Cardiology RESEARCH REVIEW™

Making Education Easy

Issue 112 – 2024

## In this issue:



**Abbreviations used in this issue**
**AF** = atrial fibrillation
**COVID-19** = coronavirus disease 2019
**CPR** = cardiopulmonary resuscitation
**HR** = hazard ratio
**NOAC** = non-vitamin K oral anticoagulant
**POTS** = postural orthostatic tachycardia syndrome
**SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2
**SAVR** = surgical aortic-valve replacement
**TAVI** = transcatheter aortic-valve implantation

# Welcome to the latest issue of Cardiology Research Review.

In this issue, Italian investigators report an increased risk of new-onset hypertension during the COVID-19 pandemic, an analysis of the REDUCE-AMI trial questions the use of beta-blockers in post-MI patients with minor myocardial injury, and a German study demonstrates the benefits of TAVI in selected patients with aortic stenosis.

I hope you find these and the other selected articles interesting and look forward to receiving any feedback you may have.

Kind regards,
**Professor Alexander Sasse**
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## Incidence of new-onset hypertension before, during, and after the COVID-19 pandemic: A 7-year longitudinal cohort study in a large population

**Authors:** Trimarco V et al.

**Summary:** This longitudinal cohort study in Italy determined the risk of new-onset hypertension before, during and after the COVID-19 pandemic. The medical records of more than 200,000 adults who were registered with a cooperative of primary physicians in 2017–2022 were analysed; 25,931 of them had a positive test for COVID-19 during the pandemic. The incidence rates of new-onset hypertension were 2.11 per 100 person-years in the three pre-pandemic years (2017–2019), 5.20 per 100 person-years during the pandemic (2020–2022), and 6.76 per 100 person-years after the pandemic (2023).

**Comment:** Another post-COVID study. Cardiovascular disorder seems to be affected by COVID infection, and the focus of this Italian study was hypertension. The study had access to patient data from 2017 to 2022 (n=244,295). In the patients affected by COVID, the incidence rate of new hypertension increased from 2.1% to 5.2% (relative risk 2.5). This trend persisted from 2020 to even 2023 but with still relatively high levels of virus circulation. The authors are unsure about the pathophysiological mechanism, and indirect effects might also play a role (quoted are stress, changes in diet and exercise and in cardiovascular prevention strategies). It would be interesting to see if the incidence rate goes back to baseline, as doubling the hypertension incidence would otherwise have quite a relevant long-term effect.

***Reference: BMC Med. 2024;22(1):127***
Abstract

## Pooled rates and demographics of POTS following SARS-CoV-2 infection versus COVID-19 vaccination

**Authors:** Yong SJ et al.

**Summary:** This systematic review and meta-analysis estimated the rates of postural orthostatic tachycardia syndrome (POTS) occurring after SARS-CoV-2 infection versus COVID-19 vaccination. Meta-analysis of data from epidemiological studies showed a pooled POTS rate of 1.08% in infected individuals (5 studies) and 0.039% in vaccinated individuals (2 studies). The time from exposure was faster for cases of post-vaccination POTS than post-infection POTS ($p<0.05$).

**Comment:** POTS in my perception used to be a niche diagnosis pre-COVID, and was largely unheard of in the public. Now it seems to be a common concern. This paper analysed studies reporting on POTS in the context of COVID-19 infection or vaccination. In the end they found only a few suitable studies and even these studies were quite heterogenous. Vaccinated and infected populations were quite different. Overall, there is limited evidence that POTS might occur following COVID vaccination, in comparison it is much more likely to occur following a COVID infection (27-fold difference). Small subgroups allowed assessment of a hazard ratio, and definite POTS had a prevalence risk ratio of 2.1 compared to an uninfected population. The absolute numbers of this paper would have to be appraised quite critically, but the increased rate of POTS following COVID-19 infection appears to be real.

***Reference: Auton Neurosci. 2023:250:103132***
Abstract

CLICK HERE to read previous issues of Cardiology Research Review

## Beta-blockers after myocardial infarction and preserved ejection fraction

**Authors:** Yndigegn T et al., for the REDUCE-AMI Investigators

**Summary:** Most trials showing a benefit of beta-blockers post MI included patients with large MIs and were conducted in an era before modern biomarker-based diagnosis of MI and treatment with PCI, antithrombotics, high-intensity statins, and renin-angiotensin-aldosterone system antagonists. This analysis of REDUCE-AMI data investigated the efficacy of beta-blockers in patients with acute MI who had undergone PCI and had preserved LVEF (≥50%). 5020 patients were randomised to receive either long-term treatment with a beta-blocker (metoprolol or bisoprolol) or no beta-blocker treatment. The primary end-point was a composite of all-cause mortality or new MI. During a median follow-up of 3.5 years, a primary end-point event occurred in 7.9% of patients in the beta-blocker group and 8.3% of patients in the no beta-blocker group (HR 0.96, 95% CI 0.79–1.16; p=ns).

**Comment:** Guidelines for beta-blockers, while showing a clear benefit, often pre-date troponin-driven medical intervention in modern times. This study with centres in Sweden, Estonia and NZ enrolled MI patients (n=5020) with minor myocardial injury (LVEF ≥50%) and relevant coronary stenosis. Patients were randomised to beta-blocker or control. Median follow-up was 3.5 years. Mortality was not different. The secondary end-point also including heart failure, MI and AF was not different. Safety also showed no difference. This is a pretty powerful trial, and beta-blocker indication in this subset of MI patients might need to be re-evaluated.

***Reference: N Engl J Med. 2024;390(15):1372–81***
Abstract

## Secondary prevention therapies in real-world patients with myocardial infarction: Eligibility based on randomized trials supporting European and American guidelines

**Authors:** Mas-Llado C et al.

**Summary:** Entry criteria for randomised controlled trials cited in US and European guidelines for secondary prevention after acute MI were applied to a cohort of patients from the EPICOR registries (n=18,117). Overall, 91.5% of post-MI patients were found to be eligible for beta-blockers, 97.7% for renin-angiotensin system inhibitors (angiotensin-converting enzyme inhibitors [ACEIs] and angiotensin II receptor blockers [ARBs]), and 4.1% were eligible for mineralocorticoid receptor antagonists (MRAs). The percentages of patients meeting eligibility criteria who were discharged with a prescription for the recommended therapies ranged from 80–85% for beta-blockers, 70–75% for ACEI/ARBs, and 29% for MRAs. Large regional variations were seen in the percentages of eligible patients who actually received the medications.

**Comment:** The prescription of key cardiovascular drugs post ACS is monitored in NZ, and compliance ranges somewhere around 74% (range 52–84%). In this study they used a large cohort of ACS patients and applied US and European guidelines to them. 92% were eligible for a beta-blocker, 98% for ACEI/ARBs, and 4% for a MRA. The real-world prescription rates were around 80% for beta-blockers, 70% for ACEI/ARBs, but only 30% for MRAs (possibly reflecting some changes in placing MRA in heart failure therapy). I guess the paper confirms that measurement and reporting of prescription rates are important, and there will always be room for improvement. But maybe our rates in NZ aren't actually that bad. And then there is new evidence about beta-blockers.

***Reference: Am J Med. 2024;137(2):137–46.e10***
Abstract

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## Transcatheter or surgical treatment of aortic-valve stenosis

**Authors:** Blankenberg S et al., for the DEDICATE-DZHK6 Trial Investigators

**Summary:** This German study investigated whether low-risk patients with severe, symptomatic aortic stenosis should undergo transcatheter aortic-valve implantation (TAVI) or surgical aortic-valve replacement (SAVR). 1414 patients (mean age 74 years, 57% male) with severe aortic stenosis who were at low or intermediate surgical risk were randomised to TAVI or SAVR; the primary outcome was a composite of all-cause mortality or stroke at 1 year. The Kaplan–Meier estimate of the primary outcome at 1 year was 5.4% in the TAVI group and 10.0% in the SAVR group (HR 0.53, 95% CI 0.35–0.79; p<0.001 for non-inferiority). The incidence of all-cause mortality was 2.6% in the TAVI group and 6.2% in the SAVR group (HR 0.43, 95% CI 0.24–0.73), and the incidence of stroke was 2.9% and 4.7% in the respective groups (HR 0.61, 95% CI 0.35–1.06).

**Comment:** A TAVI topic – and a quick disclaimer of my own bias! Patients at intermediate risk suitable for both SAVR and TAVI were randomised in this trial; minimum age 65 (actual average age 74), severe aortic stenosis. Be mindful that these trials tend to have a number of technical exclusion criteria; this is a selected group of patients. Length of stay was shorter after TAVI. Regarding the outcome of death or stroke there were 5.4% in the TAVI group and 10.0% in the SAVR group. Mortality was also different (HR 0.43), as was disabling stroke (HR 0.42) and AF (HR 0.36). Pacemakers were more common in the TAVI group (HR 1.8). According to the study layout, the result was called non-inferior. As stated earlier, I am biased.

***Reference: N Engl J Med. 2024; published online Apr 8***
Abstract



## Duration of cardiopulmonary resuscitation and outcomes for adults with in-hospital cardiac arrest

**Authors:** Okubo M et al., for the AHA's Get With The Guidelines – Resuscitation Investigators

**Summary:** This retrospective US cohort study evaluated outcomes after in-hospital cardiac arrest as a function of CPR duration. 348,996 adults who received CPR for in-hospital cardiac arrest in 2000–2021 were included. Overall, 66.9% of them achieved return of spontaneous circulation (median interval of 7 min between start of chest compressions and first return of spontaneous circulation), whereas the remainder did not (median interval of 20 min between start of chest compressions and termination of resuscitation). 78,799 (22.6%) patients survived to hospital discharge. If spontaneous circulation was achieved within 1 min of CPR, the probability of survival was 22.0% (75,645/343,866) and the probability of favourable functional outcome was 15.1% (49,769/328,771). These probabilities decreased over time and were <1% for survival after 39 min of CPR and <1% for favourable functional outcome after 32 min of CPR.

**Comment:** This is an unpleasant type reality check – the outcome of resuscitation following cardiac arrest, here within a hospital. Basis is a US registry of guideline-directed resuscitation, with 348,996 patients. The median delay to CPR was 7 min. When unsuccessful, CPR was stopped after a median of 20 min. Two-thirds of patients achieved return of circulation, but in the end only about one-quarter (22.6%) made it to hospital discharge, and only 16% had a favourable functional outcome. Critical for CPR success was the response time to CPR – after about 15 min the probability of survival was <5%, and when patients were over 80 years old this time window was down to about 10 min. Patients with witnessed and shockable rhythm had a better outcome, highlighting the benefit of monitoring and a practised response team.

***Reference: BMJ 2024:384:e076019***
Abstract

## Clinical outcomes in older patients with atrial fibrillation: Insights from the GARFIELD-AF Registry

**Authors:** Goldhaber SZ et al., for the GARFIELD-AF Investigators

**Summary:** This analysis of the GARFIELD-AF registry investigated the impact of oral anticoagulants (OACs) on clinical outcomes in older patients with AF. 52,081 adults with newly diagnosed AF were recruited into the GARFIELD-AF registry and followed up for 24 months. Approximately one-third (32.6%) of them were aged 65–74 years, 29.3% were 75–84 years, and 7.9% were ≥85 years. Treatment with OACs was associated with a reduction in all-cause mortality in patients aged ≥85 years (HR 0.77, 95% CI 0.63–0.95) and a decrease in stroke in patients aged 65–74 years (HR 0.51, 95% CI 0.35–0.76) and ≥85 years (HR 0.58, 95% CI 0.34–0.99) compared with patients of the same age-group not receiving OACs. No increase in major bleeding was observed with OACs in patients aged ≥85 years. Compared with vitamin K antagonists, NOACs were associated with a significant reduction in all-cause mortality in patients aged 65–74 years.

**Comment:** This is a common question when doing talks on AF – what about older patients, should they be anticoagulated when in AF? A study from 35 countries, patients with AF, and enrolment based on $CHA_2DS_2$-VASC. 15,252 (29.3%) were 75–84 years (52% female), and 4129 (7.9%) were ≥85 years of age (61% female) at the time of enrolment. 32% of those over 85 years did not get anticoagulated, the highest proportion when compared to the younger patients. Outcomes were measured after 24 months; mortality was reduced by 23% in the oldest group when anticoagulated, and strokes were reduced by 42%. Bleeding was unchanged (HR 0.97). And this was in a transition time between warfarin and NOACs. While not a randomised study, the result overall appears relatively clear: oral anticoagulation in patients aged ≥75 years reduces mortality and stroke. There is no increase in significant bleeding.

***Reference: Am J Med. 2024;137(2):128–36.e13***
Abstract

## Microplastics and nanoplastics in atheromas and cardiovascular events

**Authors:** Marfella R et al.

**Summary:** This study investigated the presence of microplastics and nanoplastics (MNPs) in carotid plaque specimens from patients undergoing carotid endarterectomy for asymptomatic carotid artery disease. Excised carotid plaque specimens from 304 patients undergoing carotid endarterectomy were analysed using pyrolysis-gas chromatography-mass spectrometry, stable isotope analysis, and electron microscopy. 257 patients completed a mean 33.7 months of follow-up. 150 of them (58.4%) had polyethylene detected in carotid artery plaque and 31 (12.1%) had measurable amounts of polyvinyl chloride. Electron microscopy revealed visible foreign particles among plaque macrophages and in the external debris, and radiographic examination showed that some of these particles included chlorine. Patients who had MNPs detected within the atheroma were at higher risk for a primary end-point event (MI, stroke, or all-cause mortality) than those in whom MNPs were not detected (HR 4.53, 95% CI 2.00–10.27; p<0.001).

**Comment:** This paper made it into the news cycle. This Italian group collected tissue samples from patients undergoing carotid endarterectomy (n=257 analysed) and these samples were evaluated for the presence of MNPs. 58.4% showed MNPs. MNP-positive patients were younger, more often male and more often hypertensive; they had 6.1 cardiovascular events in 100 patient-years compared to MNP-negative patients (2.1 per 100 patient-years), calculating an HR of a staggering 4.5 (p<0.001) when adjusted for risk factors. For example there were ten MIs in the MNP group compared to two MIs in the non-MNP group. The paper also shows electron microscopic images of plastic in tissue. This is a single observational study, and much broader confirmation is required. But it is an interesting angle on environmental pollution plastic and the #1 cause of death.

***Reference: N Engl J Med. 2024;390(10):900–10***
Abstract



### 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.



## Sitting time reduction and blood pressure in older adults

**Authors:** Rosenberg DE et al.

**Summary:** This study examined the impact of a reduction in sedentary behaviour on blood pressure in older adults. 283 adults aged 60–89 years with high sitting time and BMI 30–50 were randomised 1:1 to a sitting reduction intervention or a healthy living control condition for 6 months. Intervention participants received 10 health coaching contacts, sitting reduction goals, and a standing desk and fitness tracker to prompt breaks from sitting. The control group received 10 health coaching contacts to set general healthy living goals (excluding physical activity). The primary outcome was sitting time (assessed using accelerometers worn for 7 days), and was measured at baseline, 3 months, and 6 months. At baseline, 147 (51.9%) patients had a hypertension diagnosis and 97 (69.3%) of these patients took at least one antihypertensive medication. The intervention decreased mean sitting time by 31.44 min/day versus controls at 3 months (p<0.001) and 31.85 min/day versus controls at 6 months (p=0.003). The decrease in sitting time was accompanied by a reduction in systolic blood pressure at 6 months (–3.48mm Hg vs controls; p=0.03).

**Comment:** No groundbreaking data from this trial, just some motivation for keeping active. It is sometimes hard to recommend actual exercise to our older patients, but what is the benefit from keeping active? This small US study randomised 283 elderly patients (mean age 69 years) and equipped them with an accelerometer. The intervention was to encourage standing, including using a tabletop, standing desk and electronic reminders to stand. The controls received a workbook. Both groups had health coaching throughout. The intervention group was sitting for 32 min less per day at 6 months, and systolic blood pressure dropped by 3.5mm Hg (p=0.03). While I do wonder about US data and calling 69-year-olds elderly and needing an App to stand up, the message here is that even standing up and walking around is beneficial and will help lower blood pressure.

***Reference: JAMA Netw Open 2024;7(3):e243234***
Abstract

## Sex differences in association of physical activity with all-cause and cardiovascular mortality

**Authors:** Ji H et al.

**Summary:** This US study investigated whether health benefits derived through physical activity differ by sex. Survey data on leisure-time physical activity provided by 412,413 adults (55% female) were analysed to determine sex-specific associations of physical activity with all-cause and cardiovascular mortality. During 4,911,178 person-years of follow-up, there were 39,935 all-cause deaths (including 11,670 cardiovascular deaths). Compared with inactivity, regular leisure-time physical activity was associated with a 24% lower risk of all-cause mortality in women (HR 0.76, 95% CI 0.73–0.80) and a 15% lower risk of all-cause mortality in men (HR 0.85, 95% CI 0.82–0.89). Men achieved their maximal survival benefit from 300 min/week of moderate-to-vigorous physical activity, whereas women achieved similar benefit from 140 min/week. Sex-specific findings were similar for cardiovascular death, and were consistent across all measures of aerobic activity as well as muscle strengthening activity.

**Comment:** This US study analysed the previously demonstrated lower rate of engagement in physical exercise programmes by women, identifying a 'gender gap' in exercise involvement. Analysed was a survey done between 1997 and 2017 that enrolled 412,413 adults across the US (55% female); mortality was the main outcome parameter. Exercise was measured by a recurring questionnaire. 32.5% of women and 43.1% of men were engaged in regular exercise. The benefit of exercise on mortality was dose dependent. Interestingly, men derived the most benefit from 110 min/week of vigorous activity, while women derived a comparable effect after only 57 min/week. A trend seen across a number of types of exercise was that women derived greater gains in all-cause and cardiovascular mortality risk reduction from equivalent doses of leisure-time exercise. The authors hope this information will help motivate people to close the postulated 'gender gap' in exercise.

***Reference: J Am Coll Cardiol. 2024;83(8):783–93***
Abstract