Welcome to issue 17 of Acute Coronary Syndrome Research Review.

The current revascularisation guidelines are supported by the findings of a paper included in this issue, in which multivessel compared with culprit vessel revascularisation during primary percutaneous coronary intervention was associated with better outcomes (adjusted in-hospital mortality and all-cause death) in patients with ST-segment elevation myocardial infarction with cardiogenic shock and multivessel disease.

Data from another investigation suggest that a novel strategy using a simple clinical risk score, combined with the results of a single high-sensitivity troponin result, may enable immediate discharge in up to 40% of patients with suspected acute coronary syndromes. The study showed that this strategy identifies more patients suitable for early discharge, with lower false-positive rates than undetectable troponin strategies. Consistent with consensus guidelines, the study authors cannot recommend uptake of undetectable hs-cTnT rule-out strategies in the emergency department setting.

I hope you find the research in this issue useful to you in your practice and I look forward to your comments and feedback.

Kind Regards,

Professor John French
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Usefulness of ECG to differentiate Takotsubo cardiomyopathy from acute coronary syndrome

Authors: Looi JL et al.

Summary: This investigation compared the evolution of ECG changes in Takotsubo cardiomyopathy with those in myocardial infarction (MI) and sought to determine which ECG features might help to distinguish between these conditions. One hundred patients with Takotsubo cardiomyopathy and 100 with MI were enrolled. Thirty-five patients with Takotsubo cardiomyopathy had ST-segment elevation on admission. Serial ECGs performed from admission to Day 2 revealed that the patients with Takotsubo cardiomyopathy and ST-segment elevation had less prominent STE (median peak elevation 2 mm vs 3 mm; p<0.05), less reciprocal ST-segment depression and no abnormal Q-waves, as compared with ST-segment elevation myocardial infarction (STEMI) patients. By Day 2, pathological Q-waves were found in all STEMI patients versus none in the Takotsubo cardiomyopathy patients. Compared with non-ST-segment elevation Takotsubo cardiomyopathy patients, non-STEMI patients had more ST-segment depression (28.2% vs 0%; p<0.05), but less T-wave inversion (33.8% vs 11.3%; p<0.05) on admission. By Day 2, the ECG criterion that best distinguished non-ST-segment elevation Takotsubo cardiomyopathy from non-STEMI was the presence of T-wave inversion in ≥6 leads (sensitivity 74%, specificity 92%).

Comment: This paper characterises the evolving ECG patterns over the initial 2 days following hospitalisation in patients with Takotsubo cardiomyopathy compared to patients with STEMI. This relatively large cohort of 100 patients with Takotsubo cardiomyopathy did not develop Q-waves or reciprocal ST depression and they had less ST-elevation. However, it does not appear that this study provides sufficient initial ECG discrimination to allow clinicians to defer emergent coronary angiography when Takotsubo cardiomyopathy is suspected. A comprehensive prospective multicentre study describing Takotsubo cardiomyopathy presenting both to hospital and in patients presenting from non-cardiac wards, ideally with routine emergent echocardiography, is warranted to attempt to determine whether a combination of non-invasive parameters can differentiate between this disorder and STEMI with sufficient specificity to avoid emergent angiography.

Reference: Int J Cardiol. 2015;199:132-40

Abstract

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Influence of multivessel disease with or without additional revascularization on mortality in patients with ST-segment elevation myocardial infarction

Authors: Jensen LO et al.

Summary: Data from the Western Denmark Heart Registry were used to identify 8822 patients presenting with STEMI and treated with PCI between January 2002 and June 2009; 4770 patients (54.1%) had single-vessel disease and 4052 (45.9%) had multivessel disease (MVD). Cumulative mortality was 7.6% at 1 year and 24.0% at 7 years. In Cox regression analysis adjusted for potential confounding, MVD was associated with higher 7-year mortality (adjusted HR 1.45; 95% CI, 1.22 to 2.11; p=0.01) and for 1-year mortality (OR 0.51; 95% CI, 0.29 to 0.91; p=0.02).

Comment: Some Australian cardiologists consider the large and ongoing COMPLETE trial, which aims to determine the utility of complete revascularisation, compared to infarct-artery only PCI, in patients with STEMI and MVD, will not be readily applicable to Australian practice, because the revascularisation indications are too strict in the conservative arm. In this context, the findings of Jensen et al. of similar 7-year mortality rates in patients with STEMI and MVD, who underwent revascularisation in non-culprit artery(s), to those with single-vessel disease is of interest. The report’s effects of further revascularisation may have been under-estimated in those with MVD, as almost 10% of those not undergoing revascularisation had died or had been lost to follow-up at 2 months post-STEMI.

Reference: Am Heart J. 2015;170(1):70-8

Abstract

Time-dependent effects of unfractionated heparin in patients with ST-elevation myocardial infarction transferred for primary angioplasty

Authors: Giralt T et al.

Summary: These researchers examined the effect of unfractionated heparin (UFH) administered before transfer versus in the catheterisation laboratory (CathLab) on initial patency of the infarct-related artery (IRA) in transferred STEMI patients treated with primary percutaneous coronary intervention (PPCI). The study involved 1326 patients; 758 (57%) were administered UFH by ambulance crew or the physician-in-charge at the non-PPCI centre (pre-transfer group), 568 (43%) received UFH in the CathLab (post-transfer group). Initial IRA thrombolysis in myocardial infarction (TIMI) 2–3 flow was 30.3% in the pre-transfer group versus 21.2% in the post-transfer group (p=0.001). A time-dependent association was found between symptom onset and UFH administration and initial TIMI 2–3 in pre- versus post-transfer groups (<120 min: 33.2% vs 18%, p<0.001; 120–240 min: 29.2% vs 22.8%, p=0.18; >240 min: 25% vs 28%, p=0.57). No differences in major bleeding were found between groups. In logistic regression analysis, UFH administration before transfer remained an independent predictor for initial TIMI 2–3 flow (OR 1.60; 95% CI, 1.22 to 2.11; p=0.01) and for 1-year mortality (OR 0.51; 95% CI, 0.29 to 0.91; p=0.02).

Comment: ‘Upstream’ UFH, in very large doses (300 U/kg), in patients with suspected STEMI suggested benefit in the HEAP pilot study in the late 1990s. However, the subsequent HEAP trial showed no difference in the initial TIMI flow rates in STEMI patients undergoing emergent angiography, though UFH was administered in the PPCI centre; another report of non-randomised patients from the same authors suggested a similar effect to the current study of Giralt et al. They report that initial infarct artery patency (TIMI 2 or 3 flow) was higher in those STEMI patients receiving an upstream (in a non-PPCI centre or ambulance) bolus of 5000U of UFH, mainly in those presenting <120 min after symptom onset. Replication of these findings in a larger randomised trial is desirable.

Reference: Int J Cardiol. 2015;198:70-4

Abstract
Culprit or multivessel revascularisation in ST-elevation myocardial infarction with cardiogenic shock

Authors: Park JS et al.

Summary: These researchers compared the clinical outcomes of patients with STEMI, cardiogenic shock (CS) and MVD who were treated with culprit vessel revascularisation (n=386) or multivessel revascularisation (n=124) at the time of PCI. The primary outcomes were in-hospital mortality and all-cause death during a median 194-day follow-up. Compared with culprit vessel revascularisation, multivessel revascularisation had a significantly lower adjusted risk of in-hospital mortality (9.3% vs 2.4%; HR 0.46; 95% CI, 0.149 to 0.462; p<0.001) and all-cause death [13.1% vs 4.8%; HR 0.400; 95% CI, 0.264 to 0.606; p<0.001], mainly because of fewer cardiac deaths (9.7% vs 4.8%; HR 0.510; 95% CI, 0.329 to 0.790; p=0.002). In addition, multivessel revascularisation significantly decreased the adjusted risk of the composite endpoint of all-cause death, recurrent MI and any revascularisation (20.3% vs 18.1%; HR 0.728; 95% CI, 0.55 to 0.965; p=0.026).

Comment: Guidelines since the SHOCK trial (published in 1999) have recommended that patients with STEMI, CS and MVD should undergo emergent non-culprit artery revascularisation. This cohort study of Park et al. reports a lower mortality in the 1/4 of patients with CS and MVD who underwent multivessel revascularisation, compared to those who had infarct-artery only PCI; at ~6 months, rates were 13.1% and 4.8%, respectively (p<0.001). These findings support the current guidelines. However, as the reported mortality rates are dramatically lower than those in contemporary trials of CS such as the SHOCK-2 IABP (~40%), these findings, which do not appear to be due to a different definition of CS, need circumspect consideration.

Reference: Heart. 2015;101(15):1225-32

Impact of access site choice on outcomes of patients with cardiogenic shock undergoing percutaneous coronary intervention: A systematic review and meta-analysis

Authors: Pancholy SB et al.

Summary: A systematic search of the literature revealed 3652 articles reporting the outcomes of patients with CS undergoing PCI and association between choice of arterial access, 30-day all-cause mortality, and 30-day major adverse cardiac and cerebral events (MACEs). The 8 studies eligible for inclusion involved 8131 patients with CS undergoing PCI (via transradial access [TRA]: 5810 patients). At 30 days, TRA was associated with significantly reduced risk for all-cause mortality (unadjusted: RR 0.67, 95% CI 0.58 to 0.77; p<0.001, 8 included studies; adjusted: RR 0.55, 95% CI 0.44 to 0.70, p<0.001, 6 included studies) and MACE (unadjusted: RR 0.66, 95% CI 0.63 to 0.73, p<0.001, 6 included studies; adjusted: RR 0.63, 95% CI 0.52 to 0.75, p<0.001, 4 included studies) when compared with TFA.

Comment: The preferred arterial access site in patients with CS undergoing PCI is debated because some sort of circulatory support device is utilised in many patients, and that requires cannulation of an artery larger than the radial artery. So in CS, some interventionalists, even if they are experienced STEMI radial operators, choose the femoral access. This meta-analysis indicates that there is a significant mortality benefit for the radial approach: adjusted RR 0.55 (95% CI, 0.46 to 0.65; p<0.001). Confirmation of the findings in a large multicentre trial utilising circulatory additional to, or instead of, intra-aortic balloon pumping is warranted.


A novel diagnostic protocol to identify patients suitable for discharge after a single high-sensitivity troponin

Authors: Carlton EW et al.

Summary: This study demonstrates that a novel accelerated diagnostic protocol (ADP) for suspected acute coronary syndrome (ACS) can successfully identify low-risk patients suitable for discharge after a single high-sensitivity troponin (hs-cTnT) taken at presentation to the emergency department. The diagnostic performance of the Triage Rule-out Using High-sensitivity Troponin (TRUST) ADP was compared with strategies using the detection limit cut-offs of hs-cTnT (<5 ng/L and <3 ng/L). The ADP incorporates structured risk-assessment and a single presentation hs-cTnT blood draw of <14 ng/L. The primary end point was fatal/non-fatal acute myocardial infarction (AMI) within 30 days. Of the 960 participants (mean age 58.0 years), 80 (8.3%) had an AMI. The TRUST ADP classified significantly more patients suitable for immediate discharge (39.8% vs 29.3% (<5 ng/L) and 7.9% vs 3% (<3 ng/L); p<0.001), with a sensitivity for identifying AMI of 98.8% (95% CI, 92.5% to 99.9%). The hs-cTnT limit of detection cut-off of <5 ng/L had a sensitivity of 100% (94.3 to 100), as did the cut-off value of <3 ng/L (94.4 to 100). The TRUST ADP had a lower false-positive rate for AMI detection: specificity 43.3% (95% CI, 42.7% to 43.4%) vs 32.0% (hs-cTnT <5 ng/L; 95% CI, 31.5% to 32.0%) and 8.6% (hs-cTnT <3 ng/L; 95% CI, 8.1% to 8.6%), respectively.

Comment: The TRUST ADP aimed to identify patients with suspected ACS, who were at low risk and potentially suitable for early discharge and incorporated an hs-cTnT of <14 ng/L, an ECG that was non-isaemic, and a modified Goldman risk score. The TRUST ADP was compared to single hs-cTnT assays with 2 detection limits of <5 ng/L and <3 ng/L, and was shown to be superior in ruling out acute MI to either undetectable single hs-cTnT. As several Australasian emergency departments were involved, it suggests that the single assay undetectable hs-cTnT level approach to those at low risk is unlikely to be adopted locally.

Reference: Heart. 2015;101(13):1041-6
10-Year mortality outcome of a routine invasive strategy versus a selective invasive strategy in non-ST-segment elevation acute coronary syndrome: the British Heart Foundation RITA-3 randomized trial

Authors: Henderson RA et al.

Summary: The RITA-3 (Third Randomised Intervention Treatment of Angina) trial compared outcomes of a routine early invasive strategy (coronary arteriography and myocardial revascularisation, as clinically indicated) to those of a selective invasive strategy (coronary arteriography for recurrent ischaemia only) in 1810 patients with non-ST-segment elevation acute coronary syndrome (NSTEACS). At a median 5 years of follow-up, the routine invasive strategy was associated with a 24% reduction in the odds of all-cause mortality. However, this longer-term follow-up shows that after 10 years, there was no evidence of a difference in outcome between the routine invasive and selective invasive groups: all-cause deaths, 25.1% vs 25.4%, respectively (p=0.94) and cardiovascular deaths, 15.1% vs 16.1%, respectively (p=0.65). Multivariate analysis identified several independent predictors of 10-year mortality: age, previous MI, heart failure, smoking status, diabetes, heart rate, and ST-segment depression. A modified post-discharge Global Registry of Acute Coronary Events (GRACE) score was used to calculate an individual risk score for each patient and to form low-risk, medium-risk, and high-risk groups. Risk of death within 10 years varied markedly from 14.4% in the low-risk group to 56.2% in the high-risk group. This mortality trend did not depend on the assigned treatment strategy.

Comment: RITA-3 was a landmark trial in the invasive management of patients with NSTEACS, but without a total creatine kinase level >2X the upper reference limit, and initially reported in 2002. Overall, there was no difference in mortality (~25%) between those assigned a routine invasive strategy (90% angiography, 55% revascularisation) or a selective invasive strategy (21% angiography, 14% revascularisation) in respect to 10-year mortality (62% cardiovascular (~16%)). The majority of patients were defined as low risk, according to a modified post-discharge GRACE risk score, and unsurprisingly, the 10-year survival curves were essentially super-imposable with ~14% mortality, whereas the small number of patients with high GRACE scores had separation of the mortality curves (56% at 10 years) through to 8 years; the medium-risk group (as did the overall trial) showed reduced 5-year but not 10-year mortality with the routine invasive approach. While there are many interesting issues in the paper, it can be inferred from this and other studies that the rate of routine angiography in patients with NSTEACS should increase in those with highest GRACE risk.

Reference: J Am Coll Cardiol. 2015;66(5):511-20

Abstract

Independent commentary by Professor John French. Director of Coronary Care and Cardiovascular Research at Liverpool Hospital, Sydney, and conjoint Professor at the University of New South Wales. After basic physician training he undertook a PhD at the University of Adelaide, further cardiology training at Greenlane Hospital, Auckland, New Zealand, and a Wellcome Trust Postdoctoral Fellowship at University College London, UK. Prior to his current position Professor French was appointed to Greenlane Hospital and the University of Auckland from 1992-2003. Professor French has been an investigator and co-investigator in numerous randomised controlled trials, and was on the steering committee of the SHOCK, OAT, HERO-2 and CRISP-AMI trials. Professor French has served on the clinical endpoints committees of several major trials, and is currently Co-Chair of the ACI Cardiac Network NSW. Professor French’s current major research interests include the acute coronary syndromes especially ST elevation MI, and cardiac biomarkers especially high sensitivity troponins.
Assessment of fractional flow reserve in patients with recent non-ST-segment-elevation myocardial infarction: comparative study with 3-T stress perfusion cardiac magnetic resonance imaging

Authors: Layland J et al.

Summary: The British Heart Foundation Fractional Flow Reserve Versus Angiography in Guiding Management to Optimize Outcomes in Non-ST-Elevation Myocardial Infarction (FAMOUS-NSTEMI) study recently demonstrated the safety and feasibility of fractional flow reserve (FFR) measurement in NSTEMI. Outcomes are reported from the cardiac magnetic resonance (CMR) substudy, which compared the diagnostic accuracy of FFR with that of 3.0-T stress CMR perfusion among 106 patients (mean age 56.7 years) with NSTEMI who had been referred for early invasive management. FFR was measured in all major patent epicardial coronary arteries with a visual stenosis estimated at ≥30%, and if PCI was performed, an FFR assessment was repeated. Myocardial perfusion was assessed with stress perfusion CMR at 3 T. Mean time from FFR evaluation to CMR was 6.1 days. The mean left ventricular ejection fraction was 58.2%. Mean infarct size was 5.4%, and mean troponin concentration was 5.2 μg/L. There were 34 fixed and 160 inducible perfusion defects. A negative correlation was observed between the number of segments with a perfusion abnormality and FFR (r = –0.77; p < 0.0001). An FFR of ≤0.8 had an overall sensitivity and specificity of 91.4% and 92%, respectively, with positive and negative predictive values of 76% and 97%, respectively. Diagnostic accuracy was 92%. In 21 patients with NSTEMI who underwent perfusion CMR before invasive angiography, the positive and negative predictive values of FFR for flow-limiting coronary artery disease (FFR ≤0.8) were 92% and 93%, respectively. In receiver operating characteristic analysis, the optimal cut-off value of FFR for demonstrating reversible ischaemia on CMR was ≤0.805 (area under the receiver operating characteristic curve, 0.94; p < 0.0001).

Comment: In patients with NSTEMI undergoing invasive management, the functional assessment of stenosis severity is pivotal, as variability in endothelial function among other perturbations may influence angiographic severity assessment. This study, reassuringly for interventional cardiologists, shows a very high degree of association between the ischaemic myocardial territory identified by a FFR ≤0.80 and perfusion defects as identified on 3-T stress perfusion cardiac magnetic resonance imaging.

Reference: Circ Cardiovasc Interv. 2015;8(8):e002207

Prevalence, clinical features, and prognosis of acute myocardial infarction due to attributable to coronary artery embolism

Authors: Shibata T et al.

Summary: This article describes the prevalence, clinical features and prognosis of coronary artery embolism amongst 1776 Japanese patients who presented with de novo AMI between 2001 and 2013. Coronary artery embolism was diagnosed according to histological, angiographic, and other diagnostic imaging findings. The prevalence of coronary artery embolism was 2.9% (n=52), including 8 (15%) patients with multivessel coronary artery embolism. Atrial fibrillation was the most common cause (n=58, 73%). Only 39% of patients with a coronary artery embolism were treated with vitamin K antagonists, and the median international normalised ratio was 1.42. Eighteen of the 30 patients with nonvalvular atrial fibrillation in the coronary artery embolism cohort had a CHADS2 score of 0 or 1. Upon re-evaluation with the CHA2DS2-VASc, 61% of the patients were reassigned to a higher risk category. During a median 49 months of follow-up, coronary artery embolism and thromboembolism recurred in 5 atrial fibrillation patients. The 5-year MACCE rate (cardiac death, fatal arrhythmia, or recurrent thromboembolism) was 27.1%. In the propensity score–matched cohorts (n=45 each), Kaplan-Meier analysis showed a significantly higher incidence of cardiac death among patients with a coronary artery embolism as compared with patients who did not have a coronary artery embolism (hazard ratio 9.29, 95% CI, 1.13 to 76.5; p < 0.001).

Comment: This interesting paper describes the ~3% of patients identified from this Japanese cohort (the frequency could vary in other ethnic groups), who appear to have AMI due to a coronary artery embolism. Of those with a coronary embolism, ~60% with non-valvular atrial fibrillation had a CHADS score of 0-1. Patients with coronary artery embolism were at higher risk of 5-year mortality, suggesting identification at initial angiography is important to ensure close follow-up.