www.tripdatabase.com/index.html http://www.uptodate.com
4 – Primary studies	http://www.ncbi.nlm.nih.gov/sites/entrez http://sumsearch.uthscsa.edu/ http://www1.kfinder.com/newweb/

Figure 1: Each hierarchical level in the evidence pyramid and examples of Web sites available for searching.

should be to spend the most amount of time on articles with the least amount of bias and discard those that have flawed methods or results. A useful way to optimize time is to quickly assign a level of evidence to each article from retrieved abstracts of a search engine. The National Health Service Centre for Evidence-based Medicine, Oxford University, England, has developed a table of levels of evidence (Table 1) (17). By using this table, one can quickly assign a level of evidence to each article that seems relevant to a topic. In this way only the highest-level articles need to be evaluated, which can markedly reduce the reading load.

In assigning levels of evidence for our search, there were five systematic reviews evaluating cardiac multidetector CT (Table 2) (18–22). These were systematic reviews of level 2b diagnostic studies (independent, blinded comparisons of multidetector CT and coronary angiography) and were therefore classified as level 2a publications. One of the systematic reviews, which evaluated a comprehensive spectrum of generations of scanner that included four-, eight-, and 16-section CT studies and one 64-section multidetector CT study, with patient-based and segment-based analysis

in all languages with likelihood ratios (21), was considered best current evidence and was appraised in more detail. Because we wanted to include the latest generations of scanner, a later systematic review that included a more comprehensive number of 64-section CT articles with patient-based and segment-based analysis and likelihood ratios was also appraised in detail (19).

Appraising Systematic Reviews

Validity of systematic reviews.—Appraising the validity of a systematic review involves the following four basic questions: (a) Did the review explicitly address a focused clinical question? (b) Was the search for relevant studies detailed and exhaustive? (c) Were the primary studies of high methodologic quality (see the section on appraising the validity of diagnostic studies)? (d) Were assessments of studies reproducible?

Our appraisal showed that both systematic reviews asked a focused clinical question: “How does cardiac multidetector CT compare to invasive coronary angiography in the evaluation of suspected significant coronary stenosis in native coronary arteries?” The search for relevant studies was not exhaustive. Neither systematic review included all

other reviews, consulted experts directly, or searched the “gray literature” (ie, internal reports, pharmaceutical industry data, non-peer-reviewed publications/unpublished data). There may, therefore, have been publication bias; in addition, if there were recent unpublished but important “in press” study articles, these would not have been included. All included studies were of high methodologic quality. Overall study results for each scanner generation seemed reproducible. One systematic review that included only articles in English was excluded (20), and two systematic reviews that did include any 64-detector CT articles were also excluded (18,22). No systematic review included dual-source multidetector CT; therefore, from our PubMed search we found three studies that evaluated dual-source multidetector CT (23–25), one of which was a diagnostic study (level 2b), which was also appraised in detail (23).

Strength of systematic reviews.—Assessment of the strength of a systematic review of diagnostic studies can be found in the Results section of that review. The important statistical parameters include the prevalence of significant coronary artery stenosis, sensitivity, and specificity, with 95% confidence in-

Figure 2

Patient		Investigation		Comparison		Outcome	Results
Coronary artery stenosis	AND	Tomography, x-ray computed/methods	AND	Coronary angiography/methods	AND	Sensitivity and specificity	→ 14
OR							
Coronary artery	AND	Tomography, x-ray computed/methods	AND	Coronary angiography/methods	AND	Sensitivity and specificity	→ 22
OR							
Coronary artery	AND	Tomography, x-ray computed	AND	Coronary angiography/methods	AND	Sensitivity and specificity	→ 30
OR							
Coronary artery	AND	Tomography, x-ray computed	AND	Coronary angiography	AND	Sensitivity and specificity	→ 69
OR							
Coronary artery	AND	Tomography, x-ray computed	AND	Coronary angiography	AND	Diagnosis	→ 151
↓		↓		↓		↓	
23		41		3544		>50,000	

Figure 2: Search strategies can be customized to suit requirements. MeSH terms appropriate for each column of a PICO question are obtained from PubMed's (10) MeSH database, a controlled vocabulary for indexing articles. With limited time, a high specificity–lower sensitivity search using MeSH terms across a row retrieves the most important articles but may miss some relevant ones. With more time, a higher sensitivity–lower specificity search using terms down a column results in a larger retrieval of important articles but includes some less relevant ones.

tervals (CIs), predictive values, and likelihood ratios. In addition to these statistical parameters, most systematic reviews weight studies on the basis of study size. Without this inclusion, large and small studies end up with equal weights. Furthermore, one investigator may interpret the findings of a study as positive, while another investigator interprets the same study findings as negative. Finally, small but clinically important effects that may be statistically “nonsignificant” but are clinically important may be counted as “negative.” Thus, a reader cannot tell anything about the magnitude of an effect from nonweighted studies.

Our results from appraising the strength of retrieved systematic reviews are shown in Tables 3–5.

In addition to calculating the sensitivity and specificity of multidetector CT for the detection of coronary artery stenosis, most articles on this subject quoted the number and percentage of coronary artery segments (as defined by the American Heart Association [26]) that were evaluable. In the studies reviewed, the reasons most commonly cited for nondiagnostic images were irregular cardiac rhythm, sinus tachycardia, calcification, vessel motion, inadequate breath hold, poor contrast material enhancement, and anomalies of the coronary arteries. Both of the reviewed meta-analyses gave the number of interpretable segments analyzed for each study and supplied weighted averages. These data show a steady improvement in technical performance as newer generations of scanners have been introduced.

The sensitivity and specificity of multidetector CT in the detection of significant stenosis of a coronary artery (defined as narrowing of $\geq 50\%$ of the luminal diameter) is often quoted on a per-patient basis, as well as on a per-segment basis. The per-patient number refers to the detection of at least one stenotic lesion in a patient in whom one or more stenotic segments have been identified at invasive coronary angiography; for example, in a patient with stenosis in the left main and in the proximal right coronary artery, if only the left

Figure 3

Study (Year)	Source	Study (Year)	Source
4-Section		16-Section (continued)	
Kopp (2002)	PubMed	Cademartiri (b) (2005)	PubMed
Martuscelli (2004)	PubMed	Schuijf (2005)	PubMed
Hertzog (2004)	PubMed	Morgan-Hughes (2005)	PubMed
Blinder (2005)	PubMed	Garcia (2006)	SumSearch
Lau (2005)	PubMed	Dewey (b) (2006)	PubMed
Dirksen (2005)	PubMed	Cury (b) (2006)	PubMed
Gerber (2005)	PubMed	Burgstahler (2006)	SumSearch
8-Section		64-Section	
Matsuo (2004)	PubMed	Leschka (2005)	PubMed
16-Section		Raff (2005)	PubMed
Nieman (2002)	PubMed	Leber (2005)	PubMed
Cademartiri (a) (2004)	PubMed	Mollet (2005)	PubMed
Zhang (2004)	PubMed	Plass (2006)	PubMed
Hoffmann (2004)	PubMed	Ehara (2006)	PubMed
Dewey (a) (2004)	PubMed	Ropers (2006)	PubMed
Cury (a) (2005)	PubMed	Pugliese (2006)	PubMed
Gulati (2005)	PubMed	Nikolaou (2006)	PubMed
Aviram (2005)	PubMed	Dual-Source	
Gaspar (2005)	PubMed	Scheffel (2006)	PubMed
Kefer (2005)	PubMed	Achenbach (b) (2006)	PubMed
Haberi (2005)	PubMed	Flohr (2006)	PubMed
Kaiser (2005)	PubMed	Systematic Reviews	
Kuettner (2005)	PubMed	Schuijf (2005)	SumSearch
Romeo (2005)	PubMed	Sun (2006)	SumSearch
Achenbach (a) (2005)	PubMed	Van der Zaag-Loonen (2006)	SumSearch
Heuschmid (2005)	PubMed	Stein (2006)	SumSearch
Kitigawa (2005)	PubMed	Hamon (2006)	SumSearch

Figure 3: Results from searching two search engines (PubMed and SumSearch) for studies on CT by using the PICO format.

Table 1

Levels of Evidence and Grades of Recommendations for Studies from the Oxford Centre for Evidence-based Medicine

Grade/Level of Evidence	Description
A/1a	Systematic review (with homogeneity) of level 1 diagnostic studies or a CDR with 1b studies from different clinical centers
A/1b	Independent blind comparison of an appropriate spectrum of consecutive patients, all of whom have undergone both the diagnostic test and the reference standard
A/1c	Diagnostic finding for which specificity is so high that a positive result rules in diagnosis (“spin”) or for which sensitivity is so high that a negative result rules out diagnosis (“snout”)
B/2a	Systematic review (with homogeneity) of level ≥ 2 diagnostic studies
B/2b	Independent blind comparison, but either in nonconsecutive patients or confined to a narrow spectrum of study individuals (or both), all of whom have undergone both the diagnostic test and the reference standard; or a CDR not validated with a test set
B/3a	Systematic review (with homogeneity) of level 3b and better studies
B/3b	Nonconsecutive study or independent blind comparison of an appropriate spectrum, but the reference standard was not applied to all study patients
C/4	Reference standard was not applied independently or was not applied blindly
D/5	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or “first principles”

Note.—Adapted and reprinted, with permission, from reference 17. CDR = clinical decision rule.

main stenosis is identified at multidetector CT, this is still registered as a true-positive rather than a false-negative patient-based result. The opposite is also true; if one incorrect segment and 10 correct segments are read on multidetector CT images, the patient-based result is still a false-positive result, even though the majority of readings were correct. Hence, moving from a segment-based to a patient-based analysis tends to increase the sensitivity but decrease the specificity. Only one systematic review included both patient-based and segment-based analysis. It also included a comprehensive analysis based on weighting of studies. Sensitivity, specificity, and positive and negative predictive values for four-, 16-, and 64-section and dual-source coronary multi-

detector CT are quoted on a per-patient basis (Table 4) and on a per-segment basis (Table 5).

Appraising the Validity of Diagnostic Studies

When appraising an article from the diagnostic literature, two sections are evaluated. The Materials and Methods section is assessed for the validity of the study, and the Results section is evaluated for the statistical strength of the study.

Several standard questions are asked when appraising a diagnostic study for validity (27): (a) Was there an independent, blind comparison with a reference standard of diagnosis? (b) Was the diagnostic test evaluated in an appropriate spectrum of patients (like those in

whom it would be used in practice)? (c) Was the reference standard applied regardless of the diagnostic test result? (d) Was the test (or cluster of tests) validated in a second, independent group of patients?

The diagnostic article (23) we retrieved evaluated the accuracy of dual-source 64-detector CT, by using independent, blinded comparison of this technique with standard invasive coronary angiography, in a group of patients who had been clinically assessed and assigned a high pretest probability of CAD. All patients underwent invasive angiography prior to multidetector CT, with an interval of 23 days or fewer. The dual-source multidetector CT results were not validated in a second group of patients.

Table 2

Levels of Evidence for Retrieved Studies on Cardiac Multidetector CT

Category and Study	Level of Evidence	Grade of Recommendation
Systematic review		
Schuijff et al (18)	2a	B
Hamon et al (19)	2a	B
Sun and Jiang (20)	2a	B
Stein et al (21)	2a	B
van der Zaag-Loonen et al (22)	2a	B
Diagnostic study: Scheffel et al (23)	2b	B

Note.—Levels of evidence were determined by applying the criteria from the Oxford Centre for Evidence-based Medicine (Table 1).

Table 3

Coronary Artery Segments Evaluable with Successive Coronary Multidetector CT Generations

Study and Scanner Type	Analyzable Segments	Percentage
Stein et al (21)*†		
Four section	1693 of 2172	78
16 Section	6740 of 7438	91
64 Section	1005 of 1005	100
Overall	9438 of 10615	89
Hamon et al (19)†		
16 Section	Not provided	85
64 Section	Not provided	94
Overall		89
Scheffel et al (23): dual-source‡	414 of 420	99

* Limited data on eight- and 64-section CT.

† Systematic review.

‡ Diagnostic study.

Appraising the Diagnostic Radiology Literature: Additional Points for a Radiologist to Consider

In addition to answering epidemiologic questions, it is suggested that the Materials and Methods section of a radiology article should be appraised from the radiologist's perspective with five further questions (28): (a) Has the imaging method been described in sufficient detail for it to be reproduced in your department? (b) Have the imaging test being evaluated and the reference test been performed to the same standard of excellence? (c) Have "generations" of technology development within the same modality (eg, single- vs dual-source multidetector CT) been adequately considered in the study design and discussion? (d) Has radiation exposure been considered? (e) For cardiac studies, has temporal resolution been considered?

Appraising the validity of radiology publications from a radiologist's perspective, the authors described their CT technique in sufficient detail for it to be reproducible in other centers. Standard invasive coronary angiography technique was used, and these studies were interpreted according to the same guidelines as the CT images, with significant stenosis defined as vessel diameter reduction of greater than 50%. The technologic differences between dual-source

Table 4**Diagnostic Performance of Four-, 16-, and 64-Section and Dual-Source Coronary Multidetector CT: Patient-based Results**

Study and Scanner Type	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Positive Likelihood Ratio	Negative Likelihood Ratio
Stein et al (21) *†‡						
Four section	95 (61 of 64) [90, 101]	84 (21 of 25) [70, 98]	94 (61 of 65)	88 (21 of 24)	5.938	0.060
16 Section	95 (276 of 292) [92, 97]	84 (131 of 156) [78, 90]	92 (276 of 301)	89 (131 of 147)	5.938	0.060
64 Section	100 (47 of 47) [100, 100]	100 (20 of 20) [100, 100]	100 (47 of 47)	100 (20 of 20)	∞	0.000
Hamon et al (19)†‡						
16 Section§	96 (582 of 606) [95, 98]	67 (312 of 466) [63, 71]	79 (582 of 736)	93 (312 of 336)	2.906	0.059
64 Section	97 (321 of 331) [95, 99]	90 (192 of 213) [86, 94]	94 (321 of 342)	95 (192 of 202)	9.700	0.033
Scheffel et al (23): dual source	93 (14 of 15) [68, 100]	100 (15 of 15) [78, 99]	100 (14 of 14)	94 (15 of 16)	∞	0.070

Note.—Numbers in parentheses are raw data used to calculate percentages, and numbers in brackets are 95% CIs.

* Contained no patient-based data on eight-section CT and one study on 64-section CT.

† Unweighted summary statistics.

‡ Systematic review.

§ Not all 16-section studies quoted both segment- and patient-based results.

|| Diagnostic study.

Table 5**Diagnostic Performance of Four-, 16-, and 64-Section and Dual-Source Coronary Multidetector CT: Segment-based Results**

Study and Scanner Type	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Positive Likelihood Ratio	Negative Likelihood Ratio
Stein et al (21) *†‡						
Four section	84 (429 of 514) [80, 87]	93 (1613 of 1730) [92, 94]	79 (429 of 546)	95 (1613 of 1698)	12.000	0.172
16 Section	88 (1023 of 1160) [86, 90]	97 (6508 of 6741) [96, 97]	81 (1023 of 1256)	98 (6508 of 6645)	29.333	0.124
64 Section	94 (165 of 176) [90, 97]	97 (804 of 829) [96, 98]	87 (165 of 190)	99 (804 of 815)	31.333	0.062
Hamon et al (19)†‡						
16 Section§	76 (1632 of 2139) [75, 78]	92 (11229 of 12248) [91, 92]	62 (1632 of 2651)	96 (11229 of 11736)	9.171	0.259
64 Section	87 (966 of 1107) [80, 94]	96 (6326 of 6582) [95, 97]	79 (966 of 1222)	98 (6326 of 6467)	21.750	0.135
Scheffel et al (23): dual source	96 (54 of 56) [88, 100]	98 (355 of 364) [95, 99]	86 (54 of 63)	99 (355 of 357)	48.000	0.041

Note.—Numbers in parentheses are raw data used to calculate percentages, and numbers in brackets are 95% CIs.

* Contained limited data on eight-section CT and a single 64-section study.

† Unweighted summary statistics for the predictive values.

‡ Systematic review.

§ Not all 16-section studies quoted both segment- and patient-based results.

|| Diagnostic study.

64-section and older generations of helical CT scanner were discussed. Temporal resolution was also a focus of the discussion. All multidetector CT studies were performed with ECG pulsing to reduce radiation dose.

Appraising the Diagnostic Radiology Literature: Appraisal of Strength from the Results Section

These are similar to the principles for appraising a systematic review of diag-

nostic studies (as discussed previously in this article). Results were quoted both on a per-segment and a per-patient basis. The segment-based sensitivity was 96.4% (95% CIs: 91.6%, 101.3%), specificity was 97.5% (95% CIs: 95.9%, 99.1%), positive predictive value was 85.7%, and negative predictive value was 99.4%. On a per-patient basis, the sensitivity was 93.3% (95% CIs: 80.7%, 106.0%), specificity rose to 100% (95% CIs: 100%, 100%), positive predictive

value was 100%, and negative predictive value was 93.8%.

Step 4: Apply

Combining Likelihood Ratios and Pretest Probabilities: Graphs of Conditional Probability

Figure 4 shows an example of a chart available from the British Medical Journal Publishing Group allowing estima-

tion of the risk of a cardiovascular event in patients on the basis of patient age, blood pressure, diabetic status, smoking status, and total cholesterol-to-HDL ratio (29). This can be used to provide a range of pretest probabilities for a subsequent “hard cardiac event” (eg, myocardial infarction). If the likelihood ratios (provided in both appraised systematic reviews) for a given test are multiplied by the pretest odds for a given disease, the posttest probabilities for that disease are derived. The entire spectrum of pretest odds may be combined with the positive and negative likelihood ratios for a given test and

subsequently graphed. Such a graph is called a graph of conditional probabilities (GCP). The greater the distance between the two curves on a GCP, the greater the value of the diagnostic test in ruling in or ruling out the disease in question. At the extremes of the GCP, where pretest probability approaches 0% and 100%, the curves are closer together and the usefulness of the test decreases. The graph for 64-section cardiac multidetector CT is plotted in Figure 5 on the basis of the weighted summary statistics by Hamon et al (19).

For the patient in the current clinical scenario, who has an intermediate

pretest probability for a hard cardiac event, the pretest probability is 15%. Applying this as the pretest probability on the x-axis of the GCP for 64-section cardiac multidetector CT, if the finding at cardiac multidetector CT is positive, the posttest probability on the y-axis is greater than 60%, warranting further investigation. If the cardiac multidetector CT finding is negative, the posttest probability on the y-axis is less than 1%, and CAD is effectively ruled out. For patients with a low pretest probability for significant CAD (pretest probability of 9%), if the result of cardiac multidetector CT is positive, the posttest probability on the y-axis is greater than 50%, warranting further investigation. If the cardiac multidetector CT result is negative, the posttest probability on the y-axis is less than 1%, and CAD is effectively ruled out. However, for patients with a high pretest probability (pretest probability of 70%), if the cardiac multidetector CT finding is positive, the posttest probability on the y-axis is greater than 95%. If the cardiac multidetector CT finding is negative, the posttest probability on the y-axis is still greater than 10%. Either result warrants further investigation.

What Are the Overall Results of the Systematic Reviews? Clinical Closure

You present your analysis at the weekly cardiology teaching rounds. You comment that “there was an overall result in favor of improving technical performance with successive generations of scanner technology. Current best evidence coupled with Bayesian analysis shows cardiac multidetector CT to have a high sensitivity and specificity with satisfactorily narrow CIs for the detection of hemodynamically significant coronary stenosis (>50%) in patients with a low or intermediate pretest probability for CAD. We recommend its routine implementation in these patients. Our Bayesian analysis suggests 64-section cardiac multidetector CT does not have satisfactorily high sensitivity or specificity to depict significant coronary stenosis in patients with a high pretest probability for CAD, and alternative imaging modalities such as invasive coronary an-

Figure 4

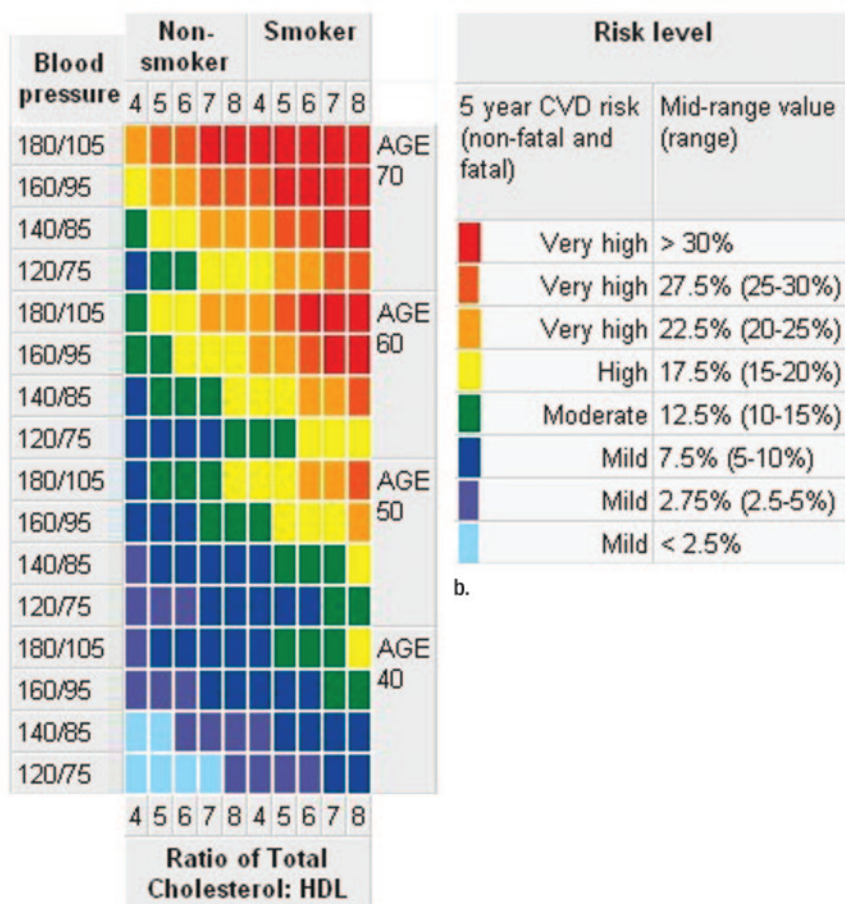


Figure 4: (a, b) Examples of charts from the series published by the British Medical Journal Publishing Group (29), adapted from the New Zealand Guidelines Group (30), that estimate a patient's absolute risk of a cardiovascular event. On the basis of patient sex, age, diabetic status, blood pressure, and cholesterol measurements, a corresponding colored box in **a** is located and checked against the guide in **b**. CVD = cardiovascular disease. (Adapted and reprinted, with permission, from reference 30.)

Figure 5

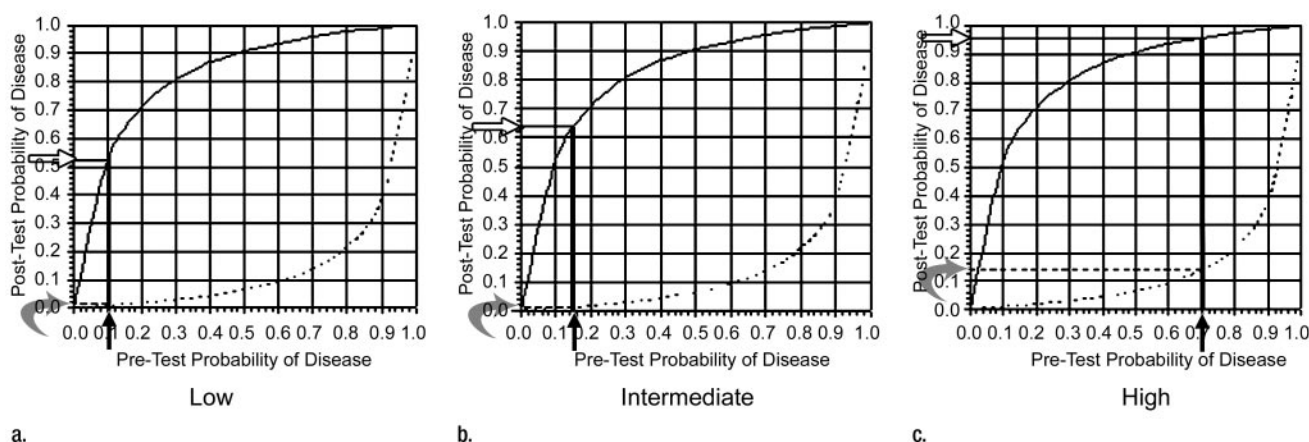


Figure 5: GCPs for diagnosis of coronary artery stenosis with 64-section CT. Bayes theorem has been used to calculate posttest probability of coronary artery stenosis for any given pretest probability, by using the patient-based sensitivity and specificity of cardiac 64-section CT derived from Tables 3 and 4. A positive test result is indicated by the solid curved line; a negative result is indicated by the dotted curved line. The GCPs are applied to patients with (a) low, (b) intermediate, and (c) high pretest probabilities for CAD (black arrow); subsequent posttest probabilities are read off the y-axis (white and curved arrows).

giography should be considered in this subgroup."

You add, "It is also important to note that substantial limitations remain for using cardiac multidetector CT in patients with extensive calcified coronary plaques or with relative or absolute contraindications such as atrial fibrillation, contrast material allergy, or renal failure."

The cardiologists agree that, allowing for these limitations and used in the correct way, cardiac multidetector CT is an excellent noninvasive test for ruling out significant CAD in selected patients. There is a group consensus that a combined multidisciplinary cardiology-radiology approach is likely to produce optimum patient outcome. You agree to participate in future cardiology rounds developing the role of cardiac multidetector CT in the noninvasive imaging strategy in patients suspected of having hemodynamically significant CAD.

Discussion

Cardiac multidetector CT is a rapidly evolving technique that allows the noninvasive depiction of the coronary circulation. A huge amount of literature is being published on the technique—so much so that it is advancing at too rapid a rate for many traditional sources

(textbooks) to have up-to-date information. Such rapidly evolving technologies are ideally suited to the principles of EBP. Such techniques are designed to efficiently ask, search, appraise, apply, and evaluate new or difficult topics. This is encompassed in the EBP paradigm, defined as "the integration of best research evidence with clinical expertise and patient values" (11). The purpose of this evidence-based review was to examine the best currently available literature regarding cardiac multidetector CT and to use this to assess the first two levels of the evaluative hierarchy: to evaluate the technical performance of multidetector CT of the coronary arteries and also to investigate its diagnostic performance by using invasive coronary angiography as the reference standard. In evaluating the technical performance of cardiac multidetector CT, our EBP analysis revealed several important issues.

Tube Current

A major concern regarding coronary multidetector CT is the radiation dose. It is interesting that no 64-section cardiac multidetector CT study used the same tube current (range 680–900 mAs; Table 6). For cardiac multidetector CT acquisitions, only a small portion of the data acquired will be used for

image reconstruction, which translates to a large amount of z-axis overlap during scanning; typically, a pitch of 0.2 is used. Such a low pitch explains why it takes a relatively long time to scan the approximately 12–15 cm of the heart; even with 64-section CT scanners, the examination takes 12–15 seconds, and coronary bypass graft evaluation takes longer. The issue of radiation dose has been addressed by the development of tube current modulation techniques by using prospective ECG gating to decrease the dose during systole, assuming all relevant data will be acquired during diastole. This leads to a dose reduction of up to 44% (31); using a lower kilovoltage in slim patients in combination with tube current modulation can lead to a dose reduction of up to 88% (32).

Contrast Agent Concentration

Considerable variability in contrast agent concentration is evident in the published literature on 64-section cardiac multidetector CT (range, 300–400 mg iodine per liter) (Table 6). Recent studies have demonstrated that the intravenous administration of iomeprol 400 provides higher attenuation of the coronary arteries and of the great arteries of the thorax in comparison with iopromide 370 administered with the same

injection parameters (33). Furthermore, high iodine concentrations of 400 mg iodine per milliliter may allow homogeneous contrast enhancement of the ventricular cavities and coronary arteries equivalent to that obtained by using a contrast medium with standard iodine concentration and can be achieved with lower overall volumes and reduced injection flow rates (34).

Triggering Technique

Two techniques, bolus tracking and use of a test bolus, have both been used successfully in cardiac multidetector CT (35). Both techniques have advantages and disadvantages. Bolus tracking uses a smaller volume of contrast material, since the test bolus (usually 10–20 mL) is obviated. One study has also shown more homogeneous contrast agent opacification by using this technique compared with test bolus strategies (36). Contrast in the proximal coronary arteries may be slightly higher by using bolus tracking. The major disadvantage of this technique is the risk of large soft-tissue contrast agent extravasations, especially at the high rates used for cardiac multidetector CT (5 mL/sec). Test bolus techniques reduce this risk, although it is theoretically possible for extravasa-

tion to occur during full volume injection rather than the test bolus.

β -Blockade

Numerous studies have demonstrated that slower heart rates result in optimal image quality (37). To achieve this in most patients, β -blockers provide safe and effective means of lowering pulse rates (38). What is less clear is whether dedicated oral or intravenous administration, or a combination of both, produces the best results. Centers vary in their preference, although with the advent of dual-source multidetector CT, medication to lower heart rates has become more controversial (25).

ECG Phase

Several studies have evaluated the optimal ECG phase in which to reconstruct images. Best image quality appears to be obtained with a reconstruction window in mid-diastole of between 60% and 65% of the R-R interval (39). At heart rates of less than 65 beats per minute, a single reconstruction at 60% provides optimal imaging of all coronary segments without the need for multiple reconstructions. At heart rates of more than 75 beats per minute, the best image quality is

acquired during systole (ECG phase of 30%–35%) (40).

Applying Pretest Probabilities to Cardiac Patients: Bayesian Analysis

For contemporary studies of cardiac multidetector CT, care must be taken to extrapolate results from dedicated research studies where the prevalence of CAD is high (prevalence of CAD in the retrieved 64-section multidetector CT studies was up to 88%). Bayesian analysis illustrates the influence of disease prevalence on diagnostic performance (Fig 5). The GCP relates the pretest probability of disease (or prevalence) to the posttest probability given a positive or negative imaging result. It is easy to see how the performance of the test is altered by a change in disease prevalence. When the prevalence is high (eg, 70%) a positive result implies a 98.2% probability of disease in the patient; a negative result still implies a more than 15% chance of disease, and therefore CAD cannot be completely ruled out. Thus, cardiac multidetector CT is perhaps best used as a potential replacement for invasive coronary angiography in patients who are at low to intermediate risk of CAD, in whom the pretest probability would be considerably lower

Table 6

Technical Parameters for Cardiac 64-Section Multidetector CT Derived from a Systematic Review

Parameter	Leschka et al	Fine et al	Pugliese et al	Ropers et al	Ehara et al	Raff et al
Collimation (mm)	64 × 0.6	64 × 0.6	64 × 0.6	64 × 0.6	64 × 0.6	64 × 0.6
Table feed (mm per rotation)	9.2	ND	3.8	3.8	11.5	3.8
Tube voltage (kV)	120	120	120	120	120	120
Tube current (mAs)	680	ND	900	750	800	750–850
Contrast agent concentration (mg iodine per milliliter)	320	ND	400	370	300–370	350
Contrast agent volume (mL)	80	ND	100	65	50–92	100
Injection rate (mL/sec)	5	ND	5	5	4	5
Triggering technique	Bolus tracking	ND	Bolus tracking	Test bolus	Bolus tracking	Test bolus
Routine β -blockade	No*	Oral and/or intravenous	Oral	Oral and/or intravenous	No	Oral and/or intravenous
Mean heart rate (beats/min)	66	ND	58	59	72	65
Section thickness (mm)	0.75	0.75	0.75	0.75	ND	ND
Increment (mm)	0.5	0.4	0.4	0.5	ND	ND
ECG-gated phase	Variable†	ND	60%–70%	70%	Variable†	65%

Source.—Reference 19.

Note.—Names in top row are studies evaluated in the systematic review by Hamon et al (19). ND = data not provided.

* Sixty percent of patients were receiving β -blockers as baseline medication.

† Different cardiac phases were used for different segments of the coronary arteries.

than this. In addition to the charts produced by the British Medical Journal Publishing Group (Fig 4), American Heart Association–American College of Cardiology statements have published CAD prevalence data based on age, sex, and type of chest pain (nonanginal chest pain, atypical angina, typical angina) (41).

In the clinical scenario described in this report, a 50-year-old nondiabetic male smoker with a blood pressure of 160/95 and a total cholesterol-to-HDL ratio of 4 has an intermediate (10%–15%) 5-year risk of a new cardiovascular event such as new angina, myocardial infarction, coronary death, and stroke (Fig 4). A nonsmoker of the same age with the same total cholesterol-to-HDL ratio who is normotensive has a low (2.5%–5%) risk. Plotting a low pretest probability of, for example, 10% on the GCP in Figure 4 shows that a negative result effectively rules out CAD (<0.1% posttest probability of disease); a positive result gives a more than 50% posttest probability. At the other end of the pretest probability spectrum, patients with a high or very high risk may not have a hemodynamically significant stenosis ruled out by a negative result; in these categories it may be prudent to consider conventional coronary angiography as an alternative test. It is clear, however, that 64-section CT is an excellent test for ruling out CAD in patients who are at low to intermediate risk. High values for sensitivity and specificity can be very useful to rule in or rule out disease by using the mnemonic devices “snout” (sensitivity–rule out) and “spin” (specificity–rule in). This means that 100% sensitivity corresponds to 100% negative predictive value (ie, rule out) and conversely 100% specificity corresponds to 100% positive predictive value (ie, rule in). For cardiac multidetector CT, the negative predictive value is high across almost all studies in every center and is therefore considered a “snout.”

Two aspects of Bayesian analysis related to the cardiac multidetector CT literature are worth noting. The prevalence of significant CAD in the population being studied in the systematic review is of relevance because it will influ-

ence the test characteristics of the GCP. The 64-section multidetector CT studies included in the retrieved systematic reviews had a variable spectrum of pretest probabilities, ranging from patients with atypical chest pain to non-ST segment myocardial infarction. Therefore, the GCP derived from the pooled systematic review sensitivities and specificities represents a GCP for 64-section cardiac multidetector CT over the range of pretest probabilities. Second, the GCP will change depending on whether a patient- or segment-based analysis is used to derive it. In the example in our study we calculated a GCP based on patient-based figures. We also calculated a GCP based on segment-based figures from the systematic review by Hamon et al (19) for 64-section multidetector CT (data not shown). As expected, sensitivity was higher and specificity was lower. For a positive test result, for a given pretest probability there was no meaningful difference in posttest probabilities between segment-based versus patient-based GCPs; however, for a negative test result, for a given pretest probability there were higher posttest probabilities for the segment-based versus the patient-based GCP. Essentially, for patients with an intermediate to high pretest probability, a GCP derived from segment-based rather than patient-based data results in a higher likelihood of there being a significant coronary lesion, despite a negative test result.

Some limitations of the current study should be noted. First, it is worth commenting that we appraised studies that applied invasive coronary angiography as the reference standard, but estimation of coronary stenosis by means of invasive coronary angiography is not as accurate as is coronary intravascular ultrasonography. This is in part because of limitations in image resolution and edge detection and also because coronary plaques are often eccentric and quantitative invasive angiography techniques ignore this fact, assuming that narrowing is concentric. In addition, angiography can result in foreshortening of lesions, and there are only a limited number of projections with which to in-

terrogate lesions. Second, EBP has been criticized for being too time-consuming. The skills required to practice EBP do take some time to master. Once learnt however, the process can be rapid. “PICO” questions can be formulated quickly. Search strategies can be narrowed to retrieve only the most important articles, thus reducing reading time. The topic of cardiac multidetector CT is a good example. Despite an enormous amount of recently published work on the subject, we appraised only three articles in detail. This is the beauty of EBP—we appraise only the article(s) on the top of the evidence-based pyramid. Calculation of statistics and/or GCPs can be performed in seconds with downloadable spreadsheets placed on office desktops or personal digital assistants. Readers interested in learning more about incorporating EBP into their radiology practice are referred to a recent series of articles in *Radiology* dealing with many aspects of EBP (12,27,42–45); a useful reference Web site can be found at www.evidencebasedradiology.net (46).

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