Welcome to issue 15 of Acute Coronary Syndrome Research Review.

Research published recently in the European Heart Journal suggests that an early discharge after a rapid rule-out of acute myocardial infarction with a single combined testing of troponin and copeptin at presentation to the emergency department or chest pain unit is safe and may also shorten length of stay in low-to-intermediate risk patients with suspected acute coronary syndrome. The study researchers call for more studies to evaluate this new strategy under routine conditions and in a larger number of patients.

Another paper reports findings from the first systematic review of the published literature concerning patients with myocardial infarction with nonobstructive coronary arteries (MINOCA). No guidelines exist as to the management of these patients. This review proposes that MINOCA be considered as a working diagnosis that requires routine evaluation for multiple treatable underlying causes.

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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Prospective validation of a 1-hour algorithm to rule-out and rule-in acute myocardial infarction using a high-sensitivity cardiac troponin T assay

Authors: Reichlin T et al.

Summary: This investigation evaluated 1320 patients presenting to the emergency department with a suspected acute myocardial infarction (AMI) to validate a novel 1-hour algorithm using high-sensitivity cardiac troponin T measurement. The algorithm classified patients as “rule-out” (59.5%), “rule-in” (16.4%), or “observational zone” (24.1%). AMI was the final diagnosis in 17.3% of patients. The rule-out zone had a sensitivity of 99.6% for AMI and a negative predictive value of 99.9%; the specificity of the rule-in zone was 95.7%, with a positive predictive value of 78.2%. The 1-hour algorithm provided higher negative and positive predictive values than the standard use of high-sensitivity cardiac troponin T cut-off values (both p<0.05). Cumulative 30-day mortality was 0.0%, 1.6% and 1.9% in the rule-out, observational and rule-in groups, respectively (p=0.001).

Comment: This study confirms other recent study findings of the ability of paired high-sensitivity troponin T levels 1h apart to rule-in or rule-out AMI in ~75% of patients evaluated for a possible AMI in emergency departments. The study contains slightly higher risk patients, with 17.3% having AMI diagnosed, compared to the prior commonly reported frequency of AMI of ~10%. The finding that ~25% of patients should remain in emergency departments for longer observation is also consistent. Whether acute CT angiography can cost-effectively expedite the management of these patients could be evaluated in future studies.

Reference: CMAJ. 2015 Apr 13. [Epub ahead of print]

Abstract
High sensitivity-troponin elevation secondary to non-coronary diagnoses and death and recurrent myocardial infarction: An examination against criteria of causality

Authors: Chew DP et al.

Summary: These researchers assessed the causal relationship between peak in-hospital troponin and subsequent MI in a cohort of 30,161 patients presenting with AMI to South Australian public hospitals over a 1-year period (September 2011 through September 2012). Using the International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM) codes, patients were discharged with coronary (n=12,645; 33.6%), non-coronary cardiac (n=3,237; 8.5%) and non-cardiac diagnoses (n=22,079; 57.9%). Troponin >14 ng/L was observed in 43.6%. In competing-risk flexible parametric survival models, the relationship between troponin and cardiac mortality was stronger among the non-coronary diagnosis group (troponin 1000 ng/L: coronary hazard ratio [HR] 5.1 [95% CI, 4.0 to 6.6] vs non-coronary HR 16.3 [95% CI, 12.6 to 22.4]). In both groups, there was a marked temporal hazard for cardiac death within 30 days. Among non-diagnostic diagnoses, the hazard for recurrent MI was higher but did not vary with time.

Comment: This study examined high-sensitivity troponin T (hs-TnT) levels measured in patients evaluated for a possible AMI in South Australia. The majority of patients had a non-cardiac diagnosis and slightly fewer than half of all patients had elevated hs-TnT levels. Interestingly, mortality incremented more steeply with higher hs-TnT levels in patients with non-cardiac rather than cardiac diagnoses. However, there is a lack of evidence regarding optimal management of these patients.

* John French is a co-author


Early discharge using single cardiac troponin and copeptin testing in patients with suspected acute coronary syndrome (ACS): a randomized, controlled clinical process study

Authors: Möckel M et al.

Summary: This study randomised 902 low-to-intermediate risk patients with suspected acute coronary syndrome (ACS) to either the standard clinical process for the acute diagnostic assessment of suspected ACS (n=451) or to a process with single combined testing of copeptin and troponin at admission (n=451). In the copeptin group, patients with negative troponin and copeptin values at admission were eligible for discharge after final clinical assessment. Over the 30-day follow-up period, an intention-to-treat analysis revealed that 22 patients (5.1%) in the standard group and 23 (5.19%) in the copeptin group developed a major adverse cardiac event (MACE, defined as death, survived sudden cardiac death, AMI, re-hospitalisation for ACS, acute unplanned percutaneous coronary intervention (PCI), coronary artery bypass grafting, or documented life threatening arrhythmias); corresponding MACE proportions in the per protocol analysis were 3.4% and 3.0%, respectively. Sensitivity analyses corroborated these results. In the copeptin group, discharged copeptin-negative patients had an event rate of 0.6% (2/362).

Comment: The early discharge of ‘troponin –ve’ patients presenting to emergency departments with chest pain suspected of ischaemic origin is an ongoing goal of systems of care in health services. While accelerated testing regimens of high-sensitivity troponin is attractive, they only rule-in or rule-out an ACS in 75–80% of cases, indicating a need for additional discriminative testing. Whether testing is another biomarker, such as copeptin, or another modality such as CT coronary angiography, needs to be tested in larger studies.


The impact of smoking on long-term outcome of patients with premature (<35 years) ST-segment elevation acute myocardial infarction

Authors: Rallidis LS et al.

Summary: Long-term outcomes are reported for 257 patients (average age of 32.2 years) who had sustained a premature ST-segment elevation AMI when aged <35 years and were followed for up to 18 years (median 9.1 years). At baseline, the vast majority were smokers (83.7%). During follow-up, 56.6% of patients reported continuation of smoking. Ninety-one (38.4%) patients had recurrent MACE (13 deaths, 59 reports of ACS, 2 arrhythmias, and 17 revascularisations). In multivariable Cox regression analysis adjusted for conventional risk factors, persistence of smoking. Ninety-one (38.4%) patients had recurrent MACE (13 deaths, 59 reports of ACS, 2 arrhythmias, and 17 revascularisations). In multivariable Cox regression analysis adjusted for conventional risk factors, persistence of smoking. Ninety-one (38.4%) patients had recurrent MACE (13 deaths, 59 reports of ACS, 2 arrhythmias, and 17 revascularisations). In multivariable Cox regression analysis adjusted for conventional risk factors, persistence of smoking. Ninety-one (38.4%) patients had recurrent MACE (13 deaths, 59 reports of ACS, 2 arrhythmias, and 17 revascularisations). In multivariable Cox regression analysis adjusted for conventional risk factors, persistence of smoking.

Comment: This paper on AMI in young patients emphasizes the pivotal role of smoking cessation in preventing further events. While there was quite a high frequency of recurrent events, the crude annual mortality rate was relatively low at 1.4%. As this commentator and others have previously reported on an increased rate of inherited thrombophilias in young MI survivors such as is reported here, data on the frequency of these mutations, their influence if any on late events and the use of anticoagulants would have been of interest.


Systematic review of patients presenting with suspected myocardial infarction and non-obstructive coronary arteries

Authors: Pasupathy S et al.

Summary: This systematic review examined the available evidence from 26 publications regarding the prevalence, clinical risk factors, and 12-month prognosis in patients with MI with nonobstructive coronary arteries (MINOCA); 46 publications were evaluated for the major underlying pathophysiological attributes of this condition. The overall prevalence of MINOCA was calculated at 6% with a mean presentation rate of 55 years among 40% women. In comparison with patients with MI associated with obstructive coronary artery disease, those with MINOCA were more likely to be younger and female but less likely to have hyperlipidaemia, although other cardiovascular risk factors were similar. All-cause mortality at 12 months was lower in the MINOCA cohort (4.7%) compared with the patients with MI associated with obstructive coronary artery disease (6.7%). Of the publications investigating the potential mechanisms responsible for MI in MINOCA, only 24% of patients had features consistent with a subendocardial infarct on cardiac magnetic resonance imaging (cMRI), 33% of patients had features of myocarditis and 26% had no detectable myocardial abnormalities. Coronary artery spasm was inducible in 28% of MINOCA patients, and there was evidence of an inherited thrombotic disorder in 14%.

Comment: The mortality for MI and non-obstructive coronary artery disease on angiography has historically been lower than in those with obstructive disease, in part probably because patients are often younger. The findings on cMRI were typical of MI in ~1/4 with slightly more having features of subendocardial infarction. Coronary artery spasm was inducible in 1/4 patients, and thrombophilias were detected in ~1/7 (similar to earlier reports). Patients with MI and non-obstructive (or no) angiographic coronary stenosis further in evaluation usually with cMRI, thrombophilia screening, though if or when provocative testing for coronary spasm should occur still requires clarification.

Reference: Circulation. 2015;131(10):861-70 Abstract

Prognostic significance of serum creatinine and its change patterns in patients with acute coronary syndromes

Authors: Marzeni G et al.

Summary: This Italian group of researchers investigated the relationship between serum creatinine (sCr) levels at baseline, changes during hospitalisation, and in-hospital mortality in 2756 patients hospitalised with ACS. sCr was measured at admission and then daily, until discharge from the coronary care unit. Patients were grouped according to the maximum sCr change observed: <0.3 mg/dL change from baseline (stable renal function group; n=2163 [78%]), ≥0.3 mg/dL decrease (improved renal function group; n=292 [11%]), and ≥0.3 mg/dL increase (worsening renal function group; n=301 [11%]). In-hospital mortality in these 3 groups was 0.5%, 2%, and 14% (p<0.001), respectively. Peak sCr value was a more powerful predictor of mortality (area under the curve [AUC] 0.86; 95% CI, 0.81 to 0.92) than the initial sCr value (AUC 0.69; 95% CI, 0.63 to 0.77; p<0.001). Combining baseline sCr and its changes over time improved the stratification of mortality risk.

Comment: This paper addressed the changes in creatinine levels in patients with ACS. The creatinine level increases of >0.27 µmol/L were associated with 14% mortality compared to those with stable or falling creatinine levels with very low mortality. While the paper is of interest, there are many baseline and interventional characteristics which are not included that confounds interpretation of this apparently simple take-home message.

Incidence, temporal trends, and prognostic impact of heart failure complicating acute myocardial infarction. The SWEDHEART Registry (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies): a study of 199,851 patients admitted with index acute myocardial infarctions, 1996 to 2008

Authors: Desta L et al.

Summary: Using data from Sweden’s nationwide coronary care unit registry SWEDHEART, these researchers examined temporal trends in the incidence and outcomes of heart failure (HF) complicating AMI amongst 199,851 patients admitted to hospital for index AMIs between 1996 and 2008. Over the study period, the incidence of HF declined from 46% to 28% (p<0.001). This decrease was more pronounced in patients with ST-segment elevation myocardial infarction (STEMI) and left bundle branch block (from 50% to 28%) compared with those with non-ST-segment elevation myocardial infarction (NSTEMI) (from 42% to 28%) (p<0.001). The in-hospital, 30-day, and 1-year mortality rates for patients who developed HF due to the index MI decreased over the years from 19% to 13%, from 23% to 17%, and from 36% to 31%, respectively (p<0.001 for all). Thirteen-year survival analysis revealed higher mortality in patients with HF compared with those without HF (adjusted HR 2.1; 95% CI, 2.06 to 2.13).

Comment: This report from the SWEDHEART registry documents the improvement in mortality among a very large cohort of patients (aged ~71 years) with MI (STEMI and NSTEMI), with or without complicating heart failure (adjusted mortality HR for CHF 2.1). Congestive heart failure (CHF) frequency declined markedly over this period, in spite of a small increase in the proportion of women. The mortality for CHF also declined over the study period. The proportion increased over the study era of patients with STEMI/LBBB receiving either fibrinolytic therapy or primary PCI. Such large registries provide useful data about the incidence and outcomes of unselected patients with CHF complicating AMI.

Reference: JACC Heart Fail. 2015;3(3):234-42

Long-term prognosis and risk heterogeneity of heart failure complicating acute myocardial infarction

Authors: de Carvalho LP et al.

Summary: This investigation examined the long-term prognosis of acute heart failure graded by Killip class in 15,235 patients hospitalised for AMI from 2000 to 2005. Vital status for each patient through to 1 March 2012 was linked to national death records. A stepwise gradient in the adjusted HR for 12-year mortality was observed with increasing Killip class: class I (n=10,123), HR 1.00 (reference group); class II (n=2913), HR 1.13 (95% CI, 1.06 to 1.21); class III (n=1217) HR 1.49 (95% CI, 1.37 to 1.62); and class IV (n=898), HR 2.80 (95% CI, 2.53 to 3.10). In a landmark analysis excluding deaths <30 days after admission, patients in Killip class IV had lower adjusted long-term mortality than those in class III. The adjusted HR for 12-year mortality comparing Killip class IV with Killip class III in patients <60 years of age was 1.71 (95% CI, 1.33 to 2.19; p<0.001) and in patients >60 years of age was 2.30 (95% CI, 2.07 to 2.56; p<0.001).

Comment: After 5 decades simple clinical features in the Killip classification robustly predicted 12-year mortality after AMI. The heterogeneity in early versus late risk in patients with Killip class IV heart failure emphasises the importance of appropriate early treatment of patients with cardiogenic shock.

Reference: Am J Cardiol. 2015;115(7):872-8

Independent commentary by Professor John French, Director of Coronary Care and Cardiovascular Research at Liverpool Hospital, Sydney, and is a 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 committees 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 AGI 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.
Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management

Authors: Vaglimigli M et al.

Summary: Patients with ACS with or without STEMI who were about to undergo coronary angiography and PCI were randomised to radial (n=4107) or femoral (n=4207) access. The 30-day co-primary outcomes were MACE (defined as death, MI, or stroke) and net adverse clinical events (defined as MACE or Bleeding Academic Research Consortium [BARC] major bleeding unrelated to coronary artery bypass graft surgery). MACE was reported in 8.8% of patients with radial access compared with 10.3% of patients with femoral access (rate ratio [RR] 0.85; 95% CI, 0.74 to 0.99; p=0.0307), non-significant at α of 0.025. Net adverse clinical events were reported in 9.8% of the radial access cohort and in 11.7% of the femoral access cohort (RR 0.83; 95% CI, 0.73 to 0.96; p=0.0092). The difference was driven by a reduction in BARC major bleeding (1.6% vs 2.3%; RR 0.67; 95% CI, 0.49 to 0.92; p=0.013) and all-cause mortality (1.6% vs 2.2%; RR 0.72; 95% CI, 0.53 to 0.99; p=0.045).

Comment: This large trial examined the outcomes after having radial versus femoral intervention, and consistent with earlier studies there was reduced BARC major bleeding, and mortality; respective risk ratios were 0.67 and 0.72. The totality of the data favouring a radial approach in patients with an ACS, with or without ST elevation, is compelling. Whether in the future there will be interventionists without sufficient femoral experience for the small number of mainly elective procedures that are desirably performed by the femoral approach is conceivable.


A randomized trial of primary PCI with or without routine manual thrombectomy

Authors: Jolly SS et al.

Summary: In this study, 10,732 patients with STEMI undergoing primary PCI were randomised to a strategy of routine upright manual thrombectomy or to PCI alone. The primary outcome (a composite of death from cardiovascular causes, recurrent MI, cardiogenic shock, or New York Heart Association class IV heart failure within 180 days) occurred in 6.9% of patients in the thrombectomy group and in 7.0% of patients in the PCI-alone group (HR in the thrombectomy group, 0.99; 95% CI, 0.85 to 1.15; p=0.88). The rates of cardiovascular death (3.1% with thrombectomy vs 3.5% with PCI alone; HR 0.90; 95% CI, 0.73 to 1.12; p=0.34) and the primary outcome plus stent thrombosis or target-vessel revascularisation (9.9% vs 9.8%; HR 1.00; 95% CI, 0.89 to 1.14; p=0.95) were also similar. Routine manual thrombectomy was associated with an increased rate of stroke within 30 days (0.7% vs 0.3%; RR 2.28; 95% CI, 1.00 to 5.19; p=0.049).

Comment: This large trial examined the role of routine thrombectomy in STEMI patients undergoing primary PCI and found no benefit, as with the slightly smaller-sized TASTE trial 18 months earlier. Indeed, stroke was increased in TOTAL, which is not particularly surprising given the challenges of ensuring all aspirated material remains in the catheter (rather than in the aorta). While there is no role for routine thrombus aspiration during primary PCI, are there specific circumstances when this is still reasonable?


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