WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

Worksheet author(s)
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Revision October 15, 2009
Final revision January 17, 2010

Clinical question.
In patients with suspected ACS (P), does the use of specific imaging techniques (e.g. CT/MRI/Nuclear testing/ECHO) (I) compared with not using them (C), improve outcome (survival, length of ED stay, hospital admission rate, cost?) (O).

Is this question addressing an intervention/therapy, prognosis or diagnosis? Therapeutic Intervention
State if this is a proposed new topic or revision of existing worksheet: New topic – no prior worksheet on this topic

Conflict of interest specific to this question
Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No

Search strategy (including electronic databases searched).

Database: Ovid MEDLINE(R) <1950 to September Week 3 2008>

Search Strategy:

Key Words: Acute coronary syndrome; chest pain; tomography; x-ray computed; magnetic resonance imaging; magnetic resonance angiography; radionucleotide imaging; cardiac nuclear scanning; MIBI; SPECT; emission-computed; single photon; myocardial perfusion scintography; echocardiography; comparative study; prognosis; infarct size; mortality; survival rate; length of stay; cost.

1 acute coronary syndrome.mp, or Acute Coronary Syndrome/ (4273)
2 chest pain.mp, or exp Chest Pain/ (51361)
3 1 or 2 (54011)
4 exp Tomography, X-Ray Computed/ (214077)
5 ct angiogram.mp. (120)
6 Magnetic Resonance Imaging/ or mri.mp. (208252)
7 Magnetic Resonance Angiography/ or mra.mp. (12255)
8 radionucleotide imaging.mp. (3)
9 cardiac nuclear scanning.mp. (0)
10 mibi.mp. (1880)
11 spect.mp, or Tomography, Emission-Computed, Single-Photon/ (22843)
12 nuclear cardiology.mp. (637)
13 myocardial perfusion scintography.mp. (0)
14 exp Coronary Angiography/ (34512)
15 6 or 11 or 7 or 9 or 12 or 14 or 8 or 4 or 13 or 10 or 5 (434294)
16 3 and 15 (8701)
17 Early Diagnosis/ or exp Diagnosis/ or Diagnosis, Differential/ (4671604)
18 16 and 17 (8627)
19 Comparative Study/ (1433552)
20 18 and 19 (1522)
21 exp Prognosis/ (651693)
22 Treatment Outcome/ (354082)
23 exp Treatment Failure/ (17678)
24 exp Mortality/ (203952)
25 exp Survival Rate/ (87804)
26 25 or 22 or 21 or 24 or 23 (804200)
27 18 and 26 and 19 (459)
28 from 27 keep 1-459 (459)

Database: updated search up to October Week 2 2009

Additional Key Word search: Myocardial infarction; chest pain; emergency department; ultrasound; hospital admission

PUBMED:
- "myocardial infarction" OR "chest pain" OR "acute coronary syndrome" limits: humans = 142379
- "emergency department" limit: humans = 24549
- ("computed tomography" OR "CT") OR ("echocardiography" OR "echo" OR "ultrasound") OR ("magnetic resonance imaging" OR "MRI") OR ("MPI" OR "nuclear scanning" OR "perfusion imaging") limit: humans = 520052
- "size" or "LV function" OR "left ventricular function" OR "survival" OR "length of stay" OR "hospital admission" OR "cost" limit: humans = 800361
- ("myocardial infarction" OR "chest pain" OR "acute coronary syndrome") AND "emergency department" AND ( "CT" OR "computed tomography" OR "magnetic resonance imaging" OR "MRI" OR "echocardiography" OR "echo" OR "ultrasound" OR "perfusion imaging" OR "MPI" OR "nuclear scanning") AND ("size" OR "LV function" OR "left ventricular function" OR "survival" OR "length of stay" OR "hospital admission" OR "cost") limits: humans = 90 (28 Review articles)

Cochrane Database:
- "Emergency department" = 2570
- "acute coronary syndrome" OR "myocardial infarction" OR "chest pain" = 13258
- ("echocardiography" OR "echo" OR "ultrasound") OR ("magnetic resonance imaging" OR "MRI") OR ("perfusion imaging" OR "MPI" OR "nuclear scanning") OR ("computed tomography" OR "CT") = 34492
- "infarct size" or "LV function" OR "left ventricular function" OR "survival" OR "length of emergency department stay" OR "length of ED stay" OR "hospital admission" OR "cost" = 77913
- "Emergency department" AND ("acute coronary syndrome" OR "myocardial infarction" OR "chest pain") AND ("echocardiography" OR "echo" OR "ultrasound") OR ("magnetic resonance imaging" OR "MRI") OR ("perfusion imaging" OR "MPI" OR "nuclear scanning") OR ("computed tomography" OR "CT") AND ("infarct size" or "LV function" OR "left ventricular function" OR "survival" OR "length of emergency department stay" OR "length of ED stay" OR "hospital admission" OR "cost") = 22

EMBASE:
- Emergency department (limit: humans) = 18529
- acute coronary syndrome OR myocardial infarction OR chest pain (limit: humans) = 84232
- (echocardiography OR echo OR ultrasound) OR (computed tomography OR CT) OR (magnetic resonance imaging OR MRI) OR (perfusion imaging OR nuclear scanning OR MPI) (limit: humans) = 494453
- "infarct size" or LV function OR left ventricular function OR survival OR length of stay OR hospital admission OR cost (limit: humans) = 539179
- emergency department AND (acute coronary syndrome OR myocardial infarction OR chest pain) AND (echocardiography OR echo OR ultrasound) OR (computed tomography OR CT) OR (magnetic resonance imaging OR MRI) OR (perfusion imaging OR nuclear scanning OR MPI) AND (infarct size or LV function OR left ventricular function OR survival OR length of emergency department stay OR length of ED stay OR hospital admission OR cost) (limit: humans) = 115

**State inclusion and exclusion criteria**

**Inclusion criteria:**
- Studies which enrolled low-intermediate risk ED patients with symptoms suggestive of ACS (chest pain), non-diagnostic ECGs and negative biomarkers
- Outcome studies addressing size of infarct; LV function; survival, length of ED stay; hospital admission rate; and cost
- Peer reviewed
- Manuscript available for review
- Human studies
- Criteria for positive result of MDCT were explicitly defined as >50% diameter stenosis

**Exclusion criteria:**
- Abstract-only studies
- Narrative review articles and case reports
- Studies that assessed imaging in stable CAD, not ACS
- Studies that utilized computer based models and not patient populations with ACS
- Studies that did not address outcome specifically
- Unknown status of biomarkers or positive markers at the time of imaging modality
- Imaging that occurred >24 hours after the onset of the acute event
- For CT studies, older generation scanners excluded (16-slice scanners) i.e. used articles that assessed 64-slice multi-detector scanners only

**Number of articles/sources meeting criteria for further review:**
- 276 articles were reviewed (abstract) and 117 (complete manuscript)
- 237 reference citations were additionally manually reviewed
- 10 articles met inclusion criteria and were included after the completed final review
- Medline: 5; Cochrane Database 0; EMBASE 1; and 4 additional articles from a comprehensive search of the references of included articles
- Level of evidence (LOE): LOE P1 = 2; LOE P2 = 0; LOE P3 = 0 LOE P4 = 8; LOE P5 = 0
## Summary of evidence

### Evidence Supporting Clinical Question

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<td>Nucifora (2007) E&lt;sup&gt;13&lt;/sup&gt;</td>
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### Types of studies:
- E<sup>1</sup> - Nuclear
- E<sup>2</sup> - CT
- E<sup>3</sup> - ECHO
- E<sup>4</sup> - MRI
- E<sup>i</sup> - Animal study

### Level of evidence:
- A = Return of spontaneous circulation
- B = Survival of event
- C = Survival to hospital discharge
- D = Intact neurological survival
- E = Other endpoint
- Italics = Animal studies

### Evidence Neutral to Clinical question

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### Level of evidence:
- A = Return of spontaneous circulation
- B = Survival of event
- C = Survival to hospital discharge
- D = Intact neurological survival
- E = Other endpoint
- Italics = Animal studies
Evidence Opposing Clinical Question

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Level of evidence

A = Return of spontaneous circulation  C = Survival to hospital discharge  E = Other endpoint
B = Survival of event  D = Intact neurological survival  Italics = Animal studies

REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

Of all of the patients who present to emergency department (ED) for evaluation of chest pain, estimates are that between 55-85% do not have a cardiac cause for their symptoms. Even though most low-risk patients are not ultimately diagnosed with an acute coronary syndrome (ACS), the majority are admitted for ‘rule out myocardial infarction’ protocols and it is estimated that approximately 6% of patients discharged with an initial negative troponin may have a final diagnosis of ACS. However, unnecessary hospital admissions lead to increasing healthcare costs, inpatient bed shortages, ED crowding, and prolonged ED stays, all of which result in poor resource utilization.

The 2007 ACC/AHA UA/NSTEMI guidelines note that the use of stress testing should be considered in low risk patients prior to discharge from an ED or a chest pain unit. It also notes that the use of MRI and MSCT coronary angiography ‘hold promise as alternative or supplementary imaging modalities for the assessment of patients presenting with chest pain syndromes with low to intermediate pretest probability of CAD in the setting of non-diagnostic ECG and negative cardiac biomarkers. However, although imaging tests are recommended for the intermediate risk patients, there are no guidelines for the use of these modalities and no assessment of whether their usage affect outcome of ACS with respect to survival, length of ED stay, hospital admission rate or costs.

Myocardial perfusion scintography (MPS) has a high negative predictive value (NPV) for ruling out acute coronary syndrome (ACS) – 99% - in patients presenting to the emergency department (ED) with acute chest pain; non-diagnostic ECG and negative cardiac enzymes. ^23^ MPS can be used as a means of triaging patients with suspected acute coronary syndrome (ACS). The patient populations best suited for an ED triage strategy with MPS are those in whom the initial history and ECG do not suggest a high or very low probability of ACS. In this patient cohort, further evaluation is necessary before a confident triage decision can be made. Patients with normal MPS do not need to be hospitalized; where as patients with positive (abnormal) MPS have a high probability of ACS and justify hospital admission for early institution of treatment.

Current European Society of Cardiology (ESC) guidelines recommend pre-discharge stress testing to provide addition prognostic information of the intermediate risk ACS patient. There have been 2 prospective randomized studies that evaluated the impact of acute
This study was a randomized controlled trial of high quality. These two LOE 4 studies (Fesmire, 2001, 207; Forberg, 2009, 9) examined the costs, length of stay, along with short (30d) and long term (6 month) cardiovascular events in a similar group of low-risk chest pain patients. Fesmire et al. describe a very large cohort of 1775 patients and demonstrates a low 30d cardiovascular event rate, while Forberg et al. describe reduced costs and lengths of stay for 40 patients.

Five studies examined the role of stress echo (traditional treadmill or pharmacologic stress) for the outcome variables above (LOE1, Nucifora, 2007, 1068; LOE 4, Bholasingh, 2003, 596; Buchsbaum, 2001, 196; Colon III, 1998, 1282; Colon III, 1999, 171). In particular, Nucifora randomized 199 patients to receive dobutamine-atropine stress echo vs. electrocardiographic exercise testing and demonstrated reduced LOS and costs within this cohort of low-risk chest pain patients. They were also able to demonstrate that stress echo was both safe and reduced costs of care. The mean lengths of stay in the hospital were 23 +/- 12 hours and 31 +/- 23 hours between the two groups favoring stress echo. No 2-month events occurred in the stress echo groups. The stress echo strategy revealed lower costs compared with exercise ECG. At 2-month follow-up, $1029 +/- 253 vs. $1684 +/- 2149, p=0.005. This study was a randomized controlled trial of high quality.

Multi-slice computed tomographic angiography (MSCT) provides high-resolution coronary angiograms and is non-invasive. Its established high negative predictive value for exclusion of significant coronary artery stenosis makes it potentially attractive for evaluation of a low-risk chest pain population. Three studies involving MDCT were identified with our search strategy (LOE 1, Goldstein, 2007, 863; LOE 4, Hollander, 2007, 112, and May, 2009, 150).

Goldstein studied ED patients with acute chest pain to compare the diagnostic safety, efficacy, and efficiency of MSCT angiography vs. nuclear stress testing protocol. This was a high quality randomized controlled trial in which 99 patients received MSCT and 98 received standard-of-care. Patients were randomized to one of the two protocols. Outcomes included safety (freedom from major adverse events over 6 months); diagnostic efficacy (clinically correct and definitive diagnosis), as well as time and cost of care. MSCT immediately excluded or identified coronary disease as the source of chest pain in 75% of patients. The remaining 25% required stress testing owing to intermediate severity lesions or non-diagnostic scans. MSCT evaluation reduced diagnostic time compared with standard of care (3.4 hours vs. 15 hours, p<0.001). And lowered costs ($1586 vs. $1872, p<0.001). Importantly, MSCT patients required fewer repeat evaluations for recurrent chest pain.

Despite this study being the largest of the three, there were still only 197 patients enrolled. Also, the MSCT was inadequate in 24/99 patients (24.1%) because scans were of non-diagnostic quality or lesions where identified that were of questionable hemodynamic significance, leading to diagnostic uncertainty and increased rates of conventional angiography. While MSCT can establish or exclude ACS as the cause of chest pain, its inability to determine the physiological significance of intermediate severity coronary lesions and cases with inadequate image quality are present limitations.

Other disadvantages of MSCT include exposure to radiation and iodinated contrast. Although nuclear testing also provides radiation exposure, it does not require iodinated contrast. Inadequate diagnostic quality scans occurred due to motion, coronary calcification or obesity. These patient groups required a second radiation exposure from nuclear testing. It should also be noted that a small group of patients in this study with either non-diagnostic scans or intermediate grade lesions, required invasive angiography as well, resulting in a third radiation exposure. The estimates of the average radiation dose of 64-slice computed coronary angiography is 13-15 mSv in men and 18-21 mSv in women. The radiation dose of one plain chest radiograph in comparison is 0.04 mSv. The estimated radiation dosage from a Sestamibi or Tetrofosmin nuclear cardiac imaging study is 10-12 mSv.

To date there are no studies that have assessed the use of MRI/MRA in the ED chest pain population to determine if there is any outcome benefit with respect to survival, ED or hospital length of stay or costs. This is likely due to MRI being a relatively new technology to aid clinicians in the diagnosis of ACS and that this is a future area of research. Kwong (2003) and Cury (2008) have demonstrated excellent sensitivity and specificity for MRI for the detection of ACS (please see diagnosis section).

Our defined outcome variables of interest include LV function, size of infarct, survival, length of stay, hospital admission, and costs. Unfortunately there were no studies identified for any of the imaging modalities that discuss LV function and size of infarct. This is likely because the ED population of importance -low risk patients who present with chest pain and have normal cardiac enzymes and a non-diagnostic ECG – likely will not have evidence of acute LV dysfunction or sizable infarcted tissue on imaging. Perhaps this is why no authors chose to include such outcomes.

Care must be taken to extrapolate the results of the studies above to individual patient populations. These studies are usually performed in centers where radiologists are highly skilled at interpreting these specialized images and rates of non-diagnostic studies may increase when applied to other centers. Costs and lengths of stay as well are dependent on institutional factors and these studies may not be generalizable to all centers.
Citation List


   LOE 4, good quality, supportive study, no industry funding.


   LOE 4, poor quality, supportive study, no industry funding.


   LOE P4, poor quality, supportive. Single group of patients exposed to the intervention; outcomes are expressed after the intervention so comparisons cannot be made. 108 patients presenting to ED with atypical chest pain received stress echo. Outcomes included 1-year cardiac event rate; stress echo was found to be 100% with a negative results.


   LOE 4.; poor quality. Supportive.


   LOE 4, fair quality, supportive study, funding from Laerdal Foundation of Acute Medicine and the Swedish Heart and Lung Foundation.


LOE 1, good study. Supportive.


LOE 4, poor study (no controls), Supportive.


LOE 4, fair quality, supportive study, no industry funding.


LOE 1. Good quality., Supportive.