atherosclerosis

Atherosclerosis newsletter

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Volume 344, Issue March 2022

Comorbidities influence the course of coronary heart disease or the efficacy of therapeutic or preventive interventions. This issue contains several reports on the impact of heart failure on preserved ejection fraction, liver transplantation, peripheral artery disease, chronic kidney disease and diabetes mellitus type 2.

Ischemic risk in patients with heart failure with preserved ejection fraction: A *post hoc* analysis of the TOPCAT data

Heart failure with preserved ejection fraction (HFpEF) accounts for about half of heart failure cases. Compared with heart failure with reduced ejection fraction (HFrEF), HFpEF has a higher burden of non-cardiac comorbidities that could predispose to ischemic vascular events. The profile of ischemic risk among HFpEF patients is not fully understood. He et al. aimed to evaluate the risk, risk factors, and prognostic significance of ischemic events among HFpEF patients.

A total of 1767 HFpEF patients from Americas in the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial (a multicenter, randomized, double-blinded, placebo-controlled trial designed to evaluate the effect of spironolactone treatment in HFpEF patients) were included in the analysis. Ischemic event was defined as myocardial infarction or ischemic stroke during follow-up. Multivariate competing risks regression model was used to identify risk factors of ischemic event. Time-dependent Cox models were constructed to evaluate the association of incident ischemic event with mortality risk.

HFpEF patients had a high risk of ischemic event, which was significantly associated with increased mortality risk. Body mass index, prior myocardial infarction, insulin use, peripheral artery disease, hypertension, and current smoking were independent risk factors of ischemic event in HFpEF patients. HF hospitalization turned out to be an important trigger of ischemic event. Risk of ischemic event increased 4.7-fold within the first month after the first HF hospitalization, and dropped rapidly thereafter. Incident ischemic event was associated with significant higher short-term risks of all-cause mortality and cardiovascular mortality.

HFpEF patients from Americas were at a high risk of ischemic events, which was associated with mortality risk. A subset of baseline characteristics and HF hospitalization during follow-up could predict ischemic event.

A prospective natural history study of coronary atherosclerosis following liver transplantation

Cardiovascular disease is the leading cause of non-graft related mortality following liver transplantation (LT), with one in three patients experiencing cardiovascular events in the first year following transplantation. Whether it may be partially attributable to accelerated development of subclinical coronary artery disease is unclear. Koshy et al. assessed the longitudinal effect of LT on coronary plaque burden.

A prospective observational study was conducted in 30 asymptomatic patients who underwent computed tomographic coronary angiography (CTCA) pre- and a median 4-years following LT. Serial changes were quantified using coronary artery calcium score (CACS) and semi-quantitative CTCA scores, in a blinded fashion. High-risk plaque (HRP) characteristics were also assessed. Plaque progression was defined using prognostically significant cut-offs.

In the study population, 93 of 459 coronary segments had plaque at baseline. On follow-up CTCA, 68 new lesions appeared in segments without plaque initially. Nineteen patients demonstrated a clinically significant rise in plaque burden on CACS and semi-quantitative indices on CTCA. CAD-RADS score rose to ≥4 in 9 patients, necessitating ischemia-guided revascularization in 3 patients. While the absence of coronary calcification or plaque pre-LT was protective, presence of HRP and development of post-transplant metabolic syndrome were both strong independent predictors of atherosclerosis progression.

These findings suggest that LT is associated with early progression of coronary atherosclerosis. Accelerated progression was noted particularly in those with HRP and post-transplant metabolic syndrome. Understanding the mechanisms of this novel observation and the potential role of preventive cardiovascular therapies in this population merits further investigation.

Impact of peripheral artery disease on prognosis after percutaneous coronary intervention: Outcomes from the multicenter prospective e-ULTIMASTER registry

Peripheral artery disease (PAD) is a common condition, with an increasing prevalence over recent decades, now estimated to occur in over 200 million people worldwide with symptoms ranging from mild to severe. Patients with peripheral artery disease (PAD) represent a high risk group, and have an increased risk of cardiovascular events and worse cardiovascular outcomes. Kobo et al. aimed to study the impact of PAD among patients undergoing percutaneous coronary intervention (PCI) with a newer-generation thin-strut drug-eluting stent (DES).

Using the all-comer, single-arm, prospective, and multicenter registry e-ULTIMASTER PCI, patients with and without known PAD undergoing PCI were compared. A propensity-score was used to adjust for differences between the groups. The primary outcome was target lesion failure (TLF): a

composite of cardiac death, target-vessel related myocardial infarction, and/or clinically driven target lesion revascularization at 1-year follow-up.

PAD was present in 2255 out of 33,880 patients included in the analysis. Patients with PAD were older with a higher burden of comorbidities, and underwent more complex interventions. Patients with PAD were less likely to present with STEMI, and more likely to undergo complex PCI. PAD was found to be independently associated with 41% increased risk for TLF. The risk for all cause death and for cardiac death was 75% and 103% higher, respectively. No difference was found in the rates of stent thrombosis, clinically driven target lesion revascularization, or myocardial infarction (MI).

Patients with PAD are at higher risk for (cardiac) death post PCI, but not target vessel or lesion repeat revascularizations. The PAD cohort represents a population with a higher risk clinical profile.

Outcome of early *versus* delayed invasive strategy in patients with non-ST-segment elevation myocardial infarction and chronic kidney disease not on dialysis

Because of paucity of published data, Kim et al. evaluated the 2-year major clinical outcomes between early invasive (EI) and delayed invasive (DI) strategies according to the stage of chronic kidney disease (CKD) in patients with non-ST-segment elevation myocardial infarction (NSTEMI), who underwent a successful newer-generation drug-eluting stent (DES) implantation.

A total of 8241 NSTEMI patients were recruited from the Korea Acute Myocardial Infarction Registry (KAMIR). Based on baseline estimated glomerular filtration rate, the patients were classified into groups A, B, C, and D. Then these 4 groups were sub-classified into the EI and DI groups. Major adverse cardiac events (MACE), defined as all-cause death, recurrent MI (re-MI), and any repeat revascularization, were evaluated.

After multivariable-adjusted and propensity score-adjusted analyses, the cumulative incidence of MACE, all-cause death, re-MI, and any repeat revascularization was similar between the EI and DI groups in the 4 different renal function groups.

In the era of newer-generation DES, EI and DI strategies showed comparable major clinical outcomes in patients with NSTEMI and CKD during a 2-year follow-up period. Randomized, large-scale, long-term follow-up studies are needed to confirm these results.

Menopausal hormone therapy and risk of cardiovascular events in women with prediabetes or type 2 diabetes: A pooled analysis of 2917 postmenopausal women

The effect of menopausal hormone therapy (MHT) on cardiovascular disease (CVD) risk among women with prediabetes or type 2 diabetes (PreDM or T2DM) is unclear. T2DM is one of the most common chronic conditions among postmenopausal women, a population that is also likely to be affected by moderate to severe vasomotor symptoms and in need of menopausal symptom

management. Yoshida et al. examined the association between ever or early use MHT and CVD risk in postmenopausal women with PreDM or T2DM, and the potential modifying effect of race.

2,917 postmenopausal women with PreDM or T2DM were pooled from 3 prospective CVD cohorts (the Atherosclerosis Risk in Communities, the Multi-Ethnic Study of Atherosclerosis, and the Jackson Heart Study). Ever (yes *vs* no) or early use of MHT (MHT initiated ≤5 *vs* > 5 years since menopause), and their associations with ischemic stroke, coronary heart disease (CHD), and atherosclerotic cardiovascular disease (ASCVD) were assessed using Cox proportional hazards models.

During a median follow-up of 15 years, 264 stroke, 484 CHD, and 659 ASCVD events were observed. In fully adjusted models, ever use of MHT was associated with reduced risk of stroke, CHD, and ASCVD n white women with PreDM or T2DM. Early use of MHT was associated with reduced risk of stroke, CHD, and ASCVD in the white group. No risk reduction with ever or early use of MHT was found for black women with PreDM or T2DM.

MHT is associated with statistically reduced CVD risk among white but not black women with PreDM or DM. Race may be an effect modifier in the association between MHT use and CVD.