Can computed tomography improve outcomes in acute coronary syndrome?

Each year, six million patients in the USA visit the emergency department for acute chest pain. Many patients are hospitalized because immediate discharge of those suspected of acute coronary syndrome could be disastrous. This review looks at whether patient outcomes could be improved by coronary computed tomography angiography.

Acute myocardial infarction is the leading cause of adult mortality in America and the west. Each year, between 6 and 10 million patients present to hospital emergency departments with sudden onset of chest pain, suspicious for the diagnosis of acute myocardial infarction or acute coronary syndrome (unstable angina or non-ST elevation myocardial infarction). Most of these patients are admitted to hospital, or remain in the emergency department for observation. Furthermore, most of them ultimately prove not to be suffering from acute ischaemic disease, and are discharged. However, a small but important minority of those individuals sent home do have an acute coronary syndrome, and have an unfavourable outcome after discharge. This article considers the current and future role computed tomography could play in improving the triage of patients presenting with acute chest pain.

Incidence of chest pain in the emergency department

Chest pain accounts for approximately 5.3% of all emergency department visits; only acute trauma is more frequent. However, acute myocardial infarction is ultimately diagnosed in only 10–15% of these individuals. The primary challenge in the emergency department is to differentiate life-threatening disease presenting with chest pain from non-lethal causes of chest pain. A good clinical history, physical examination and basic diagnostic testing (i.e. electrocardiogram and plain chest radiography) provide a wealth of information to help clinicians differentiate among these individuals.

The likelihood that symptoms reflect changes caused by myocardial ischaemia is affected by the nature of the symptoms, and other clinical and laboratory findings at the time of presentation. The likelihood that chest pain is of cardiac, particularly ischaemic, origin is increased if the presenting chest or left arm pain or discomfort reproduces the symptoms of a prior episode of documented angina pectoris. The likelihood of ischaemic aetiology is increased if the patient has a history of coronary heart disease or prior myocardial infarction, if physical signs of congestive heart failure are present at presentation, and if ST segment changes on electrocardiogram and elevated serum cardiac biomarkers are present. Thus, presentation without typical angina-like chest pain (or without chest pain), with no evidence of congestive heart failure, or in the absence of ST segment changes on electrocardiogram significantly lowers the likelihood of underlying myocardial ischaemia. *Table 1* summarizes the most common non-traumatic causes of chest pain (Selker et al, 1997).

Once non-cardiac aetiology is excluded (or judged to be of low enough likelihood to mobilize a cardiac team), emergency department physicians must consider the nature of the presenting cardiac disease. Thus, the next decision is to differentiate between ST elevation myocardial infarction and unstable angina or non ST-elevation myocardial infarction. A decision must be made to differentiate among patients presenting at high risk of developing life-threatening complications, requiring hospitalization and immediate therapy, from those who may need further evaluation, but in a less urgent and costly setting. If patients present with ST segment changes, they are identified as undergoing a ST elevation myocardial infarction, and are at high risk for further cardiac decompensation and mortality; these patients are frequently referred for emergent myocardial revascularization (percutaneous coronary angioplasty or coronary artery bypass grafting). Once ST segment changes are excluded, then the risk of further deterioration or cardiac event should be assessed to guide further intensive pharmacological management.

The diagnostic challenge for physicians

Admission rates vary between 30 and 70% in this population (Graff et al, 1997). A major factor is identifying patients in the acute coronary syndrome of whom only 20% are ultimately diagnosed correctly. The cost of excluding acute coronary syndrome has been estimated as high as $8 billion. Furthermore as many as 8% of discharged emergency department patients are later diagnosed with acute coronary syndrome. Moreover the mortality rate in these patients is 25%, and twice that of those admitted (Fineberg et al, 1984; Lee et al, 1987; Pope et al, 2000).

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Risk stratification and consequences

Once non-cardiac aetiology is excluded, precise cardiac diagnosis is needed. Rapid risk profiling of these patients is imperative. Early institution of medical therapy is indicated because of the significant chance of rapid cardiac decompensation. Thus, objective criteria are needed to direct therapeutic decision making.

To this end Antman et al (2000) reviewed the baseline characteristics of patients in the Thrombosis in Myocardial Infarction (TIMI) 11B and Efficacy and Safety of Subcutaneous Enoxaparin in Unstable Angina and Non-Q-Wave MI (ESSENCE) trials. Seven clinical characteristics were identified as predictor variables for developing at least one component of a primary end-point (all-cause mortality, new or recurrent myocardial infarction, or severe recurrent ischaemia requiring urgent revascularization): age >65 years, at least three risk factors for coronary heart disease (family history of coronary artery disease, hypertension, hypercholesterolaemia, diabetes mellitus, or being a current smoker), prior coronary artery stenosis of ≥50%, ST segment deviation (transient ST elevation or persistent ST depression) on electrocardiogram at presentation, at least two anginal events within the last 24 hours, use of aspirin in the past 7 days, and elevated cardiac markers. A value of 1 was assigned for the presence of a particular characteristic, and 0 if absent, and a risk score was calculated as the sum of risk characteristics. Using this method, the rate of all-cause mortality, myocardial infarction and severe recurrent ischaemia prompting urgent revascularization increased significantly as the risk score increased (*Table 2*).

Table 1. Common potential causes of non-traumatic chest pain

Life-threatening	Acute coronary syndrome
	Pulmonary embolism
	Aortic dissection
	Intramural haematoma
	Penetrating aortic ulcer
	Aortic aneurysm or rupture
	Oesophageal rupture
	Pericardial tamponade
	Tension pneumothorax
Non-life-threatening	Pneumonia or pulmonary parenchymal disease
	Pulmonary, mediastinal or pleural neoplasm
	Musculoskeletal injury or inflammation
	Cholecystitis
	Pancreatitis
	Herpes zoster
	Hiatus hernia, gastro-oesophageal reflux disease or oesophageal spasm
	Pericarditis or myocarditis
	Simple pneumothorax

From Stillman et al (2007)

Table 2. Rate of composite end point* as a function of risk factors

TIMI risk score	Rate of composite end point (%)
0/1	4.7
2	8.3
3	13.2
4	19.9
5	26.2
6/7	40.9

TIMI = Thrombosis in Myocardial Infarction. *i.e. all-cause mortality, myocardial infarction and severe recurrent ischaemia. From Antman et al (2000)

When this method of risk assessment was used in a prospective observational cohort study of 1458 consecutive emergency department chest pain patients (Hoekstra et al, 2002), the calculated TIMI risk score correlated strongly with the incidence of 30-day death, acute myocardial infarction and revascularization. They did not demonstrate discrete strata of risk as defined by TIMI score, but rather a continuum of risk across all groups, tending toward increasing incidence of adverse outcomes at higher risk scores; patients with a TIMI risk score of 0 had a 1.7% incidence of adverse outcomes.

In a similar study (Morris et al, 2006) 1000 consecutive patients presenting to the emergency department were stratified by TIMI risk score, and followed up to hospital discharge or 30 days after enrollment: 980 patients had complete data for analysis. An increasing rate of adverse events was found with increasing TIMI risk score (*Table 3*). As both studies show, this method of risk stratification improves the ability to identify patients at increased risk of an adverse outcome, but does not differentiate individuals at high risk from those at low risk.

Pletcher et al (2004) reviewed four studies reporting measurement of coronary calcium score in asymptomatic individuals and follow up of those patients for coronary events. Relative risk estimates for those with coronary calcium scores >100 Agatston units ranged from 3.0 to 17.0, but varied significantly among studies. However, they found a relative risk of 2.1 (95% confidence interval 1.6–2.9) for a coronary calcium score of 1 to 100 Agatston units, and concluded that coronary calcium score is an independent predictor of coronary heart disease events.

Greenland et al (2004) performed a prospective observational population-based study of 1461 asymptomatic adults with coronary risk factors. Adults >45 years of age with at least one Framingham risk factor underwent computed tomography for coronary calcium score. Participants were contacted yearly for up to 8.5 years. They found an increasing hazard ratio for coronary heart disease death or non-fatal myocardial infarction with increasing coronary calcium score. Compared with the group with a coronary calcium score of 0 Agatston units, a coronary calcium

score >300 Agatston units predicted coronary heart disease. The risk of coronary artery death or non-fatal myocardial infarction for individuals in the highest (>20% estimated 10-year risk) Framingham risk group was 14.3 times than that of individuals with Framingham lowest risk (<10% estimated 10-year risk). A coronary calcium score >300 Agatston units was associated with a significant increase in coronary event risk compared with that determined by Framingham risk factors alone. This supports the hypothesis that a high coronary calcium score can modify predicted risk and alter clinical decision making, especially in individuals of intermediate Framingham risk, for whom decision making is most uncertain.

Choi et al (2008) performed a retrospective analysis of 1000 middle-aged asymptomatic individuals who underwent computed tomography coronary arteriography as part of a general health evaluation. They found atherosclerotic plaque in 22% of individuals; 5% had significant coronary artery stenosis (>50%), and 2% had severe stenosis (>75%). The incidence of atherosclerotic plaque, significant stenosis and moderate to severe coronary calcification increased with patient age. Non-calcified plaques were the only sign of coronary artery disease in 4% of subjects. These individuals were younger than subjects with other types of plaques, and 95% were classified as low and moderate National Cholesterol Education Program risk. In contrast, the proportion of non-calcified plaque in each age quartile was lowest in the oldest group.

These clinical series point out that atherosclerotic coronary heart disease is prevalent in asymptomatic individuals and, furthermore, significant disease may be present in individuals estimated to be of low or intermediate risk for coronary heart events. In other words, conventional risk assessment may underestimate the prevalence and severity of coronary heart disease.

Computed tomography: current and future role

Computed tomography first became available in the mid-1970s, and rapidly revolutionized medicine. However, limited temporal resolution precluded the application of computed tomography to evaluation of cardiac disease. The use of computed tomography angiography for the evaluation of patients with heart disease was limited to demonstration and evaluation of cardiac calcification, namely pericardial or valvular changes.

Early feasibility studies with single slice scanners showed that computed tomography could identify ischaemic myocardium, quantitate infarct size, and measure myocardial perfusion and left ventricular functional indices (Lipton, 2007). Millisecond scanning became possible with the development of electron beam computed tomography, which allowed visualization of coronary and intracardiac anatomy, and reliable, accurate measurement of coronary arterial calcification. This lead to a non-invasive means of estimating coronary artery disease risk – coronary calcium scoring.

Most recently, electrocardiogram-gated multidetector computed tomography (MDCT) scanners have proved useful for diagnosing coronary artery disease. MDCT couples very rapid acquisition with highly sensitive photon detectors, allowing reliable visualization of intracardiac and, more importantly, epicardial structure, in particular the epicardial coronary arteries. A large and growing body of experience (Mollet et al, 2004; Raff et al, 2005; Raff and Goldstein, 2007) has shown that MDCT provides highly accurate coronary arterial visualization. MDCT has a very high negative predictive value, providing a powerful clinical tool for eliminating coronary artery disease as the aetiology in patients referred with chest pain. Nevertheless, selective catheter coronary artery angiography remains the gold standard for definitive diagnosis of coronary heart disease. Furthermore, selective coronary cannulation at angiography is the method of choice for performing acute coronary arterial intervention (angioplasty and stent placement). Although the accuracy of MDCT for the diagnosis or exclusion of coronary heart disease is established, the question remains whether or not MDCT can be successfully used to triage patients with chest pain and safely improve management in a cost-effective manner.

Goldstein et al (2007) compared the safety, diagnostic efficacy and efficiency of MDCT with standard diagnostic evaluation of low-risk patients presenting with chest pain to an emergency department. They randomized 197 patients to either MDCT coronary angiography or a standard 'rule-out myocardial infarction' diagnostic algorithm, using serial electrocardiograms and cardiac enzymes, followed by rest and/or stress imaging examination. Individuals who underwent coronary computed tomography angiography were discharged if they had no coronary stenosis greater than 25% or a coronary calcium score greater than 100 Agatston units. Individuals in whom significant (>70%) stenosis was detected by MDCT were referred for invasive coronary arteriography, and patients with intermediate (26–70%) stenosis, coronary calcium score over 100 Agatston units or non-diagnostic MDCT were referred for nuclear stress testing. Patients rand-

Table 3. Relation between TIMI score and event rate in 980 patients seen in an emergency department with chest pain

TIMI risk score	Event rate (%)
0	0
1	7
2	13
3	24
4	24
5	49
6/7	72

TIMI = Thrombosis in Myocardial Infarction. From Morris et al (2006)

omized to the 'standard' protocol were discharged home if they had serial negative electrocardiograms, negative cardiac biomarkers and a negative nuclear stress test. Patients who developed electrocardiographic abnormalities, positive biomarkers or abnormal stress nuclear imaging were referred for invasive coronary angiography.

The authors found no test complications in any MDCT or standard algorithm patient. Of the 24% of patients undergoing MDCT angiography in whom intermediate coronary disease was found, or in whom a non-diagnostic examination was obtained, nuclear stress testing was negative in 21 of 24 patients (87%), and they were discharged home. Among patients in the standard algorithm group, 94% had normal nuclear scans and were discharged home. Five (5.1%) patients in the standard algorithm group had abnormal stress nuclear scans, and three underwent invasive coronary angiography.

Overall, 88 of 99 patients (89%) in the MDCT group and 97% of the patients in the standard group were directly discharged home from the emergency department. None of these patients suffered a major adverse cardiovascular event over a 6-month follow-up period.

Comparison of MDCT coronary angiography with invasive coronary angiography (*Figures 1–4*) in the 12 patients who underwent both tests showed that eight of nine patients with significant stenosis on MDCT had angiographic correlation (true positives), and one of the nine was a false positive. Of the nine patients undergoing invasive angiography, four went on to percutaneous coronary angioplasty, two were sent to coronary artery bypass surgery, and two were treated medically. Thus, 96 of 99 (97%) of patients who underwent MDCT coronary arteriography had a clinically correct diagnosis.

Figure 1. Axial contrast-enhanced acquisition image obtained in a 54-year-old man presenting to the emergency department with chest tightness. In the emergency department, ST depression was found; serum troponin was negative. The right coronary artery lumen (large arrow) is very narrow. Low attenuation, non-calcified plaque (arrowheads) is seen adjacent to the narrowed lumen.

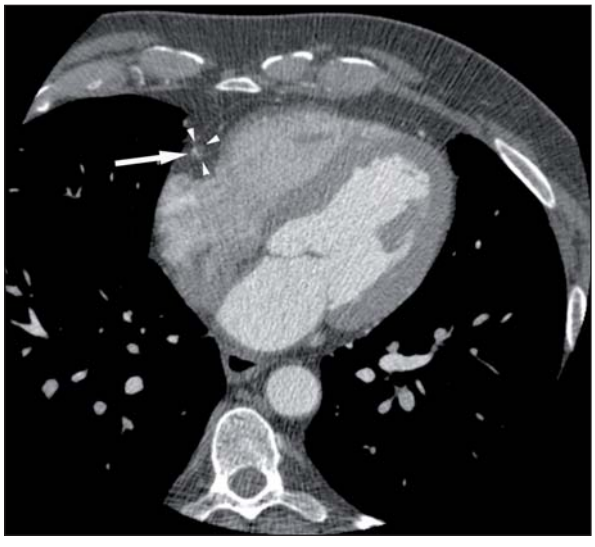


Figure 2. Multiplanar reformatted image reconstructed from axial acquisition imagery displays the severe mid-right coronary artery stenosis (arrow).

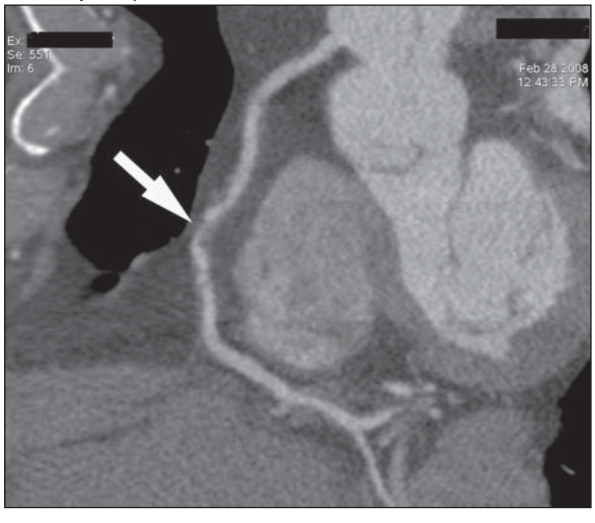


Figure 3. Same patient as shown in* Figure 2. *Frame from a right coronary arteriogram obtained in left anterior oblique projection, confirming the severe mid-right coronary arterial stenosis (arrow) found on computed tomography.

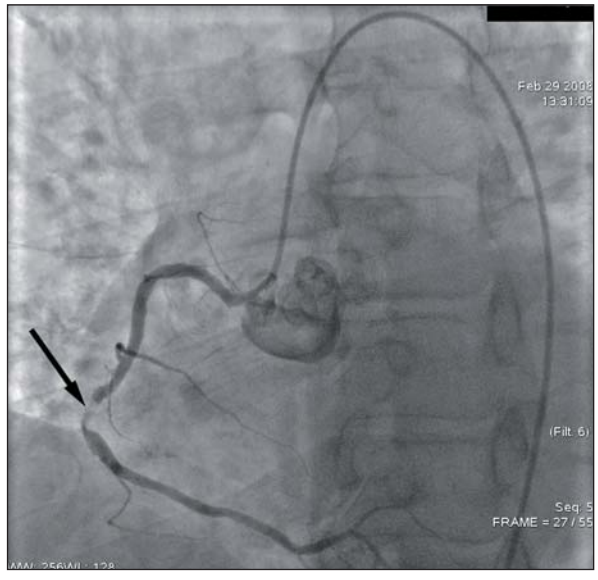
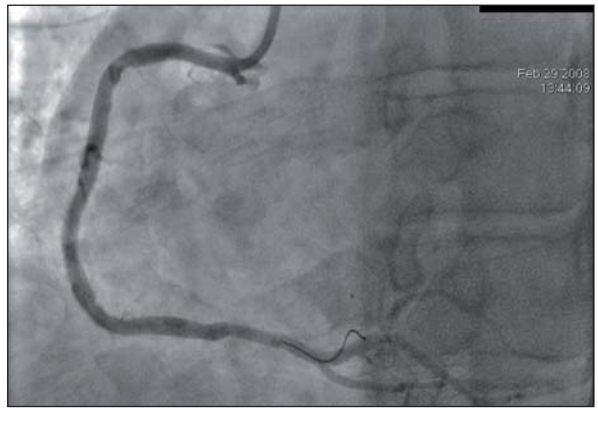


Figure 4. Frame from the repeat right coronary arteriogram obtained after stent placement shows resolution of the focal stenosis.



Seven of 98 (7%) of patients who underwent the standard algorithm went on to invasive coronary angiography. A further four patients went on to invasive angiography during 6 months follow up. In this group, 96 of 98 patients (98%) had a clinically correct diagnosis.

Conclusions

MDCT cardiac angiography is a novel modality for which excitement about its ability to depict the epicardial coronary arteries exceeds the volume of evidence-based data available to evaluate its benefit (Schoenhagen, 2007; Stillman et al, 2007). As the volume of imaging reports grows, and the data become more reliable, patients will be identified for whom MDCT provides important morphological or functional information, as well as clinical scenarios in which MDCT provides important information for clinical decision making. Use of MDCT to evaluate the thoracic great arteries and veins will continue to refine techniques, as well as better defining patient groups who benefit from it. Adequate facilities and specially trained technical and medical staff are needed for MDCT coronary arteriography to be optimally used. If it is to be used in emergency departments, then 24-hour availability of scanner facilities, as well as examination, interpretation with post processing and reporting is needed. Expanding MDCT into this setting necessitates specialized training in cardiac medicine and pharmacological intervention for radiologists, as well as physics, principles of electrocardiogram-gated MDCT, and image manipulation for cardiologists. Radiation dose and the toxicity of intravenous contrast administration must be considered when choosing whether or not to perform the test. Continued non-cardiac as well as cardiac use will drive the development of faster, lower dose imaging protocols.

Magnetic resonance angiography has been used for coronary artery imaging but computed tomography angiography appears more practical (Lipton and Manning, 2007). In properly chosen patients, a negative coronary calcium score associated with a contrast-enhanced MDCT showing no segmental luminal stenosis is associated with an event-free interval. Such a patient may be safely discharged from the emergency department. Weighing the short-term benefit of such a discharge against the long-term cost of radiation exposure and limited long-term outcome data may just show that MDCT is worth performing. **BJHM**

Table 1 *is reproduced from Stillman et al (2007) by kind permission of* European Radiology.

Conflict of interest: Dr L Boxt and Dr M Lipton serve as consultants for Fuji Medical Systems.

Antman EA, Cohen M, Bernick PJLM et al (2000) The TIMI risk score for unstable angina/non-ST elevation MI. *JAMA* **284:** 835–42

Choi E-K, Choi SI, Rivera JJ et al (2008) Coronary computed tomography angiography as a screening tool for the detection of occult coronary artery disease in asymptomatic individuals. *J Am Coll Cardiol* **52:** 357–65

Fineberg HV, Scadden D, Goldman L (1984) Care of patients with a low probability of acute myocardial infarction. Cost effectiveness of alternatives to coronary-care-unit admission. *N Engl J Med* **310**(20): 1301–7

Goldstein JA, Gallagher MJ, O'Neill WW et al (2007) A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. *J Am Coll Cardiol* **49:** 863–71

Graff LG, Dallara J, Ross MA et al (1997) Impact on the care of the emergency department chest pain patient from the chest pain evaluation registry (CHEPER) study. *Am J Cardiol* **80**(5): 563–8

Greenland P, LaBree L, Azen SP et al (2004) Coronary calcium score combined with Framingham score for risk prediction in asymptotic individuals. *JAMA* **291:** 210–15

Hoekstra JW, Pollack CV Jr, Roe MT et al (2002) Improving the care of patients with non-ST-elevation acute coronary syndromes in the emergency department: the CRUSADE initiative. *Acad Emerg Med* **9:** 1146–55

Lee TH, Rouan GW, Weisberg MC et al (1987) Clinical characteristics and natural history of patients with acute myocardial infarction sent home from the emergency room. *Am J Cardiol* **60**(4): 219–24

Lipton MJ, Manning WJ (2007) Relative merits of coronary CTA and coronary MRI. In: Di Carli MF, Lipton MJ, eds. *Cardiac PET and PET/CT Imaging*. Springer, London: 204–14

Lipton MJ (2007) Myocardial perfusion, viability, and functional assessment with contrast CT. In: Di Carli MF, Lipton MJ, eds. *Cardiac PET and PET/CT Imaging.* Springer, London: 270–82

Mollet NR, Cademartiri F, Nieman K et al (2004) Multislice spiral computed tomography coronary angiography in patients with stable angina pectoris. *J Am Coll Cardiol* **43:** 2265–70

Morris AC, Caesar D, Gray S, Gray A (2006) TIMI risk score accurately risk stratifies patients with undifferentiated chest pain presenting to an emergency department. *Heart* **92:** 1333–4

Pletcher MJ, Tice JA, Pignone M, Browner WS (2004) Using the coronary artery calcium score to predict coronary heart disease events. *Arch Int Med* **164:** 1285–92

Pope JH, Aufderheide TP, Ruthazer R et al (2000) Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med* **342**(16): 1163–70

Raff GL, Gallagher MJ, O'Neill WW (2005) Diagnostic accuracy of noninvasive coronary arteriography using 64-slice spiral computed tomography. *J Am Coll Cardiol* **46:** 552–7

Raff GL, Goldstein JA (2007) Coronary angiography by computed tomography. *J Am Coll Cardiol* **49:** 1830–3

Schoenhagen P (2007) The role of coronary CT angiography (CTA) for patients presenting with acute chest pain. Defining problem-specific evidence-based indications of a novel imaging modality. *Int J Cardiovasc Imaging* **23:** 429–32

Selker HP, Zalenski RJ, Antman EM et al (1997) An evaluation of technologies for identifying acute cardiac ischemia in the emergency department: a report from a National Heart Attack Alert Program Working Group. *Ann Emerg Med* **29:** 13–87

Stillman AE, Oudkerk M, Ackerman M et al (2007) WhiteUse of multidetector computed tomography for the assessment of acute chest pain: a consensus statement of the North American Society of Cardiac Imaging and the European Society of Cardiac Radiology. *Eur Radiol* **17:** 2196–207

KEY POINTS

- Acute chest pain is a frequent presenting symptom in the emergency department.
- There is a wide aetiological spectrum.
- Acute coronary syndrome may be difficult to diagnose because of delayed enzyme elevation and normal electrocardiogram.
- Hospital admission may be essential for observation and further investigations.
- The cost of this in terms of lost work days and medical expense is billions.
- Computed tomography angiography may be helpful in enabling rapid triage and cost saving.
- Experience with electrocardiogram-gated multidetector computed tomography, using state of the art scanners and trained personnel, is mandatory if the programme is to be successful.