Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary

Oxygen therapy in acute stroke

Report by Katherine Potier de la Morandiere,
Specialist Registrar
Checked by Darren Walter, Consultant

Abstract
A short cut review was carried out to establish whether supplemental oxygen reduces long term disability and mortality in patients attending the emergency department with stroke who do not require resuscitation. Altogether 18 papers were found using the reported search, of which one presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of this best paper are tabulated. A clinical bottom line is stated.

Clinical scenario
A 73 year old woman presents to the emergency department with a six hour history of left sided hemiparesis. She has a past history of hypertension. On examination she is GCS 15 with a dense left hemiparesis and her basic observations are stable. You wonder whether the use of supplemental oxygen in the acute stage is needed and will have any effect on long term prognosis.

Three part question
In a [patient presenting to the emergency department with a stroke who does not need resuscitative measures] is [supplemental oxygen better than no oxygen] at [reducing long term disability and mortality]?

Search strategy

Search outcome
Altogether 18 papers were found of which one directly addressed the three part question (table 1).

Comment(s)
This large, well conducted study shows no statistically significant difference between the two groups. It shows there is no benefit to giving oxygen routinely to stroke patients, and suggests if given to non-hypoxic patients with mild to moderate strokes may increase mortality. The results for severe stroke patients were inconclusive. The authors hypothesise (based on a small number of animal studies) that this may be attributable to oxygen free radicals.

Clinical bottom line
In non-hypoxic patients with minor or moderate strokes supplemental oxygen is of no clinical benefit.


CT pulmonary angiogram compared with ventilation-perfusion scan for the diagnosis of pulmonary embolism in patients with cardiorespiratory disease
A short cut review was carried out to establish whether V-Q scintigraphy has better utility than CT in investigating possible pulmonary embolus in patients with chronic respiratory disease. A total of 239 papers were found using the reported search, of which one presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of this best paper are tabulated. A clinical bottom line is stated.

Clinical scenario
A 70 year old known COPD patient presents to your emergency department with pleuritic chest pain and dyspnoea suggestive of pulmonary embolus. As part of your diagnostic strategy, you wonder if V-Q scintigraphy has better diagnostic utility than CT for pulmonary embolus.

Three part question
In [patients with chronic respiratory disease] does [V-Q scintigraphy have greater diagnostic utility than computed tomography] in the [investigation of pulmonary embolus]?

Search strategy
Medline 1966-07/03 using the OVID interface. (exp Tomography, Spiral Computed OR exp Tomography, X-Ray Computed OR “CT” OR exp Tomography AND (exp Ventilation-Perfusion OR “VQ” OR “V-Q”) OR ventilation angiogram OR “VQ” angiograms OR VQ scans OR “VQ” scan OR VQ scans OR VQ scans OR V/Q scans OR “V-Q” scans OR V/Q scans OR pulmonary embolism OR pulmonary embolism) LIMIT to human AND English.

Table 1
<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Key results</th>
<th>Outcomes</th>
<th>Study weaknesses</th>
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</thead>
<tbody>
<tr>
<td>Hartmann I, Petronella H, Melissant C, et al, 2000, Netherlands</td>
<td>627 patients (91 COPD, 536 non-COPD) with suspected PE diagnosis</td>
<td>Diagnostic study</td>
<td>Proportion of diagnostic VQ scans and CT pulmonary angiograms from both groups</td>
<td>54% of VQ scans in COPD group ruled in/out PE v 79% of VQ scans in non-COPD group</td>
<td>Observational groups not evenly matched</td>
</tr>
<tr>
<td>PE inclusion (angiography or high probability V-Q) PE Exclusion (normal angiography or perfusion scintigraphy)</td>
<td>Sensitivity and specificity of VQ and CT in both groups</td>
<td>All CT pulmonary angiograms gave a rule in/rule out result. No statistical difference between the two groups</td>
<td>Questionable inclusion COPD criteria</td>
<td>No power calculation</td>
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Table 2
<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Key results</th>
<th>Outcomes</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Running OM and Gulhöv G, 1999, Norway</td>
<td>550 patients presenting within 24 hours after stroke onset</td>
<td>RCT (randomised on birth dates)</td>
<td>Disability at seven months (Barthel Index)</td>
<td>No difference between the two groups on disability (p = 0.07) or impairment scores (p = 0.67)</td>
<td>Quasi-randomised</td>
</tr>
<tr>
<td>Exclusion criteria: age &lt;60, onset&gt;24 hours, subarachnoid, TIA</td>
<td>Impairment at seven months (Scandinavian Stroke Scale) Survival at one year</td>
<td>No statistical significant difference (p = 0.3) in survival rates. One year survival greater in control group (72.9% v 68.8%)</td>
<td>Effects of being treated in a stroke unit</td>
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</table>

Search outcome
Altogether 239 were papers found of which 238 did not address the exact question. One paper was of relevance (table 2).

Comment(s)
Surprisingly few comparative studies. Ultimately small number studied in the study in question. Rigid definition of study population and reporter bias pose difficulties in such a study group. Diagnostic utility of V-Q questionable because of high proportion of inconclusive results—resource and economic factors are thus of relevance.

► CLINICAL BOTTOM LINE
There is not enough evidence to support V-Q Scintigraphy as the initial investigation of choice in COPD patients.


Combining clinical probability and ventilation-perfusion scan for diagnosis of pulmonary embolism
Kerstin Hogg, Clinical Research Fellow
Ged Brown, Specialist Registrar

Abstract
A short cut review was carried out to establish whether clinical probability estimates improve the utility of VQ scan results in patients being investigated for possible pulmonary embolus. Altogether 387 papers were found using the reported search, of which six presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of this best paper are tabulated. A clinical bottom line is stated.
outcomes, results and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

**Clinical scenario**
A 20 year old woman presents to the emergency department with shortness of breath and chest pain. Her D-dimer level is abnormal and you have sent her for a ventilation-perfusion scan. The scan result is reported as “low probability for pulmonary embolic disease, however this does not rule out pulmonary embolism”. You have assigned her a low clinical probability of pulmonary embolism score and wonder if this helps interpret the scan.

**Three part question**
In [patients who have undergone ventilation-perfusion scans for possible pulmonary embolus] does [combining clinical probability of pulmonary embolism and ventilation-perfusion scan result] increase the [diagnostic utility]?

**Search strategy**
Medline using the OVID interface 1966-07/03. [exp pulmonary embolism/ OR pulmonary embol$.mp. OR PE.mp. OR exp thromboembolism/ OR pulmonary infarct$.mp.] AND [exp nuclear medicine/ OR exp ventilation-perfusion ratio/ OR ventilation-perfusion.mp. OR ventilation perfusion.mp. OR

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<th>Table 3</th>
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<tbody>
<tr>
<td>Author, date and country</td>
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<tr>
<td>PIOPED investigators, 1990, USA 931 PE patients at six centres. All underwent clinical probability scoring, VQ scan and pulmonary angiogram. 69 patients with normal VQs and 106 others did not undergo the pulmonary angiogram. All followed up clinically for a year</td>
</tr>
<tr>
<td>Miniati M et al, 1996, Italy 890 patients PE had a perfusion scan. 413 of 670 patients with abnormal perfusion scan had a pulmonary angiogram. All abnormal perfusion scan patients were followed up for one year</td>
</tr>
<tr>
<td>Wells PS et al, 1998, Canada 1239 patients PE underwent a clinical probability assessment, VQ scan +/- serial Doppler scans. All patients negative for PE were followed up clinically for three months</td>
</tr>
<tr>
<td>Perrier A et al, 2000, Quebec and Geneva 180 patients from two centres Prospective study with non-diagnostic (low and intermediate probability) lung scan and low clinical probability, followed up for three months</td>
</tr>
<tr>
<td>Baraghouth G et al, 2000, Switzerland 143 consecutive PE patients in acute medical ward. Nine lost to follow up excluded. Decision algorithm used to isolate those requiring pulmonary angiogram, based on VQ scan result and clinical probability score</td>
</tr>
<tr>
<td>Nilsson T et al, 2001, Sweden 1707 PE patients 1991–1994. All had clinical probability score, Q or VQ scan, pulmonary angiogram, and six month follow up</td>
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</table>

Search outcome
Altogether 387 papers found of which six addressed the question and are shown in table 3.

► CLINICAL BOTTOM LINE
All ventilation-perfusion scans must be interpreted with an independent clinical probability score.


Serum amylase and acute pancreatitis

Report by John Butler, Consultant
Checked by Damian Bates, Specialist Registrar

Abstract
A short cut review was carried out to establish whether a normal serum amylase value rules out the diagnosis of acute pancreatitis. Altogether 191 papers were found using the reported search, of which four presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

Clinical scenario
A 44 year old man presents to the emergency department with a four hour history of severe epigastric pain. You consider a diagnosis of pancreatitis and organise a serum amylase to be taken. You wonder whether a single normal serum amylase result is sufficiently sensitive to rule out pancreatitis in this patient.

Three part question
In [patients with abdominal pain] does [a normal serum amylase] exclude [the diagnosis of pancreatitis]?

Search strategy
Medline 1966-07/03 and Embase 1980-07/03 using the OVID interface. {((exp Abdominal pain/ OR abdominal pain.mp) OR (exp Pancreatitis/ OR pancreatitis.mp) OR pancreatitis, alcoholic/ OR pancreatitis, acute necrotising/ OR pancreatitis.mp) AND [exp Amylases OR amylase$ OR amylase.mp]) AND [exp Sensitivity and Specificity OR (sensitivity.mp AND specificity.mp) LIMIT to human AND English].

Search outcome
Altogether 191 papers found of which four papers were relevant to the original question (table 4).

Comment(s)
The gold standard for the diagnosis of pancreatitis is considered to be surgical examination at laparotomy or pancreatic histology. Often in practice such information is either unavailable or obtained at postmortem examination. In the absence of a readily available gold standard it becomes necessary to evaluate serum diagnostic markers against radiological methods such as CT. Only two studies used an independent “gold standard” for all patients to compare the

<table>
<thead>
<tr>
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<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steinberg WM et al, 1985, USA</td>
<td>39 patients with pancreatitis were compared with 127 controls with abdominal pain</td>
<td>Diagnostic study</td>
<td>Sensitivity and specificity of two amylase serum assays for pancreatitis. Using upper limit of normal. Using best cut off</td>
<td>Amylase 1 = sensitivity 94.9% specificity 88.9%. Amylase 2 = sensitivity 94.9% specificity 86.0%.</td>
<td>Various techniques used to confirm diagnosis including CT scans, laparotomy, USS scans</td>
</tr>
<tr>
<td>Lin XZ et al, 1989, Taiwan</td>
<td>62 consecutive patients with image verified pancreatitis, and 414 patients with an acute abdomen</td>
<td>Diagnostic study</td>
<td>Sensitivity and specificity of serum amylase at selected cut off three times above upper limit of normal</td>
<td>Sensitivity of serum amylase: 84% in image proven pancreatitis 92% in patients with or without image verified disease</td>
<td>Various techniques used to confirm diagnosis including CT scans, laparotomy, USS scans</td>
</tr>
<tr>
<td>Clavien PA et al, 1989, Canada</td>
<td>352 consecutive attacks of acute pancreatitis in 318 patients</td>
<td>Diagnostic study</td>
<td>Sensitivity and specificity of serum amylase (&lt;160 IU/l) compared with gold standards of CT or laparotomy</td>
<td>Sensitivity of 81% at presentation</td>
<td>Various techniques used to confirm diagnosis including CT scans, laparotomy, USS scans</td>
</tr>
<tr>
<td>Winslet M et al, 1992, UK pancreatitis</td>
<td>417 patients with acute pancreatitis</td>
<td>Diagnostic study</td>
<td>Sensitivity of serum amylase (&lt;1000 IU/l) for detecting acute pancreatitis at hospital admission</td>
<td>Mild cases 96.1%. Severe cases 87.4%. Alcohol subgroup 86%</td>
<td>Various techniques used to confirm diagnosis including CT scans, laparotomy, USS scans</td>
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</table>
diagnostic test under consideration. Despite this weakness all the above studies except one reported sensitivities below 95%, especially in alcohol related pancreatitis cases.

**Clinical Bottom Line**

In patients presenting to the emergency department with acute abdominal pain a normal serum amylase concentration is not sufficiently sensitive to rule out the diagnosis of acute pancreatitis.


**Ultrasonic guidance and the complications of central line placement in the emergency department**

<table>
<thead>
<tr>
<th>Author, date and country</th>
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<tbody>
<tr>
<td>Randolph AG et al, 1996, USA</td>
<td>Eight randomised controlled studies identified from Medline search from 1966 to 1995</td>
<td>Meta-analysis</td>
<td>Meta-analysis of the relative risk of various clinical variables</td>
<td>Central line placement failure 0.32 (0.18 to 0.55)</td>
<td>Medline search only, no systematic review</td>
</tr>
<tr>
<td>NICE guidelines, 2002, UK</td>
<td>Systematic review of the literature</td>
<td>Systematic review and meta analysis</td>
<td>Recommendations</td>
<td>Use of 2-D USS should be considered in most clinical situations where a central line is necessary electively or in an emergency</td>
<td>Poor search strategy</td>
</tr>
<tr>
<td></td>
<td>20 RCTs evaluating ultrasound guidance for central line placement found</td>
<td></td>
<td>Meta-analysis of relative risks of various clinical outcome measures</td>
<td>No. failed catheter placements RR: 0.16 (0.09 to 0.3)</td>
<td>Grades of recommendation not provided</td>
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<td>No. complications odds: 0.36 (0.17 to 0.36) risk of failure RR: 0.29 (0.39 to 0.88)</td>
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<td>Number of fewer attempts RR</td>
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<td>Number of seconds saved 76 (96–63)</td>
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<td>Number of arterial punctures saved 90 per 1000 patients</td>
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<td>The extra cost is likely to be about £10 patient, although the machines cost £7000–£15000 initially</td>
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<tr>
<td>Miller AH et al, 2002, USA</td>
<td>122 emergency medical patients designated as “difficult insertions” randomised to the Landmark technique (n = 71) or 2-D USS guidance technique (n = 51)</td>
<td>Cohort study</td>
<td>Time from needle touching skin to successful flashback</td>
<td>Landmark group 463 s +/- 627 s SS group 93 s +/- 176 s p &lt; 0.0001</td>
<td>The insertion time may only represent a small amount of the total time taken to set up an USS guided central line insertion</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Number of attempts</td>
<td>Landmark group 3.54 +/- 2.7 USS group 1.55 +/- 1 p &lt; 0.0001</td>
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<td></td>
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<td>Complications</td>
<td>Landmark group 14% USS group 12% p = 0.780</td>
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</table>
Three part question
In [patients in the emergency department requiring a central line] is [USS guidance better than blind landmark techniques] at [reducing the complications of insertion]?

Search strategy
Medline 1966-07/03 using the OVID interface. [(exp Ultrasonography/ OR ultrasound.mp) AND (exp Catheterization, Central Venous/ OR central venous catheter.mp OR central line.mp)] LIMIT to human AND English

Search outcome
Altogether 349 papers were found of which two represented the best evidence. This included a meta-analysis and an additional paper. In addition a second meta-analysis not indexed on Medline was identified by cross referencing (table 5).

Comment(s)
Two meta-analyses were identified in this area and only one additional paper could be found that neither meta-analysis included. Both meta-analyses provide strong evidence that USS guided placement significantly reduces complications during catheter placement, number of attempts at insertion and reduction in the number of attempts at insertion for both neck and femoral line insertion. In addition and the NICE meta-analysis provides evidence that insertion time is quicker although this evidence is less convincing. NICE also imply that if used regularly the cost implication could be as little as £10 per patient although they acknowledge a projected £29 million cost for initial NHS implementation for equipment and training.

► CLINICAL BOTTOM LINE
There is good evidence that USS guided placement of central lines reduces the complication rate associated with this procedure.


The utility of the tongue blade test for the diagnosis of mandibular fracture

Report by Rashmi Malhotra, Medical Student
Checked by Joel Dunning, RCS Research Fellow

Abstract
A short cut review was carried out to establish whether the tongue blade test is useful in the clinical assessment of patients with mandibular trauma. Altogether 269 papers were found using the reported search, of which two presented the best evidence to answer the clinical question. The author, date and country of publication, patient group

Table 6

<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alonso LL and Thomas TB, 1995, USA</td>
<td>110 consecutive patients in the emergency department with jaw pain</td>
<td>Diagnostic study</td>
<td>Patient ability to grasp a tongue blade/depressor between his teeth and hold the blade against a twisting motion, with the ability to crack the tongue blade on both sides defined a negative test</td>
<td>Sensitivity of tongue blade test: 45 positive of 47 fractures, specificity 95.7%, CI (85.5 to 99.3%)</td>
<td>No sample size estimates—sample used too small</td>
</tr>
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<td></td>
<td>Exclusion criteria: patients unable to cooperate because of age, language barrier, inability to open mouth because of pain, intoxication or head injury</td>
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<tr>
<td>Robert A et al, 1998, USA</td>
<td>119 patients with jaw pain after trauma presenting at the emergency department</td>
<td>Diagnostic study</td>
<td>Patient ability to grasp a tongue blade/depressor between his teeth by and then to hold the blade against mild resistance by the examiner</td>
<td>Sensitivity of tongue blade test: 42 positive of 44 fractures, specificity 95%</td>
<td>&quot;Gold standard&quot; radiologist interpretation</td>
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<td></td>
<td>Exclusion criteria: airway compromise, inability to perform or cooperate with clinical examination, edentulousness</td>
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<td>Single radiologist to report radiographs—no double reporting</td>
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<td>No OPG despite panoramic series known to be more sensitive than mandibular series in detecting mandibular fracture</td>
<td>Single radiologist to report radiographs—no double reporting</td>
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<td>No interobserver variability measurements</td>
<td>No sample size estimates—number too small should have used Fisher’s exact test</td>
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<td>No radiographs—no double reporting</td>
<td>No CIs calculated</td>
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</tbody>
</table>

Sensitivity of tongue blade test: 42 positive of 44 fractures, specificity 95%
Specificity of tongue blade test: 23 positive TBT of 63 non-fractures, specificity 63.5%, CI (50.4 to 75.3%)

Sensitivity measured in an other study in this hospital and was found to be only 95.5%
Single radiologist to report radiographs—no double reporting
No OPG despite panoramic series known to be more sensitive than mandibular series in detecting mandibular fracture
Single radiologist to report radiographs—no double reporting
No interobserver variability measurements
No CIs calculated
Incorrect use of y2 test—number too small should have used Fisher’s exact test
No sample size estimates—sample used too small

Inability to hold tongue blade against resistance on either hemimandible defined as a positive test
Sensitivity measured in an other study in this hospital and was found to be only 95.5%
studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

Clinical scenario
You are evaluating a patient who has attended the emergency department having just been punched on the jaw. He is having difficulty opening his mouth and talking but you can see no step deformity or loose teeth. You recall that while you were on elective you saw the tongue blade test being used routinely in America to select patients for mandibular imaging. For this test the patient is asked to bite on the tongue blade and if the examiner can break the blade while the patient grips it, the patient does not need a mandibular radiograph. You wonder whether this is a sensitive test to use in this patient.

Three part question
In [patients with mandibular trauma] is [the tongue blade test] a good diagnostic test for [mandibular fracture]?

Search strategy
Medline 1966-7/03 using the OVID interface. [(mandibular fracture.mp.OR exp Mandibular Fractures/) OR {(exp fractures OR fracture$.mp) AND (exp mandible OR mandible$.mp or mandibular.mp)}] AND exp diagnosis OR diagnosis.mp AND maximally sensitive RCT filter LIMIT to human AND English.

Search outcome
Altogether 269 papers were found of which two were relevant and are listed in table 6.

Comment(s)
No confidence intervals were calculated by Roberts et al for the reported sensitivity of the tongue blade test so we calculated this ourselves: sensitivity 95.4% (CI 84.53% to 99.44%). The confidence intervals are comparatively wide and so the tongue blade test could not stand on its own as a single diagnostic tool in screening for mandibular fractures since missing these fractures can lead to serious long term complications.

The high sensitivities reported by both these studies do suggest, however, that the tongue blade test is a useful screening tool in evaluating patients with mandibular fracture but other clinical predictors must also be considered.

► CLINICAL BOTTOM LINE
The tongue blade test is useful in evaluating patients with possible mandibular fracture
