

ABSTRACTS OF SOCIETIES

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Long Term Outcome of Asymptomatic Left Ventricular Dysfunction in an Urban Population

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Background: Numerous clinical trials and hospital based series have documented the high mortality rate associated with left ventricular systolic dysfunction. Population data, however, are scarce. We report on the long term mortality associated with left ventricular dysfunction (both symptomatic and asymptomatic) in a population-based cohort randomly sampled from an urban community. **Methods:** Two thousand men and women aged 25-74 were randomly sampled from the North Glasgow population in 1992-3. Of these, 1640 had an echocardiogram to document LV systolic function. A left ventricular ejection fraction $\leq 30\%$ was defined as significant

systolic dysfunction (LVD). Symptomatic LVD was LVD with dyspnoea or the prescription of a loop diuretic agent. A 12-lead ECG, full medical history and plasma BNP concentrations were also documented. The cohort has been followed up for a mean duration of 12.2 years. **Results:** At the baseline screen in 1992/1993, 2.9% of the cohort had LVD, 1.5% symptomatic LVD and 1.4% asymptomatic. At a mean follow up of 12.2 years, the all cause mortality rate in the entire cohort was 15.9% and 5.6% in those free of cardiovascular disease. The mortality rates in those with symptomatic and asymptomatic LVD were 60% and 40% respectively. A baseline BNP concentration in the top quartile was associated with a hazard ration for mortality c.f the lowest quartile of 4.7 (95% CI 3.0-7.3), $p < 0.0001$. In a Cox Proportional Hazard model, the independent predictors of mortality are shown in the table (see www.smj.org.uk). **Conclusions:** The long term prognosis of LVD in the general population is poor. Asymptomatic LVD also confers a high mortality rate. BNP was an accurate test at diagnosing LVD in this population. It also identifies those at highest risk of a poor outcome. Strategies to detect and treat LVD earlier using BNP may help improve its adverse outcome.

Endothelial Tissue Plasminogen Activator Release Predicts Future Adverse Cardiovascular Events in Patients with Stable Coronary Heart Disease

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Background: The fibrinolytic factor tissue plasminogen activator (t-PA) is rapidly released from the endothelium and is a major determinant of vessel patency and clinical sequelae following acute coronary plaque rupture. We assessed whether acute t-PA release predicts future atherothrombotic events in patients with stable coronary heart disease (CHD). **Methods:** Plasma t-PA and plasminogen activator inhibitor (PAI-1) antigen concentrations and net release of t-PA were determined in response to intra-arterial substance P infusion (2-8 pmol/min) in 97 patients with proven CHD (stable anginal symptoms for ≥ 3 months). Forearm blood flow was measured during infusion of substance P and sodium nitroprusside (2-8 $\mu\text{g}/\text{min}$). Cardiovascular events, including death from cardiovascular causes, myocardial infarction (MI), ischaemic stroke (CVA) and hospitalisation for myocardial ischaemia, were determined through the Information and Statistics Division of the National Health Service and the General Register Office in Scotland. **Results:** Patients experiencing cardiovascular events ($n=20$; median follow-up, 34 months) had similar baseline characteristics to those free of events ($P=\text{ns}$ for all). Substance P caused a dose-dependent increase in plasma t-PA antigen ($P<0.001$, ANOVA) but not PAI-1 ($P=\text{ns}$) concentrations. Net release of t-PA was reduced by 91% in patients with death/MI/CVA, and 44% for those with Death/MI/CVA/hospitalisation for myocardial ischaemia ($p=0.02$; ANOVA for both). Major adverse cardiovascular events increased with decreasing t-PA release ($P=0.04$, log rank) with the lowest quartile having the highest rate of adverse events ($P=0.02$, versus upper 3 quartiles). Endothelium-dependent and independent vasodilatation did not differ between the groups. **Conclusion:** Endothelial fibrinolytic capacity, as measured by stimulated t-PA release, predicts the future risk of adverse cardiovascular events in patients with coronary heart disease. We suggest that endothelial fibrinolytic capacity is a powerful novel determinant of cardiovascular risk and that therapeutic interventions augmenting acute t-PA release represent a novel approach to the prevention of future cardiovascular events.

First North American Experience with Percutaneous Aortic Valve Replacement (CoreValve) in Patients Unsuitable for Surgical Aortic Valve Replacement

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Background: Percutaneous aortic valve replacement (PAVR) is an emerging, alternative to palliative medical therapy for non-surgical patients with severe aortic stenosis (AS). We describe the first North American experience of PAVR with the CoreValve

Revalving™ system, which includes a self-expandable porcine bioprosthesis within a nitinol frame. **Methods:** Patients with symptomatic, severe (area $< 0.6 \text{ cm}^2/\text{m}^2$) AS who had been refused aortic valve surgery because of comorbidity were enrolled. Exclusion criteria included severe peripheral vascular disease and major comorbidity (life expectancy < 1 year). A multi-disciplinary approach involved general anaesthesia, surgical peripheral arterial access and femoral vein-femoral artery cardiopulmonary bypass. Aortic balloon valvuloplasty was performed first, then retrograde CoreValve PAVR. **Results:** Between March 2005–2006, 9 men and 9 women (mean age 82(10) years; range 64–90 years) were referred for PAVR. Two men and 4 women were offered PAVR and gave informed consent. Procedural success was achieved in 4 patients. One patient who had obstructive coronary artery disease simultaneously treated with percutaneous coronary intervention (PCI). In all 4 cases, the aortic bioprosthetic valve area was $> 1.2 \text{ cm}^2$ and paravalvular regurgitation was \leq Grade I. In the unsuccessful cases, the CoreValve system could not be advanced because of aorto-iliac disease. No major complications occurred. Follow-up (range 1 to 4 months) confirmed haemodynamic and functional improvements in all PAVR cases. Four of the referred patients who did not undergo PAVR died. **Conclusions:** PAVR is feasible in selected patients. Procedural success may improve through careful screening and anticipated improvements in device design.

Does Scotland Need a Left-ventricular Assist Device Programme?

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Introduction: Patients with severe acute heart failure (HF) are at high risk of death. Interventional options include urgent cardiac transplantation and implantation of left ventricular assist devices (LVADs). Patients who are eligible for cardiac transplantation receive LVADs if they are failing on supportive measures. LVADs can be implanted as destination therapy. Only 2 Scottish patients have received LVADs. Does Scotland need an LVAD programme? **Aim:** We aim to characterise and quantify the population in Scotland that might benefit from an LVAD. **Methods:** All coronary care units (CCUs) in Scotland were invited to participate in the audit. Charge nurses were asked to prospectively record admissions of all patients admitted with either: 1) acute decompensated, inotrope-dependent, HF or 2) patients with post-myocardial infarction (MI) cardiogenic shock. The audit ran for a two-month period in 2005. **Results:** 93% ($n=25$) of Scotland's CCU units agreed to participate. 10 patients were identified. 8 were male, 2 were female. Mean age was 59.9 (range: 45 - 68). 2 patients had acute decompensated, inotrope-dependent HF. 8 patients had post-MI cardiogenic shock. 3 patients with post-MI cardiogenic shock had had percutaneous intervention and insertion of an intra-aortic balloon pump (IABP). 60% ($n=6$) died before discharge from CCU (5 post-MI; 1 acute HF). 5 (50%) had a contraindication to transplantation. 3 (30%) had an absolute contra-indication to VAD implantation. **Conclusion:** During this 2-month period, 7 acutely unwell patients in this Scottish audit were identified that may have benefited from LVAD. If we extrapolate this figure to achieve an annual figure, 42 patients in Scotland could enter a VAD programme per year.

Diesel Exhaust Inhalation Increases Thrombus Formation In Man

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Background: Epidemiological data suggest that transient exposure to traffic-derived particulate air pollution may be a trigger for acute myocardial infarction although the mechanism is unclear. In urban areas, diesel engines are considered to be the source of particulate air pollution. In an animal model, tracheal instillation of diesel exhaust particles enhances arterial and venous thrombus formation *in vivo*. The aim of this study was to investigate the effect of inhalation of diesel exhaust on thrombus formation in man using an *ex vivo* model of thrombosis. **Methods:** In a double-blind randomised cross-over study, 7 healthy men were exposed to diluted diesel exhaust (300 µg/m³) or air during intermittent exercise for 2 hours. Thrombus formation was measured at 6 hours using the Badimon *ex vivo* perfusion chamber at low (212 s⁻¹) and high (1,690 s⁻¹) shear rates with porcine aortic tunica media as the thrombogenic substrate. Aortic specimens were fixed and stained with combined Masson's trichrome-elastin stain. Total thrombus area was measured histologically using computerized planimetry. All data are expressed as mean ± SEM. **Results:** Compared to air, diesel exhaust inhalation increased thrombus area under both high (27%±9%; n=7; P=0.02) and low (20%±9%; n=7; P=0.08) shear stress flow conditions. **Conclusions:** Inhalation of diesel exhaust increases *ex vivo* thrombus formation in man. These findings provide a potential mechanism that links exposure to traffic-derived air pollution with acute atherothrombotic events including acute myocardial infarction.

Connexin 43 Mediates Endothelium-Dependent Hyperpolarising Factor Induced Vasodilatation in Human Resistance Arteries

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Background: The nature of endothelium-derived hyperpolarising factor (EDHF) is controversial but gap junctions appear to have a central role. Connexin mimetic peptides (CMPs), designated as ^{37,43}Gap27, ⁴⁰Gap27 and ⁴³Gap26 according to homology with the three major vascular connexins (Cx37, 40 and 43), were used to assess the role of gap junctions in EDHF-mediated relaxation of human arteries. **Methods and Results:** Resistance arteries were obtained from subcutaneous fat of healthy women undergoing elective cesarean section. Using wire myography, responses to the endothelium-dependent vasodilator bradykinin (BK) were assessed after precontraction. L-NAME and indomethacin (nitric oxide synthase and cyclooxygenase inhibitors respectively) attenuated maximal relaxation to BK (R_{max}) by ~50% (n=27).

Co-incubation of vessels with L-NAME, indomethacin and the combined CMPs (37,43Gap27, 40Gap27 and 43Gap26, 300 µmol/L each) almost abolished relaxation to BK (R_{max} 12.2 ± 3.7% [n=6]). After incubation with L-NAME and indomethacin, the addition of either ^{37,43}Gap27 or ⁴⁰Gap27 (900 µmol/L) had no effect on R_{max} whilst ⁴³Gap26 (900 µmol/L) caused marked inhibition (R_{max} 21 ± 6.4%, p = 0.005 vs. L-NAME plus indomethacin alone; n=5 for each). Endothelium-independent vasorelaxation to sodium nitroprusside was unaffected. Immunohistochemistry revealed Cx37, 40 and 43 in the endothelium and vascular smooth muscle. **Conclusions:** In pregnant women, EDHF-mediated vasorelaxation of subcutaneous resistance arteries is dependent on Cx43 and gap junctions. This is the first study to demonstrate the central role of connexins in human EDHF-mediated vasorelaxation.

Post-operative Cardiac Troponin I Levels Predict Outcome from Cardiac Surgery

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Background: Cardiac surgery may be associated with significant peri-operative myocardial damage. A number of factors may contribute to this. Interpretation of troponin levels in the post-operative period may, therefore, be complex and the clinical implications are uncertain. The current study assesses the prognostic importance of post-operative troponin release, taking into account potential confounding variables. **Methods:** Between April 2000 and September 2002, 1,442 consecutive patients underwent cardiac surgery at our institution. Eighty-six patients were excluded having undergone emergency surgery, congenital repair, or who had suffered recent (<7 days) myocardial infarction. Two patients died intra-operatively. Cardiac troponin I (cTnI) was measured 24 hours post-operatively in the remaining 1,365 patients, using the Bayer ADVIA Centaur automated immunoassay. Baseline clinical and demographic data was obtained including EuroSCORE, details of medication and peri-operative electrocardiographic changes. The primary endpoint was all-cause mortality using a vital event search by the General Register Office for Scotland. **Results:** Mortality at 30 days, 1 and 3 years after operation was 3%, 5% and 9% respectively. In a logistic regression analysis with backward stepwise selection, cTnI was found to be independently predictive of mortality even after adjustment for all other variables including operation complexity and EuroSCORE; 30 days (odds ratio [OR] 1.14 per 10µg/L, 95% CI 1.05-1.24; p = 0.002), 1 year (OR 1.10 per 10µg/L, 95% CI 1.03-1.18; p = 0.006), and 3 years (OR 1.07 per 10µg/L, 95% CI 1.00-1.15; p = 0.04). After adjustment for EuroSCORE and operation type, patients with cTnI in the upper quartile were at greatest risk (X² 14.50 v quartile 1, p<0.001). **Conclusion:** Elevated cTnI levels 24 hours following cardiac surgery are associated with poor short, medium and long-term outcomes, and remain independently predictive when adjusted for other potentially confounding variables. Cardiac TnI levels in the highest quartile at 24 hours are associated with a particularly increased mortality.

Treatment Delays in the Referral of Patients with ST-Segment Elevation Myocardial Infarction (STEMI) for Emergency Percutaneous Coronary Intervention (PCI)

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Background: The benefit of reperfusion therapy for ST-Elevation Myocardial Infarction (STEMI) is time-dependent. For thrombolytic therapy, complete prevention of myocardial infarction requires administration within 30 minutes of the onset of STEMI. Beyond this time window, the degree of myocardial salvage progressively diminishes with little benefit beyond 6 hours. The importance of time to presentation on mortality has also been shown in randomised controlled trials of primary percutaneous coronary intervention (PCI) versus thrombolytic therapy. 30-day mortality increases with treatment delay for both therapies, with a greater mortality for those receiving thrombolysis at equivalent times from onset of symptoms. **Methods:** We carried out a 6-month audit (September 05 - March 06) of all patients referred to the Western and Royal Infirmarys, Glasgow, for emergency PCI for STEMI. We recorded data on gender, age, referring hospital, STEMI site and reason for referral. We also analysed the time of symptom onset, call for medical assistance, diagnostic ECG, "90" minute ECG (to assess reperfusion), referral for emergency transfer, arrival at PCI site, and door to balloon time (ACC/AHA target < 30 mins). **Results:** 158 patients were transferred for emergency PCI. 116 patients were male and 42 female. The age range was 32-84 years (mean 60). The site of STEMI was 56.3% inferior/posterior, 43.0% anterior and 0.6% LBBB. The majority of patients were referred for rescue PCI (71.5%). 116 patients went directly to the cath lab and 101 had PCI. The mean time from referral to arrival at PCI site was 109 minutes (range 35-515). **Conclusions:** Significant delays were identified in determining the need for emergency PCI and in subsequently transporting patients to and within the PCI sites. These delays potentially compromise the outcome of emergency PCI for STEMI. In order to provide this service effectively in the West of Scotland, healthcare systems need to organise prompt assessment and selection of appropriate patients for rapid and safe ambulance transfer to a PCI centre.

Magnetic Resonance Myocardial Perfusion Imaging (MRMPI) for the Detection of Myocardial Ischaemia as Determined by Pressure Wire Derived Fractional Flow Reserve (FFR)

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Background: Magnetic resonance myocardial perfusion imaging (MRMPI) for the detection of functionally significant coronary heart disease (CHD) has previously been validated by comparison with radioisotope perfusion imaging and/or quantitative coronary angiography (QCA).

Neither of these techniques represents a true gold standard and in particular there is only an approximate relationship between angiographic parameters of lesion severity and functional significance. In previous studies, pressure wire derived fractional flow reserve (FFR) values <0.75 correlate very closely with objective evidence of reversible ischaemia. Accordingly we have compared MRMPI with FFR to determine the sensitivity, specificity, positive (PPV) and negative predictive values (NPV) of this technique. In addition we have also compared MRMPI with QCA. **Methods:** Eighty-six patients with chest pain were referred for coronary angiography or intervention and underwent MRMPI in the week prior to angiography. This was performed on a Siemens Sonata 1.5Tesla scanner (Erlangen, Germany) with perfusion imaging of 3 short axis slices obtained using a turboFLASH sequence (TI 90ms, TE 0.99ms, TR 173ms, Flip Angle 8°, Matrix 80 x 128). Maximal hyperaemia was achieved using intravenous adenosine (140µg/kg/min). The first pass bolus contained 0.1mmol/kg of gadolinium (Omniscan, Amersham Health, Oslo, Norway) power injected at 5ml/sec (Medrad, Pittsburgh, PA) followed by a 20ml saline bolus. During coronary angiography the FFR was recorded in all patent major epicardial coronary arteries using a coronary pressure wire (RADI™, Uppsala, Sweden) with hyperaemia induced using intravenous adenosine as above. An FFR value of <0.75 was taken as the cut off for the diagnosis of significant CHD. MRMPI scans were analysed by a blinded independent experienced observer. QCA was also performed for all major epicardial coronary arteries with stenoses ≥70% being considered significant (Centricity Cardiology CA1000, GE). **Results:** Sixty-three of 86 (73%) patients were male. The mean age was 60 years (SD=9, Range 37-80). MRMPI revealed 102 perfusion defects in 256 coronary artery segments (40%). Ninety-one of these were confirmed to be physiologically abnormal with an FFR < 0.75, giving a PPV of 89%. There were 154 normally perfused coronary artery territories on MRMPI, 147 of which had an FFR ≥ 0.75 giving a NPV of 96%. The sensitivity and specificity of MRMPI for the detection of significant CHD were both 93% using FFR as the gold standard. Of the 102 hypoperfused territories identified by MRI, only 63 had a stenosis of ≥70% in the corresponding coronary artery using QCA. However, of the 155 territories with normal perfusion on MRMPI, 153 had <70% stenosis on QCA. Therefore, the sensitivity, specificity, PPV and NPV are 97%, 80%, 62% and 99% when QCA is used as the gold standard test. **Conclusion:** First pass perfusion MRI can detect significant CHD with a good sensitivity, specificity, PPV and NPV when compared to FFR. The specificity and PPV are lower when you compare this technique with QCA. This adds support to the growing evidence for the use of this technique as an alternative to nuclear perfusion techniques and the diagnostic coronary angiogram.

Implementing Early Treatment of Acute Coronary Syndromes – a national audit.

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Background: National Health Service policy encourages the rapid transfer of patients from accident and emergency (A&E) departments to medical admission units (MAU) to reduce waiting times. This may result in treatment delays. We sought to examine acute coronary syndrome (ACS) management nationally in a telephone audit. **Methods:** In every Scottish hospital, we contacted by telephone a middle grade A&E doctor

and medical doctor, and an A&E nurse. All were asked prespecified questions regarding local management of ACS. This included estimating to the nearest 10% the number of patients treated in A&E with either low molecular weight heparin (LMWH) or clopidogrel. **Results:** Estimates correlated highly between medical and nursing staff ($r=0.88$, $p<0.0001$). This high interdisciplinary agreement suggests results accurately reflect daily practice. Hospitals directly admitting patients to a dedicated chest pain assessment area ($n=6$) were excluded from the analysis. Estimated use of LMWH or clopidogrel in the remaining 19 A&E departments varied according to local policy, falling into three categories (figure 1, see www.smj.org.uk). **1)** 16% aim to transfer patients to MAU for treatment – in these, 16% of patients are treated in A&E prior to transfer. **2)** 53% have no specific policy – in these, 39% of patients are treated in A&E prior to transfer. **3)** 31% aim to treat patients before transfer – in these, 62% of patients are treated in A&E prior to transfer. LMWH was available in all A&E departments but only 79% stocked clopidogrel. **Conclusion:** Early directed therapy saves lives. Despite this, less than a third of the hospitals in Scotland have a policy of commencing therapy in A&E. Even in these, only around two thirds of patients actually receive treatment in the department with resultant potential for treatment delays. Treatment should ideally be started either in A&E, or in dedicated chest pain assessment areas to which patients may be directly admitted. This issue merits urgent national consensus opinion.

Initial Experience in the Remote Monitoring of Implantable Cardioverter Defibrillators

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Background: Internal electrograms (IEGMs) and device parameters are essential to interpret the appropriateness of implantable cardioverter-defibrillator (ICD) therapy and monitor safe functioning of the device but up to now this has required interrogation of the device in the clinic. We report our initial experience with an ICD system capable of monitoring such data automatically within the patient's local environment (so called 'Home Monitoring'); such a system may have considerable advantage to the Scottish patient, particularly where their home is remote from their follow-up centre. **Methods:** We have compared the routine daily data transmitted from Biotronik ICDs capable of 'Home Monitoring', such as lead impedance, with stored lead impedance data obtained at routine clinic follow-up. A transmitter unit collects data from the ICD when placed in a 2-3 meter range of the device. Using roving mobile phone technology, data on device parameters and events is sent to the manufacturers in Berlin and then clinically relevant events are relayed to the patient's cardiologist, usually via e-mail. The daily data transmission rates and the reasons for failure were also assessed using the Biotronik 'Home Monitoring' web site and technical/telephone follow-up. Interpretation of the IEGMs of tachy-arrhythmias detected (and the appropriateness of the devices classification of the arrhythmia) was carried out by experienced observers (CR, PB) on both the transmitted data and also the full data downloaded at the time of a clinic visit. **Results:** 13 patients, from Tayside to Orkney, have so far received an ICD capable of Home Monitoring implanted in Aberdeen Royal Infirmary. Lead impedance data was available for comparison at the 1 month follow up point for both stored and online data in 10 of the 13 patients giving a mean difference

of $1.3\pm 22\Omega$. Two episodes of ventricular tachycardia and 1 episode of supraventricular tachycardia were confirmed as appropriately classified on the basis of the IEGM transmitted by 'Home Monitoring' and confirmed at follow-up. Patient acceptance appears good, none declining the technology or returning the monitoring unit. Overall the rate of data capture was good with $> 80\%$ in $\frac{3}{4}$ of the patients and $> 90\%$ in 5 patients. The mean number of days that no message had been received from the patients ICDs was 32 ± 61 , the majority of missed days arose from 2 Home Monitoring equipment malfunctions that were resolved with the issue of new transmitters. **Discussion:** Our initial experience of Home Monitoring of ICDs suggest that it is feasible and may prove to be the preferred means of follow-up in the future, particularly for patients who live remote from their follow-up centre. Studies assessing system reliability and cost effectiveness are on-going or planned. Further refinement in the technology is anticipated which would enhance clinical utility.

Detection of Additional Cardiac Abnormalities in Patients with Myocardial Infarction using Cardiac Magnetic Resonance Imaging

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Background: Trans-thoracic echocardiography (TTE) is considered the mainstay of assessment of cardiac function following acute myocardial infarction (MI). Contrast enhanced cardiac magnetic resonance imaging (ceMR) is now recognised as a "gold standard" technique for assessing cardiac structure, function and delineation of MI. We report on abnormalities detected, in addition to left ventricular myocardial infarction, using ceMR in patients admitted with acute coronary syndrome. **Methods:** 171 patients (mean age 59 years [range 27-88], 78% male) admitted with ACS underwent TTE and contrast-enhanced CMR ceMR was performed 10 minutes after injection of 0.2 mmol/kg gadolinium-DTPA using a breath-hold segmented turbo FLASH inversion-recovery sequence. **Results:** 127 had an ST-elevation MI (STEMI), 44 a non-STEMI. Infarct site was anterior and antero/lateral in 93 (54%) and inferior in 79 (46%). Left ventricular thrombus was detected in 17 (10%) on ceMR but only 5 (3%) on TTE. Even when the TTE was repeated after the CMR, thrombus was not detectable in 9 of the 12 "TTE negative, ceCMR positive" patients. LV thrombus only occurred in the apex of patients with an anterior MI and the incidence within this subgroup was 17/93 (18%). 14 patients (13 inferior and 1 anterior) had significant right ventricular (RV) infarction identified on ceMR. Two were detected by TTE, one of which had a clinical diagnosis of RV infarction complicating inferior MI. In one patient, a small atrial myxoma was identified on CMR that had not been detected on TTE; this finding led to successful excision of the lesion 6 weeks post-MI. Three patients had a pattern of contrast enhancement that spared the subendocardium and did not match a coronary territory and had normal coronary angiography. One underwent RV endomyocardial biopsy that was in keeping with myocarditis. **Conclusion:** Additional information that altered clinical management was provided by ceMR in 12% (20) of patients admitted with ACS when ceMR was performed together with the current post MI investigations. The improved accuracy in the diagnosis of ACS and its complications using ceMR suggests that this technique should become part of the mainstay of post MI assessment and may be shown to be cost effective.