

# Cardiology

## RESEARCH REVIEW™

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Issue 2 – 2020

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#### Abbreviations used in this issue

**AF** = atrial fibrillation  
**AS** = aortic stenosis  
**CT** = computed tomography  
**CTCA** = CT coronary angiography  
**CVD** = cardiovascular disease  
**ECG** = electrocardiogram  
**HR** = hazard ratio  
**LVEF** = left ventricular ejection fraction  
**MACE** = major adverse cardiovascular events  
**NT-proBNP** = N-terminal pro-B-type natriuretic peptide  
**STEMI** = ST-elevation myocardial infarction

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## Welcome to the latest issue of Cardiology Research Review.

This selection comes in very different times. A number of publications are emerging on COVID-19, but as expected few of them represent systematic research yet. Included are two excerpts from Chinese data, including inherent inconsistencies. Heart disease has not gone away, if anything the COVID-19 crisis will likely make it worse.

Please stay safe in these times and thank you for your support.

Kind regards,

**Professor Alexander Sasse**

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### Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China

**Authors:** Shi S et al.

**Summary:** This study explored the association between cardiac injury and mortality in patients with COVID-19. 416 patients (median age 64 years; 50.7% female) hospitalised with COVID-19 at Renmin Hospital of Wuhan University were included. Common symptoms included fever (80.3%), cough (34.6%), and shortness of breath (28.1%). 82 patients (19.7%) had cardiac injury; these patients were older (median age 74 vs 60 years;  $p < 0.001$ ) and had more comorbidities (e.g. hypertension, diabetes, coronary heart disease, cerebrovascular disease, chronic heart failure, chronic obstructive pulmonary disease and cancer) than patients without cardiac injury. Patients with cardiac injury were more likely to have COVID-19 related complications such as acute respiratory distress syndrome (58.5% vs 14.7%;  $p < 0.001$ ) and acute kidney injury (8.5% vs 0.3%;  $p < 0.001$ ), and had a higher mortality rate (51.2% vs 4.5%;  $p < 0.001$ ) than those without cardiac injury.

**Comment:** 416 COVID patients from a single centre were analysed for this study. 19.7% had evidence of cardiac injury, defined by high-sensitivity troponin I levels. Among other parameters, NT-proBNP levels were higher in this population, symptoms were similar, but chest pain was more common, and patients were older (74 vs 60 years). Only 26% of these patients had an ECG. The mortality rate was higher among patients with versus without cardiac injury (51.2% vs 4.5%;  $p < 0.001$ ). The mechanism of cardiac injury and the impact of treatment remain unclear.

**Reference:** *JAMA Cardiol* 2020; published online Mar 25

[Abstract](#)


  
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## Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19)

**Authors:** Guo T et al.

**Summary:** This study evaluated the association of underlying CVD and myocardial injury with fatal outcomes in patients with COVID-19. 187 patients (mean age 58.5 years) with confirmed COVID-19 disease at the Seventh Hospital of Wuhan City were included. 66 (35.3%) patients had underlying CVD including hypertension, coronary heart disease and cardiomyopathy, and 27.8% had myocardial injury (elevated troponin T [TnT] levels). Mortality rates during hospitalisation were 7.62% for patients without underlying CVD and normal TnT levels, 13.33% for those with underlying CVD and normal TnT levels, 37.50% for those without underlying CVD but elevated TnT levels, and 69.44% for those with underlying CVD and elevated TnT levels. Patients with elevated TnT levels had more frequent malignant arrhythmias, and were more likely to need glucocorticoid therapy (71.2% vs 51.1%) and mechanical ventilation (59.6% vs 10.4%) than patients with normal TnT levels.

**Comment:** Another paper that retrospectively summarised data from COVID patients, fairly raw data up for interpretation. Elevated TnT levels were used as a discriminator, and 28% of patients were allocated to significant myocardial injury. This group was older and had more cardiovascular risk factors. D-dimer levels were also much higher in this group. Mortality was markedly higher in patients with elevated plasma TnT levels than in patients with normal TnT levels (59.6% vs 8.9%). The authors noted that cardiovascular injury went along with inflammatory changes. Little reference was made to ECG and echo. The in-hospital mortality in this cohort was 8.9%.

**Reference:** *JAMA Cardiol* 2020; published online Mar 27

[Abstract](#)

## Egg consumption and risk of cardiovascular disease

**Authors:** Drouin-Chartier J-P et al.

**Summary:** This analysis of 3 large cohort studies (Nurses' Health Study [NHS] 1980–2012, NHS II 1991–2013, and Health Professionals' Follow-Up Study 1986–2012) investigated the association between egg intake and CVD. During 32 years of follow-up (>5.54 million person-years), 14,806 participants in the 3 cohorts had incident CVD. Pooled multivariable analysis showed that consumption of at least 1 egg per day was not associated with incident CVD risk after adjustment for lifestyle and other dietary factors. An updated meta-analysis (1,720,108 participants, 139,195 CVD events) found that an increase of 1 egg per day was not associated with CVD risk. Results were similar for coronary heart disease and stroke. In analyses stratified by geographical location, no association was found between egg consumption and CVD risk among US or European cohorts, but an inverse association was seen in Asian cohorts.

**Comment:** Lifestyle, diet and cardiovascular risk. These are related but difficult to measure. Here we are talking eggs. The data are from about 210,000 nurses, and most of them ate 1–5 eggs per week. Higher egg consumption was associated with higher body mass index and more red meat consumption. Furthermore, the data were used as the basis for a meta-analysis of other published data. Brief summary: eating 5 or fewer eggs per week does not increase cardiovascular risk.

**Reference:** *BMJ* 2020;368:m513

[Abstract](#)

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## Electrical versus pharmacological cardioversion for emergency department patients with acute atrial fibrillation (RAFF2)

**Authors:** Stiell IG et al.

**Summary:** The RAFF2 trial compared electrical and pharmacological cardioversion for patients with acute AF. 396 patients with acute AF at 11 hospital emergency departments in Canada were randomised to attempted pharmacological cardioversion with intravenous procainamide (15 mg/kg over 30 min) followed by electrical cardioversion if necessary (up to 3 shocks, each of  $\geq 200$  J), or placebo infusion followed by electrical cardioversion. Conversion to sinus rhythm occurred in 96% of patients in the drug-shock group and 92% in the shock-only group (absolute difference 4%; 95% CI 0–9;  $p=0.07$ ). 97% and 95% of patients in the respective groups were discharged home. Conversion to sinus rhythm was not affected by pad position (anterolateral or anteroposterior).

**Comment:** A prospective, randomised trial of current practice in cardioversion. Half of the patients were shocked, the other half also took anti-arrhythmic medication (procainamide). Also pad position was randomised. 52% of patients in the drug-shock group converted after drug infusion only. Electrical cardioversion was highly successful (92–96%). Pad position made no difference. Both pathways were successful, and the authors concluded that there are benefits for the drug-facilitated pathway as it avoids the more resource-intensive sedation associated with cardioversion in about half the patients.

**Reference:** *Lancet* 2020;395(10221):339-49

[Abstract](#)

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## Prognostic value of N-terminal pro-form B-type natriuretic peptide in patients with moderate aortic stenosis

**Authors:** Ito S et al.

**Summary:** This study evaluated the prognostic value of plasma NT-proBNP levels in patients with moderate AS. 261 patients (median age 78 years, 64% male) with moderate AS (aortic valve area 1.0–1.5cm<sup>2</sup>) had serum NT-pro BNP levels measured within 3 months of their echocardiographic assessment. The median NT-pro BNP level of the cohort was 888 pg/dl. The mortality rate during a median 2.7 years of follow-up was 3-fold higher in patients with NT-pro BNP levels above the median than in those with NT-pro BNP levels below the median (HR, 3.11; 95% CI 1.78–5.46; p<0.001), even in patients who underwent aortic valve replacement (AVR).

**Comment:** Recently the focus has been on the treatment of moderate AS – does earlier treatment improve outcomes? In this retrospective study, patients with moderate AS were divided into 2 groups using median NT-proBNP level (888 pg/dl) as the cut-off. A higher than median NT-pro BNP level was significantly associated with worse overall survival outcomes even after adjusting for comorbid conditions (HR, 2.52; 95% CI 1.58–4.02; p<0.001). Mortality rates were independent of AVR performed (in 31% of patients) throughout the observation period. Hence the study highlights the prognostic importance of BNP, but was not designed to evaluate the timing and role of AVR.

**Reference:** *Am J Cardiol* 2020; published online Feb 11

[Abstract](#)

## Initial invasive or conservative strategy for stable coronary disease

**Authors:** Maron DJ et al., for the ISCHEMIA Research Group

**Summary:** The ISCHEMIA trial compared an initial invasive strategy and a conservative strategy in patients with stable coronary disease. 5179 patients with moderate or severe ischaemia were randomised to an initial invasive strategy (angiography and revascularisation when feasible) plus medical therapy or to an initial conservative strategy of medical therapy alone and angiography if medical therapy failed. Over a median follow-up of 3.2 years, 318 primary outcome events (death from cardiovascular causes, myocardial infarction, hospitalisation for unstable angina, heart failure, or resuscitated cardiac arrest) occurred in the invasive-strategy group compared with 352 in the conservative-strategy group. Cumulative event rates were 5.3% and 3.4%, respectively, at 6 months and 16.4% and 18.2%, respectively, at 5 years. 145 patients in the invasive-strategy group and 144 in the conservative-strategy group died (HR, 1.05; 95% CI 0.83–1.32).

**Comment:** In patients with stable coronary artery disease, despite intuition telling us that improving blood flow through revascularisation intervention should help, the evidence has been somewhat lacking. In this trial, patients also had evidence of ischaemia, and the majority also had a CT scan to rule out proximal prognostic disease. Following this, patients were randomised to invasive or medical therapy. After 3.2 years there was no significant difference regarding MACE between the two groups. Early peri-procedural events contributed to MACE numbers in the invasive group, also 21% in the medical group ended up having an intervention. Not sure what this really means, as how likely is it that we do an ischaemia test, a CT in all, and a further angiogram in a quarter of patients to then call this medical management?

**Reference:** *N Engl J Med* 2020;382:1395-1407

[Abstract](#)

## Health-status outcomes with invasive or conservative care in coronary disease

**Authors:** Spertus JA et al., for the ISCHEMIA Research Group

**Summary:** This secondary analysis of the ISCHEMIA trial assessed angina-related outcomes after an initial invasive or conservative strategy in patients with stable coronary disease. Angina-related symptoms, function, and quality of life were assessed using the Seattle Angina Questionnaire (SAQ) at baseline and at months 1.5, 3, and 6, and every 6 months thereafter in patients randomised to an invasive treatment strategy (n=2295) or a conservative strategy (n=2322). The primary outcome was the SAQ summary score (ranging from 0–100, with higher scores indicating better health status). At baseline, 35% of patients in each group reported having no angina in the previous month. SAQ summary scores increased in both treatment groups, with increases at 3, 12, and 36 months that were 4.1 points (95% CI 3.2–5.0), 4.2 points (95% CI 3.3–5.1), and 2.9 points (95% CI 2.2–3.7) higher in the invasive strategy group than in the conservative strategy group. Differences were larger in patients who had more frequent angina at baseline.

**Comment:** Following the main publication of the ISCHEMIA trial, this paper assessed angina burden and treatment in the study population by using an angina questionnaire. After 12 months there was a small mean difference for the entire population that was sustained throughout follow-up. However, the baseline frequency of angina was a relevant determinant for benefiting from invasive management. Simply put, patients with daily and weekly angina tended to benefit more from invasive management.

**Reference:** *N Engl J Med* 2020;382:1408-19

[Abstract](#)

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### Independent commentary by Professor Alexander Sasse

Professor Alexander Sasse is Consultant Cardiologist and Clinical Director of the Cardiology Department at Wellington Hospital/CCDHB. His clinical interests include the various modalities of cardiac imaging, structural heart disease and intervention, general cardiology and the prevention of stroke. He went to Medical School in Bonn and did his training at the RWTH Aachen (Germany) and has been a Cardiologist since 2004. In 2007 he moved to Wellington and has been there since. Appointments include being a senior lecturer at Wellington School of Medicine (University of Otago) since 2007, and adjunct Professor at the School of Biological Sciences (Victoria University) Wellington since 2012.



## Increased long-term mortality in women with high left ventricular ejection fraction: Data from the CONFIRM (coronary CT angiography evaluation for clinical outcomes: an international multicenter) long-term registry

**Authors:** Gebhard C et al.

**Summary:** This analysis of the CONFIRM registry determined the clinical relevance of an increase in LVEF in women and men. 4632 patients from the CONFIRM registry (44.8% women; mean age 58.7 years in men and 59.5 years in women) who had LVEF measured by CTCA were categorised according to LVEF (low <55%, normal 55–65%, and high >65%). The prevalence of high LVEF was similar in both sexes (33.5% in women and 32.5% in men). After 6 years of follow-up, no difference in mortality was observed in patients with high LVEF in the overall cohort. However, a subgroup analysis showed that women with high LVEF died more often from any cause than women with normal LVEF (8.6% vs 7.1%;  $p=0.032$ ) and an opposite trend was seen in men (5.8% vs 6.8%;  $p=0.89$ ).

**Comment:** Bigger is better, right? LVEF is influenced by a number of factors, gender being a more important one. In this prospective trial, LVEF was measured by CTCA. The primary outcome was mortality and the secondary outcome was MACE. Low ejection fraction was clearly associated with adverse outcomes. However, women with LVEF >65% had a higher mortality ( $p=0.031$ ) especially in the presence of obstructive coronary artery disease (CAD;  $p=0.003$ ); no difference in MACE was detected. Microvascular dysfunction, myocardial infarction with nonobstructive coronary arteries (MINOCA) and heart failure with preserved ejection fraction were discussed as underlying pathophysiologies. But mostly the conclusion was that CAD presents differently in men and women.

**Reference:** *Eur Heart J Cardiovasc Imaging* 2020; 21(4):363-74

[Abstract](#)

## Meta-analysis comparing complete versus infarct-related artery revascularization in patients with ST-elevation myocardial infarction and multivessel coronary disease

**Authors:** Osman M et al.

**Summary:** This meta-analysis compared outcomes after complete revascularisation (CR) or infarct-related artery revascularisation (IRA) in patients with STEMI. Data from 10 randomised controlled trials that compared CR ( $n=3574$ ) with IRA ( $n=3849$ ) after STEMI were included. Meta-analysis of the data found that during a 2-year follow-up there was a significant reduction in MACE with CR compared with IRA (10.7% vs 18.6%, relative risk [RR], 0.64; 95% CI 0.51–0.81;  $p=0.002$ ). CR was also associated with lower rates of repeat revascularisation (4.0% vs 11.7%; RR, 0.44; 95% CI 0.28–0.70;  $p<0.0001$ ), and a nonsignificant trend toward lower cardiovascular mortality (2.8% vs 3.7%; RR, 0.78; 95% CI 0.60–1.03;  $p=0.08$ ). However, there were no differences between the 2 strategies in all-cause mortality, myocardial infarction, stroke, or contrast-induced nephropathy.

**Comment:** 60% of patients presenting with STEMI have multi-vessel coronary artery disease. This meta-analysis tried to identify the most appropriate treatment options for non-infarct related vessels. In the past, studies tended to come up with somewhat conflicting results. 10 trials with 7423 patients ended up in the analysis. CR had a better outcome regarding MACE with a better result in earlier revascularisation. CR did not lower all-cause mortality although cardiovascular mortality was improved. It appears that data and discussion at the recent European Society of Cardiology favour CR, but as usual a case by case assessment seems to be the best approach.

**Reference:** *Am J Cardiol* 2020;125(4):513-20

[Abstract](#)

## Acute effects of Red Bull energy drinks on atrial electromechanical function in healthy young adults

**Authors:** Özde C et al.

**Summary:** This study evaluated the acute effects of energy drinks on atrial electromechanical conduction times in healthy young adults. 54 healthy young adults fasted for 12h before consuming 330ml of a Red Bull® energy drink. Echocardiographic tissue-Doppler imaging at baseline and 2h showed significant increases in atrial electromechanical coupling-lateral time (+4.4 msn;  $p=0.001$ ), atrial electromechanical coupling-septal time (+2.9 msn;  $p=0.032$ ) and interatrial electromechanical delay (AEMD; +3.7 msn;  $p=0.010$ ) after energy drink ingestion.

**Comment:** Red Bull® might give you wings, but how about the heart? Six of 60 healthy volunteers could not drink a full can and were excluded due to nausea, leaving 54 participants. Volunteers were examined with ECG and echocardiography; systolic blood pressure and heart rate increased. Interestingly, the AEMD, measuring from onset of P to onset of contraction in the atrium was significantly increased. AEMD in other studies has been linked to AF. None of the volunteers had AF, but the authors concluded that this electromechanical effect of Red Bull® could contribute to the onset of AF in young and otherwise healthy consumers. Not flying anywhere.

**Reference:** *Am J Cardiol* 2020;125(4):570-4

[Abstract](#)