Journal Watch

1. Perioperative myocardial injury: A silent complication

Evidence Mounts for Myocardial Injury After Noncardiac Surgery - Medscape - Dec 11, 2017

The BASEL-PMI study, a prospective study showed that perioperative myocardial injury (PMI) is a common and problematic complication after non-cardiac surgery.

Although there was an increased CV risk, 82% patients did not show any ischemic symptoms and only 6% had chest pain. In addition, only 29% patients fulfilled any of the additional criteria required for spontaneous acute MI, such as loss of viable myocardium on imaging or ECG findings suggestive of myocardial ischemia.

The prognosis was poor despite the screening, and based on an absolute rise of high-sensitivity cardiac troponin T (hs-cTnT) of >14 ng/L from presurgery to postsurgery levels in 2000 patients, PMI occurred in 16% of the study population. The adjusted risk of death was almost threefold higher at 30 days and nearly twofold higher at 1 year.

This study was an extension to the findings of the VISION trial, which used multiple hs-cTnT thresholds, did not report 1-year mortality, and enrolled 21,050 patients at least 45 years of age irrespective of preexisting atherosclerotic disease. On the contrary, this study included patients at least 65 years or at least 45 years with preexisting coronary artery disease (CAD), peripheral arterial disease, or stroke.

This study showed that in most cases, cardiomyocyte injury was likely caused by supply-demand mismatch due to hypotension, anemia, and tachycardia and that people who are at increased risk of heart damage can suffer heart damage during major operations. The researchers recommend coronary angiography only after cardiology consultant in only 10% of PMI patients, to ensure improved, more focused cardiac management

2. CTA: The Best test for chest pain?

Is CT Angiography the Best First Test for Chest Pain? - Medscape - Oct 11, 2017

A recent meta-analysis of 13 randomized clinical trials showed that coronary computed tomography angiography (CTA) is associated with significantly fewer MIs than standard functional stress testing in patients with suspected CAD and acute or stable chest pain. On the contrary, it is also indicated that CTA may result in significantly more downstream invasive coronary procedures, CAD diagnoses, and aspirin and statin prescriptions without an overall reduction in mortality or cardiac hospitalizations.

The study consisted of 10,315 patients that were assigned to coronary CTA and 9777 patients assigned to a functional stress-testing strategy that included no testing, myocardial perfusion imaging, exercise-treadmill or bike electrocardiography testing, and stress echocardiography.

It was observed that CTA and functional stress testing had similar rates of death (1.0% vs 1.1%) and cardiac hospitalizations (both 2.7%). However, use of coronary CTA significantly lowered the risk of MIs overall and for patients with stable chest pain, but not for those with acute chest pain. Subsequent invasive coronary angiography (ICA) was significantly higher with the CTA strategy overall as were revascularizations.

According to researchers, the benefits of CTA are likely largely driven by changes in preventive therapies and may allow better selectivity for ICA and revascularization.

In the US, single-photon emission computed tomography (SPECT) remains the dominant noninvasive test for CAD; however, the updated NICE guidelines recommend coronary CTA as the initial test for all patients with chest pain and suspected CAD.

The limitation for this study was that they did not use individual patient-level data and were unable to make an assessment of differences in radiation exposure or the impact of incidental cardiac and pulmonary findings identified with cardiac CTA.

3. Hypertension Guideline Update

New ACC/AHA Hypertension Guidelines Make 130 the New 140 - Medscape - Nov 13, 2017

The ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults by the American College of Cardiology (ACC) and the American Heart Association (AHA) has revised the definition of hypertension from 130 to 139 mm Hg systolic or 80 to 89 mm Hg stage 1.

This revision provided a comprehensive guideline for diagnosis, prevention, evaluation, treatment, and very important strategies to improve control rates during treatment. The guidelines emphasized on:

- Blood-pressure measurement, both accuracy of blood-pressure measurements and using the average of measures taken over several visits, as well as an emphasis on out-of-office blood-pressure measurements
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- A new blood-pressure classification system, updating the previous Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7) guidelines
- A new approach to decision-making for treatment that incorporates underlying cardiovascular risk.
- Lower targets for blood pressure during the management of hypertension.
- Strategies to improve blood-pressure control during treatment with an emphasis on lifestyle approaches.

Blood Pressure Classification by JNC7 and 2017 ACC/AHA Hypertension Guidelines

Systolic, Diastolic Blood Pressure (mm Hg)	JNC7	2017 ACC/AHA
<120 and <80	Normal BP	Normal BP
120–129 and <80	Prehypertension	Elevated BP
130–139 or 80–89	Prehypertension	Stage 1 hypertension
140–159 or 90–99	Stage 1 hypertension	Stage 2 hypertension
> 160 or >100	Stage 2 hypertension	Stage 2 hypertension

Despite change in recommendations, lifestyle modification remains an essential part for treatment of hypertension.

4. Adding Rivaroxaban to Aspirin: Economical and Clinical Gains

Adding Rivaroxaban to Aspirin Cuts Costs in Secondary Prevention - Medscape - Dec 05, 2017

In patients with CAD or peripheral artery disease (PAD), addition to low-dose rivaroxaban to a low-dose aspirin regimen for secondary prevention reduces costs compared to aspirin alone. This reduction in costs accounts for both CV events and related procedures, and the cost is lowest in patients with PAD or with extensive atherosclerosis as opposed to CAD alone. A significant amount of the cost reduction was a result of averted strokes and PAD-related events, rather than from prevention of MI or other cardiac events.

The COMPASS study comprised 27,395 patients with stable atherosclerotic vascular disease who were randomized to 1:1:1 to 2.5-mg twice-daily rivaroxaban plus 100-mg daily aspirin, 5-mg twice-daily rivaroxaban, or 100-mg daily aspirin. Most of the patients (91%) had CAD, 27% had PAD, 62% had a history of MI, and 4% had a previous stroke. The trail was stopped at 23 months due to superiority of rivaroxaban plus aspirin vs. aspirin alone for the primary composite outcome of cardiovascular death, stroke, or MI (HR, 0.76; 95% CI; 0.66–0.86; P<0.001), although there was more major bleeding with the combined therapy.

Patients who received rivaroxaban and aspirin had lower rates of stroke, MI, severe limb ischemia, resuscitated cardiac arrest, venous thromboembolism, and angina. However, they also had higher rates of heart failure, cardiac arrhythmia, syncope, transient ischemic attack (TIA), and bleeding requiring an ER visit or hospitalization. Those who received both rivaroxaban and aspirin also had fewer peripheral angioplasties, PCI, limb amputations, vascular surgery, and coronary angiography, but also more CABG, pacemaker/ICD implantations, and carotid angioplasty. Overall, the cost savings, mainly from reduction in strokes, was approximately $4.2 million US dollars.

In summary, the COMPASS study emphasized that for patients with established CAD or PAD, addition of low-dose rivaroxaban to low-dose aspirin may provide meaningful cost offsets—particularly for patients with PAD or extensive atherosclerosis.

5. Outcomes of the CANVAS Program

Mahaffey KW, Neal B, Perkovic V, et al. On behalf of the CANVAS Program Collaborative Group. Circulation. 2017

The Canagliflozin Cardiovascular Assessment Study (CANVAS Program) compared the effects of canagliflozin among patients with type 2 diabetes mellitus and elevated cardiovascular risk (secondary versus primary prevention). Canagliflozin is a sodium glucose cotransporter 2 inhibitor that significantly reduces the composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke.

In this study, 10142 subjects with type 2 diabetes mellitus were randomly assigned to canagliflozin or placebo. The primary prevention cohort comprised individuals ≥ 50 years of age with ≥2 risk factors for cardiovascular events but with no prior cardiovascular event, and the secondary prevention cohort comprised individuals ≥30 years of age with a prior cardiovascular event. The results showed that patients were younger, were more often female, and had a longer duration of diabetes mellitus compared with secondary prevention participants.

The primary end point event rate (a composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke) was higher in the secondary prevention group compared with the primary prevention group. The primary end point was reduced in the group assigned canagliflozin compared with placebo. Although this study showed that canagliflozin reduced cardiovascular and renal outcomes with no statistical evidence of heterogeneity of the treatment effect across the primary and secondary prevention groups, further studies are warranted.

6. Dyslipidemia and abdominal aortic aneurysms

Elevated Lipids Probably a Cause of AAA: Genomic Study - Medscape - Dec 04, 2017

In a meta-analysis of >50,000 cases and controls, which used Mendelian randomization, researchers attempted to correlate the presence of several single-nucleotide polymorphisms (SNPs) linked with higher levels of LDL cholesterol and triglycerides and lower levels of HDL cholesterol with abdominal aortic aneurysms (AAAs). This indicates that AAAs are at high risk and treatment should aim at modifying lipid levels.

Data on the relationship between lipid subfractions and AA is scarce, and therefore, the current study was the first definitive large-scale genetic analysis. This study mainly highlighted that HDL cholesterol may play a causal role in abdominal aortic aneurysm.

The study considered at SNPs associated with the lipid subfractions and the treatment targets among 4914 cases of AAA and 48,002 non-AAA controls from five genomewide association studies, each in different countries. The molecular targets included HMG-coenzyme A reductase for statins, proprotein convertase subtilisin/kexin type 9 (PCSK9) for the PCSK9 inhibitors, and cholesteryl ester transfer protein (CETP) for the CETP inhibitors.

It was observed that a one–standard-deviation genetic elevation in LDL-C was associated with an odds ratio (OR) of 1.66 for AAA. The corresponding OR for triglyceride elevation was 1.69. The OR for AAA for a one-standard-deviation increase in HDL-C was 0.67. The allele of rs12916 associated with reduced LDL-C in the HMG-coenzyme A reductase gene HMGCR conferred an OR 0.93 for risk of AAA.

Among LDL-C-reducing alleles of PCSK9, rs11206510 was "weakly associated" with lower AAA risk, while rs2479409 showed no association. The allele of rs3764261 in CETP associated with increased HDL-C levels conferred an OR of 0.89 for risk of AAA.

The results of this study suggest that patients with AAA may be predisposed to higher LDL-C and that SNPs play a role in aneurysm screening.

7. Liraglutide and cardiovascular risk

Davies MJ, Aronne LJ, Caterson ID, et al. Diabetes, Obesity and Metabolism. 2017;26

Five randomized, double-blind, placebo-controlled clinical trials were evaluated post hoc to understand the cardiovascular safety of liraglutide, a glucagon-like peptide-1 receptor agonist approved for weight management at a dose of 3.0 mg. The post hoc study consisted 5908 participants who were randomized to liraglutide or a comparator group (placebo or orlistat). The researchers attempted to understand whether cardiovascular risk was increased with liraglutide treatment. The primary composite outcome of this time-to-event analysis was the first occurrence of cardiovascular death, nonfatal myocardial infarction or nonfatal stroke. With liraglutide 3.0 mg, eight participants had positively adjudicated cardiovascular events compared to 10 participants in the comparators group. These observations indicated that liraglutide 3.0 mg treatment was not associated with excess cardiovascular risk.

8. Understanding STEMI Survival Gains After Early Aldosterone Inhibition

STEMI Survival Gains After Early Aldosterone Inhibition Seen in Trials - Medscape - Sep 01, 2017

In two randomized controlled trials, ALBATROSS and REMINDER, conducted over 7 months, it was observed that treatment with aldosterone antagonists started within 3 days of acute ST-segment elevation MI (STEMI) onset, along with standard therapy, appeared to lower the risk of death. Besides the risk of mild hyperkalemia, the benefits of spironolactone and eplerenone, also called mineralocorticoid receptor antagonists (MRAs), there were only a few side effects.

The patient-level data included in the study was:

- The STEMI population subset of the ALBATROSS trial, which tested early spironolactone 25 mg/day for acute MI of any stripe, in the absence of heart failure
- The REMINDER trial looking at early eplerenone 25 to 50 mg/day in patients with STEMI but no HF or LV dysfunction

The researchers randomized 1118 patients with STEMI to receive an MRA, either spironolactone or eplerenone, and

1123 to placebo, both on top of standard therapy. In the ALBATROSS trial, spironolactone did not show a clinical benefit, although eplerenone was beneficial in the REMINDER trial when biomarkers were included along with the clinical events. However, none of the trails gave any statistical clinical outcome.

However, in the current analysis, the patients who received an MRA showed 0.4% mortality over a median follow-up of 190 days, compared with 1.6% in the placebo group (P = 0.006). Nevertheless, it would be incorrect to conclude that MRA should be started within 1 to 3 days of onset of any acute STEMI. Another study with results similar to the current analysis, the EPHESUS trial, also demonstrates that MRAs should be given to patients with left ventricular dysfunction after a recent acute MI.

Therefore, it can be concluded that MRAs may benefit largely by attenuating myocardial fibrosis after infarction, lessening risk of adverse structural and electrical remodeling. It can also be suggested that MRAs stem the damage caused by acute ischemic injury and subsequent myocardial necrosis might explain why spironolactone and eplerenone improve survival in STEMI but not NSTEMI or other forms of ACS, where necrosis is less of a factor.

9. Canakinumab: Reduces risk of CV events

CANTOS: Anti-Inflammatory Drug Cuts CV Events, Cancer - Medscape - Aug 27, 2017

Canakinumab is an anit-inflammatory drug that selectively inhibits the proinflammatory cytokine interleukin-1 beta (IL-1ß). The results of the CANTOS trial have shown that canakinumab significantly decreases the risk of recurrent major CV events without any effect on cholesterol and also cuts the rates of new lung cancer and lung-cancer mortality.

The study population comprised 10,061 high-risk patients, who had a prior MI and persistently elevated high-sensitivity C-reactive protein (hs-CRP) levels. Most participants (66.7%) had undergone PCI, and 93.4% were on high-dose statins. More than a third of patients had diabetes and almost a quarter were current smokers. It was observed that patients who received subcutaneous canakinumab 150 mg every 3 months had a 15% reduced risk for the composite primary end point of nonfatal MI, nonfatal stroke, and CV death compared with those receiving placebo. In addition, the risk of unstable-angina hospitalization leading to urgent revascularization was reduced by 17%.

A 300-mg dose of canakinumab produced similar reductions but failed to meet the prespecified threshold after adjustment for multiplicity for statistical significance, while a 50-mg dose had no effect.

It was observed that the treatment benefitted all the patient groups and treatment with the monoclonal antibody also reduced the need for revascularization by about 30%. Cholesterol levels remained constant in the study, while hs-CRP median reductions in the 50-mg, 150-mg, and 300-mg groups were 26%, 37%, and 41% greater than that in the placebo group (P <0.001).

10. Lowering BP and its relation with stroke

No Increased Stroke Risk With Intensive Systolic BP Lowering - Medscape - Oct 23, 2017

The findings of a recent study have shown that intensive lowering of systolic blood pressure (SBP) does not increase the risk for stroke. These observations indicate that SBP can be safely lowered, even to levels below 120 mm HG, when treating patients with hypertension, and there will be no risk of a stroke through cerebral hypoperfusion by lowering blood pressure too much.

Clinical recommendations have set the target at 140 mm Hg for the prevention of stroke and cardiovascular events; however, the Systolic Blood Pressure Intervention Trial (SPRINT) tried to more intensively lower levels to below 120 mm Hg to further reduce fatal cardiovascular events and mortality. The results of SPRINT showed that patients who did achieve SBP below 120 mm Hg in the study showed higher rates of hypotension, which could have led to decreased cerebral perfusion pressure and an increased stroke risk.

In order to better understand these results, the current study evaluated data on 8844 participants in SPRINT, establishing mean arterial pressure (MAP) and pulse pressure (PP) from the patients' SBP and diastolic blood pressure measurements. The patients were followed up for 32.6 months, and during this time, there were 132 stroke cases and 187 syncope cases. The mean minimal MAP was 78.21 mm Hg and the mean minimal PP was 45.10 mm Hg. Although lower MAP and PP were associated with an increased risk for hypotension and syncope, they did not indicate an increase in stroke risk. The stroke risk did increase consistently by approximately 31% with every 5-mm Hg increase in MAP and approximately 30% with every 5-mm Hg increase in PP. In addition, the risk in syncope increased by 39% with every 5-mm Hg increase in MAP and by 14% with every 5-mm Hg increase in PP.

Conclusively, this study reiterates that lowering SBP using medications in the setting of a diagnosis of hypertension will lower the risk for cardiovascular diseases, stroke, and death.