Clinical question.

In patients with suspected ACS in various settings (e.g. prehospital, emergency or in-hospital) and normal oxygen saturations (P), does the use of supplemental oxygen (I), compared with room air (C), improve outcomes (e.g. chest pain resolution, infarct size, ECG resolution, survival to discharge, 30/60 d mortality) (O)?

Is this question addressing an intervention/therapy, prognosis or diagnosis? Intervention/therapy

State if this is a proposed new topic or revision of existing worksheet: Revision

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).

The following databases were searched:

MEDLINE via PUBMED (1950 to May 2009)
1. myocardial infarction
2. acute coronary syndromes
3. unstable angina
4. chest pain
5. oxygen therapy

1 and 5: 22 relevant hits out of 2180 total hits
2 and 5: 1 additional relevant hit
3 and 5: no additional relevant hits
4 and 5: no additional relevant hits

OVID/EMBASE
1 and 5: 133 hits, 2 additional relevant hits
2 and 5: 25 hits, no additional relevant hits
3 and 5: 37 hits, no additional relevant hits
4 and 5: 78 hits, no additional relevant hits

COCHRANE LIBRARY
1 relevant hit

AHA ENDNOTE
No additional hits

CLINICAL TRIALS.GOV
No additional hits

UpToDate ONLINE VERSION 17.1
No additional hits

GOOGLE SCHOLAR
No additional hits

In addition all references of identified articles and in particular the references of the following relevant review articles were checked: (Nicholson 2004), (Beasley, Aldington et al. 2007) and (Wijesinghe, Perrin et al. 2009)

• State inclusion and exclusion criteria

Inclusion criteria:
Use of oxygen therapy in patients with ST elevation myocardial infarction or acute coronary syndromes

Exclusion criteria:
Intracoronary oxygen, Hyperbaric oxygen. Abstracts only. Editorials.
Number of articles/sources meeting criteria for further review: 13

Two randomized trials were identified: (Rawles and Kenmure 1976) and (Wilson and Channer 1997)

Five relevant human (mechanistic) studies were identified: (Thomas, Malmcrona et al. 1965), (Kenmure, Murdoch et al. 1968), (Foster, Casten et al. 1969), (Horvat, Yoshida et al. 1972) and (Madias, Madias et al. 1976).

Six relevant animal studies were identified: (Maroko, Radvany et al. 1975), (Malm, Arborelius et al. 1977), (Ribeiro, Louie et al. 1979) (Weisse, Moore et al. 1982), (Ishikawa, Kanamasa et al. 1986) and (Kelly, Hursey et al. 1995)
# Summary of evidence

## Evidence Supporting Clinical Question

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<th>Good</th>
<th>Fair</th>
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<th>Level of evidence</th>
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<td>A = Return of spontaneous circulation</td>
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<td>B = Survival of event</td>
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<td>C = Survival to hospital discharge</td>
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<td>Italics = Animal studies</td>
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### Evidence Neutral to Clinical question

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<tr>
<td>Fair</td>
<td>Nicholson 2004 systematic review Rawles 1976; E=incidence of arrhythmias</td>
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<td>Weisse 1982; E=infarct size</td>
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<td>Poor</td>
<td>Wilson 1997; E=arrhythmia; ST changes</td>
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A = Return of spontaneous circulation  C = Survival to hospital discharge  E = Other endpoint  
B = Survival of event  D = Intact neurological survival  Italics = Animal studies

### Evidence Opposing Clinical Question

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<td>Fair</td>
<td>Rawles 1976; C E=infarct size Wijesinghe 2009; C</td>
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<td>Kenmure 1968; E=cardiac output Foster 1969; E=cardiac output</td>
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<td>Poor</td>
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<td>Thomas 1965; E=cardiac output Malm 1977; E=infarct size</td>
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A = Return of spontaneous circulation  C = Survival to hospital discharge  E = Other endpoint  
B = Survival of event  D = Intact neurological survival  Italics = Animal studies
Oxygen has been used in the treatment of myocardial infarction and acute coronary syndromes for many years. Evidence in support of this approach is primarily derived from animal models, in which the administration of oxygen during and/or after experimental coronary artery occlusion reduces the extent of myocardial necrosis in some (Maroko 1975, Ribeiro 1979, Kelly 1995, Ishikawa 1986), but not all studies (Malm 1977, Weisse 1982). Few human studies conducted in small number of patients suffering a myocardial infarction reported diminished cardiac output during oxygen therapy (Thomas 1965, Kenmure 1968, Foster 1969). One human case study found improvement in ST changes with the use of oxygen (Madias 1976). Rawles and Kenmure conducted a blinded randomized controlled trial in 157 patients suffering myocardial infarction (oxygen versus room air inhalation). Aspartate aminotransferase levels, as surrogate for infarct size, were higher in the oxygen group (P<0.05). There were 11.3% deaths in the oxygen group and 4% in the air group, relative risk of death 2.9 (95% CI 0.8-10.3, P=0.08). Ventricular tachycardia occurred in 13.8% of the oxygen group and 6.5 % of the air groups, relative risk 2.1 (0.8-5.8, P=0.13). The authors concluded that there was suggestive evidence of a deleterious effect of oxygen. This study lacked statistical power to detect clinically important outcomes. Wilson and Channer conducted a parallel-group, non-blinded controlled study of oxygen therapy. Fifty patients with myocardial infarction treated with streptokinase were randomized to oxygen or room air for 24h. The study was not designed to compare outcomes measured by infarct size or mortality. Ventricular tachycardia occurred in 23% of the oxygen group and 25% of the air group (P=NS). Also there was no significant difference in opiate use. Severe hypoxemia occurred in 8 patients (1 in the oxygen group versus 7 in the air group, P<0.05)

There is insufficient evidence to support the use of oxygen in the treatment of uncomplicated myocardial infarction (Nicholson 2004, Wijesinghe 2009). The routine use of oxygen in this situation may increase infarct size and possibly increase the risk of mortality. There is a need for randomized controlled trials of the use of oxygen therapy in uncomplicated myocardial infarction that are sufficiently powered and performed in the current reperfusion era.

Acknowledgements:

Citation List

Level 1, neutral, funding: none sought or received
Key points: historical overview including the randomized trial from Rawles and Kenmure. The authors stress the need for randomized controlled trials.

Level 5, opposing, funding: NIH USA grant
Key point: small study 14 pts acute myocardial infarction and 4 volunteers receiving 4 combinations of oxygen. Effects on hemodynamics studied.

Level 5, supporting. funding: NIH USA grant
Key points: small study, 11 patients with CAD, right atrial pacing to determine angina threshold, when oxygen was given (patients were unaware) the threshold was higher

Level 5, supporting, funding: not clear
Key points: animal experiment 22 dogs, LAD occlusion, oxygen 40% improved coronary saturation and shifted myocardial lactate production to utilization, also ST segment elevation on epicardial ECG improved.


Level 5, supporting, funding: academic Rush Medical College
Key points: dogs underwent 90 minutes coronary occlusion, one group received room air, the other group oxygen. Infarct size (histochemical staining technique) was lower and EF better in the oxygen group.


Level 5, opposing, funding: British Heart Foundation
Key points: myocardial infarction patients were treated with oxygen, CO and SV diminished, vascular resistance and BP increased.


Level 4, supporting, funding: USPHS and AHA grants
Key points: 17 patients with acute anterior myocardial infarction admitted to the CCU. Measurement of blood gasses and ST segment monitoring during ambient air and 66 minutes oxygen. Sum of ST elevation and number of sites showing elevation was lower with oxygen. PaO2 was higher. Clinical status remained unchanged.


Level 5, opposing, funding: swedish medical research council
Key points: 23 dogs, LAD ligation induced medium sized infarction, infarct size measurement with thermography, ventilation with 100% oxygen during 15 minutes. Control series of 4 dogs. the infarcted area under the influence of oxygen did not diminish in size in any cases.


Level 5, supporting, funding: NIH-NHLI and John A Hartford Foundation Grant
Key points: protocol A: LAD ligation in 36 dogs, in 15 dogs 2 x 20' 20% oxygen, in 15 dogs 20' 20% oxygen and 20' 40% oxygen, in 6 dogs 40% and 100% oxygen. Effects on ST segments. Protocol B 15 control dogs and in 9 dogs 40% oxygen. Effects on CPK and histological infarct size. 40% oxygen reduced ECG evidence of acute myocardial injury and extent of myocardial necrosis.


Level 1, neutral, funding: not clear


Level 1, neutral (mortality, arrhythmias) and opposing (infarct size:AST levels), funding: not clear.
Key points: double-blind controlled oxygen versus air during first 24h of uncomplicated myocardial infarction. AST higher in oxygen group (P<0.05). 9 deaths in oxygen, 3 in air group (P=NS). More sinus tachycardia in oxygen group (P<0.05).


Key points: 23 dogs, acute occlusion LAD. 15 dogs 100% oxygen; 8 dogs room air. Determination of regional myocardial blood flow. In treated dogs, flow at remote sites from occlusion decreased and increased in the ischemic sites.


Key points: 6 patients studied at day 1 and 2 of myocardial infarction, hemodynamics. Air or oxygen breathing. With oxygen HR lower, CO lower, SV lower, SBP higher, peripheral resistance higher


Key points: 31 dogs, four groups based on differences in ventilation and blood gases, ligation of LAD. Tissue data demonstrated no beneficial effects of oxygen administration.


Key points: included only randomized controlled trials (Rawles and Kenmure and Wilson and Channer) insufficient evidence for routine use of oxygen, potentially harmful.


Key points: Two parts. 1) survey of use of oxygen and pulse oximetry in English CCU's. Hypoxemia is frequent in patients not given oxygen. 2) prospective study in 50 myocardial infarction patients randomizing to oxygen or air. Measurement of oxygen saturation and ST segment changes. Severe hypoxemia in 8 patients (7 in the no-oxygen group). No significant differences between groups in the incidence of arrhythmias or ST segment changes or the type of arrhythmia in each group.