Question sheet

Hoffmann et al. Coronary Computed Tomography for Early Triage of Patients With Acute Chest Pain. Journal of the American College of Cardiology 2009;53:1642-1650.

1. Provide a no more than 200 word summary of this paper. Only the first 200 words will be considered – short bullet points are acceptable. Maximum of 8 points available.

   Answer

   - *Diagnostic observational cohort study (1 point – ½ mark if only observational, or only diagnostic. No marks for cohort only)*

   - *Study population – Patients presenting to the ED with chest pain with non-ischaemic initial ECG and normal initial troponin (1 point – must get all three elements to get mark)*

   - *Both clinicians and investigators were blinded (1 point)*

   - *Test of interest – Coronary computed tomography angiography (1 point)*

   - *Reference (gold) standard – Diagnosis of ACS according to American Heart Association/American College of Cardiology/European Society Guidelines (after hospitalisation) (1 point)*

   - *Results*

     For plaque on CTA (presence of coronary artery disease):

     Sensitivity 100% (95% CI 98-100%)
     Negative predictive value 100% (85% CI 89-100%)
     Specificity 54% (95% CI 49-60%)

     (1 point – must get all three for mark, ½ mark if 2 out of three)

     For stenosis on CTA (> 50% luminal narrowing):

     Sensitivity 77% (95% CI 59-90%)
     Negative predictive value 98% (85% CI 95-99%)
     Specificity 87% (95% CI 83-90%)

     (1 point – must get all three for mark, ½ mark if 2 out of three)
     Likelihood ratio also accepted

- *Conclusion – the authors conclude that because half of low to intermediate risk chest pain patients were free of CAD and had no ACS, early coronary CTA may significantly improve patient management in the ED. (1 point)*

  'Coronary CTA diagnosed CAD independent of TIMI score or troponin etc' not accepted.

2. List six features of the study <u>design</u> in this paper that enhance the quality of the study. (6 points)

Answer

(a) Prospective design (1 point)

Test applied to appropriate patients that we would see in the ED and who there is uncertainty about i.e. relevant population (chest pain possibly of cardiac origin with normal initial ECG/troponin) (1 point)

Coronary CTA (test of interest) carried out on all patients (1 point)

Appropriate reference (gold) standard (1 point) (Note: while the reference standard (diagnosis of ACS according to widely agreed guidelines) is not as objective as, for example, a blood test or anatomic measure, it is standard clinical practice and is backed up by the outcome data provided in the paper)

Gold standard also applied to all patients (1 point)

Appropriate sample size calculation (1 point)

Both those reporting the investigation under evaluation and those applying the reference standard were blinded to the other Blinding of CT interpretation to reference diagnosis; blinding of reference diagnosis to CT result (1 point - 1/2 mark for any mention of blinding, 1 if mention both are blinded)

Maximum of 6 points

3. In this paper, the CT images were interpreted by investigators blinded to the subject's clinical presentation and history. The diagnosis of ACS was established by a panel of 3 investigators blinded to the results of coronary CT.

(a) Explain how or why bias might arise if the blinding outlined above had not been undertaken in this study? (1 point)
(b) Give one circumstance in which lack of blinding in a diagnostic test evaluation study may not lead to significant bias. (1 point)

Answer

(a) The CT interpretation was carried out blinded to the clinical presentation and the reference diagnosis. If those interpreting the CT images knew what the presentation or reference diagnosis was, that knowledge might influence their interpretation of the images, particularly 'borderline' images e.g. they might be more likely to diagnose CAD if they knew that the final outcome diagnosis was ACS. (1/2 point for understanding along these lines)

The reference diagnosis was established without knowledge of the CT result. Given that the reference was to some extent subjective i.e. based on consensus opinion rather than on a purely objective measure, then knowledge of the CT result could have influenced the assignation of the reference diagnosis. (1/2 point for understanding along these lines)

Must mention both ways of bias for full marks

(b) If either reference test or test under investigation is absolutely categorical and doesn't rely on interpretation – must be clear that it is the result that is strongly categorical that cannot be biased. (1 point)

OR

If the result of either the test of interest or the reference diagnosis test is generated by a strongly objective process e.g. a numerical test result from an automated blood analyzer, then blinding of that aspect may not lead to bias as much as if the interpretation is subjective e.g. image interpretation. (1 point)

4. Table 3 of the paper is reproduced below. The questions below refer to the table.

Table 3 Diagnostic Accuracy of Coronary CTA for the Detection of Acute Coronary Syndrome and Myocardial Infarction During Index Hospitalization Among Patients With Acute Chest Pain Based on the Presence of Any Coronary Plaque or the Presence of Coronary Artery Stenosis (>50% Luminal Narrowing)

Coronary CTA Finding	Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	LR+	LR−
Acute coronary syndrome						
Any plaque	31/31 (100%) [89%–100%]	183/337 (54%) [49%–60%]	31/185 (17%) [12%–23%]	183/183 (100%) [98%–100%]	2.2	0.0
Coronary stenosis	24/31 (77%) [59%–90%]	293/337 (87%) [83%–90%]	24/68 (35%) [24%–48%]	293/300 (98%) [95%–99%]	5.9	0.3
Myocardial infarction						
Any plaque	8/8 (100%) [63%–100%]	183/360 (51%) [46%–56%]	8/185 (4%) [2%–8%]	183/183 (100%) [98%–100%]	2.0	0.0
Coronary stenosis	5/8 (63%) [24%–91%]	297/360 (83%) [78%–86%]	5/68 (7%) [2%–16%]	297/300 (99%) [97%–100%]	3.7	0.45

CI = confidence interval; CTA = computed tomography angiography; LR+ = likelihood ratio given positive test result; LR− = likelihood ratio given negative test result; NPV = negative predictive value; PPV = positive predictive value.

(a) You see a patient who has no stenosis on coronary CT. Which performance measure (sensitivity, specificity etc) is most useful in advising the patient about their chances of having ACS? (1 point)
Explain why you think this performance measure is most useful. (1 point)
What would you tell the patient about their chances of having ACS? (2 points)

(b) Coronary CTA can be reported in terms of presence of plaque or presence of stenosis. Comment on the utility these two results in ruling out ACS.
(2 points)

Answer

(a) Negative predictive value (NPV) (1 point)

NPV tells you the probability of disease in those with a negative test result (no stenosis in this case) and so is most useful in advising an individual with that result. (1 point for understanding along these lines)

The NPV for 'no stenosis' on CT is 98%. You could tell the individual that with a negative result our estimate is that they have a 2% chance of having ACS (1 point), but that the chance could be as high as 5% or as low as 1% (as given by the 95%CI) (1 point)

(b) The CTA results are provided at two levels – 'no plaque' and 'no stenosis'

If using the presence or absence of plaque as the result, then sensitivity is 100% and the absence of plaque is useful to rule out ACS. (1 point)

If using presence or absence of stenosis as the result, then sensitivity is 77% meaning that 23% of patients with ACS have no stenosis on CT and so 'no stenosis' does not adequately rule out ACS. (1 point)

5. In relation to coronary stenosis for the diagnosis of ACS, table 3 of the paper gives the likelihood ratio of a positive test (LR+) as 5.9 and the likelihood ratio of a negative test (LR-) as 0.3.

(a) Define a likelihood ratio? (1 point)
(b) What does LR + 5.9 mean? (1 point)
(c) Give one advantage of likelihood ratios over sensitivity, specificity, negative predictive value and positive predictive value? (1 point)

Answer

(a) A likelihood ratio is a number, derived from test performance characteristics, that provides an indication of the degree (magnitude and direction) to which a given test result will alter the probability (strictly speaking odds) of disease after application of the test.

Likelihood ratios indicate by how much a given diagnostic test result will raise or lower the pre-test probability of the target disorder.

It is derived from the other performance characteristics and gives an indication of the change to the pre-test probability. A likelihood ratio of 1 means that the post-test probability is the same as the pre-test probability (not a useful test). Likelihood ratios of greater than 1 increase the probability that the target disorder is present. Likelihood ratios less than 1 decrease the probability that the target disorder is present.

Sensitivity/1 – specificity also acceptable

(1 point for understanding along these lines)

(b) A positive result (coronary stenosis) is 5.9 times more likely to be found in an individual with ACS than one without ACS. This is the literal meaning. Another acceptable interpretation is that a patient with a positive result is 5.9 times more likely to have ACS than you thought they were prior to doing the test. This results in a moderate shift in pre- to post- test probability. (1 point for the numerical interpretation or interpretation of the shift in probability)

(c) The advantage of likelihood ratios is that they are applicable to patients in any population, regardless of prevalence (1/2 point – must mention prevalence)
By contrast positive and negative predictive values vary with prevalence of disease and cannot be applied to different populations (1/2 point).

(1 point for understanding along these lines)

6. The following quote is taken from the results section of the paper:

‘ the presence of stenosis was associated with a more than 20-fold increased risk of ACS (OR: 22.8, 95% CI: 9.3 to 56.1; p < 0.0001).’

(a) What does 95% CI: 9.3 to 56.1 mean? (1 point)
(b) What does p < 0.0001 mean? (1 point)
(c) Give one advantage of confidence intervals over p values when interpreting the results. (1 point)

Answer

(a) This 95% confidence interval means that although our point estimate of the odds ratio is 22.8, it may be less or it may be more. We can be 95% confident that the true value lies between 9.3 and 56.1. (1 point)

OR

If we repeated this study 100 times, the result would be between 9.3 and 56.1 95 times. (1 point)

OR

The ‘true’ result lies between 9.3 and 56.1 95% of the time. (1 point)

(b) The probability of seeing an odds ratio of 22.8 when there is, in fact, no difference in the odds of ACS with stenosis on CT is less than one in ten thousand. This is considered a highly statistically significant result. (1 point – ½ point for mentioning one in ten thousand, ½ mark for mentioning that this is the probability of the Odds ratio being incorrect. Just stating ‘statistically significant’ does not get the mark)

(c) Confidence intervals provide information on the best and worse case scenarios for a given result, whereas the p value simply gives an indication of the probability of observing a point estimate by chance. As such, CI’s are more informative.

For example, while the p value above is impressive, we might decide that an odds ratio below 12 would not be useful to us and, with the confidence interval telling us that ‘true’ result could be as low as 9.3 (below our threshold), we might be less impressed with the result than if relying solely on the p value.

(1 point for understanding along these lines – CI more informative than p value, must mention best and worst case scenarios as opposed to simply referring to a range)

7. An editorial accompanying the publication of this paper described the use of coronary CTA in low risk patients as a 'promising development' but stopped short of pronouncing it the answer to the problem of low risk patients with chest pain.

Having read this paper, give six reasons why you would not implement coronary CTA for low risk patients in your ED. (6 points)

Answer

(a) Exclusion criteria - A significant number of patients were excluded because of elevated creatinine. This may limit the applicability of coronary CTA.

(b) Follow-up – The loss to follow-up was 8%. While this is not bad, rare but serious events (major adverse cardiac outcomes) may have occurred in this group (perhaps explaining their loss to follow-up)

(c) Test performance – the sensitivity of 'no plaque' is good at 100%, but the associated specificity is moderate (54%) meaning that large numbers of patients would be subjected to further assessment who don't have ACS.

(d) Test performance – The sensitivity of 'no stenosis' (77%) is not good enough to allow safe discharge i.e. doesn't rule out, even though the specificity is better (87%).

(e) The CT resource may not be widely available in UK/Irish practice.

(f) We don't know how this test would compare with standard care for admission rates, rates of further invasive testing, duration in ED etc.

(g) No cost analysis (must include that it may or may not have been more expensive, not just that it would be more expensive)

(h) Expertise of researchers limits applicability

(i) Concerns over Independence of researchers given funding reported on first page

(j) Lower specificity if older – but these are most important

(k) Single centre study so possibly not generalisable

(l) Sample size not reached

(m) No inter-rater reliability

(n) High number of refusals or drop outs

1 mark for each valid point to a maximum of 6. Other points not made above, but deemed appropriate by examiners, may be accepted. Radiation risk not accepted as not mentioned in the paper.