Cardiovascular disease in the literature: A selection of recent original research papers

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Tenosynovial and Cardiac Amyloidosis in Patients Undergoing Carpal Tunnel Release. J Am Coll Cardiol 2018;72:2040–50.

Background: Bilateral carpal tunnel syndrome is common in patients with cardiac amyloidosis, especially the transthyretin type (TTR), and usually precedes it by 5-10 years. Sperry et al. from Cleveland Clinic Foundation, Ohio performed a cross-sectional prospective study of 98 patients (median age 68 years, 51% men, 85% bilateral symptoms) undergoing carpal tunnel release surgery to determine the prevalence and type of amyloid deposits in the tenosynovium in addition to cardiac involvement.

Findings: On tenosynovial biopsy, 10 patients (10.2%) had amyloid deposits by Congo red staining (7 ATTR and 2 AL by mass spectrometry). Of these 10 patients, 2 had cardiac amyloidosis; one had AL amyloid with increased septal thickness by echocardiography, elevated NT-proBNP and cardiac troponin T and heart failure by exam. The other patient had TTR amyloid with septal hypertrophy by echocardiography and a positive technetium PYP scan with grade 3 myocardial uptake. The first patient was treated with dexamethasone, cyclophosphamide, and bortezomib with complete hematologic response. The second patient was treated with diflunisal, a TTR stabilizer.

Significance: Of patients undergoing carpel tunnel release for idiopathic carpel tunnel syndrome, a substantial proportion (10% in this study) has amyloid deposits on tenosynovial tissue biopsy. Importantly, 20% of these patients had previously undiagnosed cardiac amyloidosis which was subsequently treated. With the development of pharmacologic interventions targeting TTR cardiac amyloid, early diagnosis using tissue biopsy or advanced imaging as proposed in this study will become increasingly attractive.

Complete Versus Culprit-Only Lesion Intervention in Patients With Acute Coronary Syndromes. J Am Coll Cardiol 2018;72:1989–99.

Background: In patients with STEMI, complete revascularization has been shown to associate with lower mortality and recurrent MI compared to culprit-only revascularization. Rathod et al. from Barts Health NHS Trust, London, United Kingdom performed an observational cohort study of 21,857 patients with NSTEMI and multivessel disease (mean age 67 years, 74% men, 30% diabetes) using data from 8 London heart attack centers who collect data in a prospective British registry (British Cardiac Intervention Society dataset) to evaluate the long-term outcome of complete vs. culprit-only revascularization. Patients with cardiogenic shock, prior CABG, and chronic total occlusion were excluded.

Findings: Complete revascularization was performed in 54% of patients. Patients who underwent complete revascularization were older, more likely to be female, diabetic, have renal disease, have prior MI and prior revascularization. In-hospital MACE was similar between the 2 groups (3.8% culprit, 4.1% complete) with higher rate of death in the complete revascularization group and higher rate of reintervention PCI in the culprit group. During a median follow-up of 4.6 years, the complete revascularization group had significantly lower rate of mortality (22.5% vs. 25.9%, p=0.0005). In an adjusted model, the hazard ratio for mortality associated with complete revascularization was 0.90 (95%

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CI 0.85-0.97). Similar results were found in propensity-matched cohorts (0.89, 95%CI 0.76-0.98).

Significance: This large prospective observational multicenter study demonstrates a lower long-term risk of mortality associated with complete revascularization in patients with NSTEMI and multivessel disease. There is a growing body of evidence supporting complete revascularization in NSTEMI and STEMI with multivessel disease but randomized studies are needed in NSTEMI patients.

Stratified Medical Therapy Using Invasive Coronary Function Testing In Angina: CorMicA Trial. ***JACC 2018,*** https://doi.org/10.1016/j.jacc.2018.09.006.

Background: Almost half of patients undergoing elective coronary angiography have non-obstructive CAD. This group includes those with non-cardiac chest pain, but also microvascular and vasospastic angina that are associated with increased morbidity, impaired quality of life, and frequent hospitalization. In order to test whether a stratified medical therapy guided by an interventional diagnostic procedure improves outcomes of this cohort of patients, Ford et al. from West of Scotland Heart and Lung Centre, Golden Jubilee National Hospital, UK, randomized 151 patients with angina and non-obstructive CAD to stratified medical therapy guided by interventional diagnostic procedure (n=76) and to blinded control group (n=75, standard care). All patients underwent vasoreactivity testing with acetylcholine infusion per standard protocols, and were diagnosed accordingly as having vasoreactive angina, microvascular angina, or non-cardiac chest pain; however, the treating physician and patients in the control group were blinded to these results. The primary endpoint was the mean difference in angina severity at 6 months (assessed by the Seattle Angina Questionnaire summary score).

Findings: The left anterior descending was the target artery in the majority of patients. The intervention resulted in an improvement of 11.68 units (95% CI [4.99 - 18.37]; p = 0.001), that was driven by reduced angina limitation (p <0.001), frequency (p = 0.04), and related quality of life (p=0.015). In addition, the intervention led to improvements in the mean quality of life score (p = 0.024), without any major adverse events (p = 1.00).

Significance: Coronary angiography often fails to identify patients with vasospastic and/or microvascular angina. In this randomized blinded control study of patients without obstructive CAD at angiography, a stratified medical therapy based on the results of subsequent coronary vasoreactivity testing was safe, feasible, and clearly improved angina frequency, limitation, and quality of life. The mechanism of symptoms improvement is not fully understood. In part, it could be related to better medical therapy (patients in the intervention arm were more likely to take calcium channel blockers; relative risk 2.4, p=0.001), better engagement, and more informed patients and referring physician. Another cause of chest pain without obstructive disease that was not well entertained is myocardial bridging, which is sometimes missed on coronary angiogram and confirmed on computed CT angiography. Whether all patients with angina and non-obstructive disease should undergo coronary vasoreactive testing needs to be further explored in larger multicenter studies.

Decade Long Trends (2001-2011) in the Incidence Rates of Initial Acute Myocardial Infarction. ***The American Journal of Cardiology*** (2018), https://doi.org/10.1016/j.amjcard.2018.10.002

Background: CAD remains the leading cause of death in the Western World. Advances in medicine including preventive measures, better diagnosis and treatment have resulted in increased age longevity of patients and improved survival. However, little data exist on whether the incidence of acute myocardial infarction (AMI) has been declining in the last decade. Goldberg et al. from the department of Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, MA, evaluated the trends in the incidence rates of first hospitalized episodes of AMI between 2001 and 2011 among 3737 adult residents of central Massachusetts (mean age 70 years, 43% women, 90% White) from 11 medical centers.

Findings: Patients hospitalized in 2009-2011 were younger, had more co-morbidities and less in-hospital complications compared to those admitted earlier in the study (2001-2003). Between 2001 and 2011, the overall age-adjusted hospital incidence rates of first AMI (per 100,000 persons), declined from 319 to 163, and almost by half for men (422 to 219), and women (232 to 120). Also, the age-adjusted incidence rates (per 100,000) of an initial STEMI decreased from 129 to 56, as did the age-adjusted incidence rates of an initial NSTEMI from 190 to 107.

Significance: In this clinical and epidemiological study, the decline in the annual incidence rates of AMI during the last decade is encouraging. Although the study was limited to the area of Massachusetts, and included predominately Caucasian patients (more than 90%), these results were in line with those of the Atherosclerosis Risk in Communities (ARIC) Study that showed a declining annual incidence rates of AMI of 4.3% among white men, 3.8% among white women, 2.9% among black women, and 1.5% among black men between 1987 and 2008. Still, every 40 seconds, one person develops AMI in the United States. We are far from conquering this disease. Prevention and early

screening for risk factors remains key in the management of this global pandemic.

Association of Unrecognized Myocardial Infarction With Long-term Outcomes in Community-Dwelling Older Adults. The ICELAND MI Study. JAMA Cardiol. https://doi.org/10.1001/jamacardio.2018.3285.

Background: Unrecognized myocardial infarction (UMI) has been associated with poor outcomes but long-term prognosis is not known. Acharya et al. from the National Heart, Lung, and Blood Institute, Bethesda, Maryland investigated the long-term prognosis of UMI by CMR in a 935 patient subset (mean age 76 years, 52% women) of the Age, Gene/Environment Susceptibility (AGES)–Reykjavik prospective cohort (5764 Icelandic, community-dwelling, older individuals).

Findings: UMI (17%) was more common than recognized MI (RMI, 10%). Infarct size was smaller for UMI vs. RMI (4% vs. 9.6%) and LVEF was higher (60% vs. 53%). During a follow-up period of up to 13.3 years three were 424 deaths, 174 nonfatal MI and 220 heart failure events. Although at 3 years, UMI mortality rates were not significantly different from the no MI rate (3% for both) and lower than RMI (9%, p=0.03), at 10 years the rates of UMI and RMI were similar (49% and 51%) and significantly higher than no MI (30%, p<0.001). After adjusting for age, sex, and diabetes the hazard ratio for UMI for mortality (1.61, 95% CI 1.27-2.04) and MACE (1.56, 95% CI 1.26-1.93) were not different from RMI.

Significance: In this community-dwelling older population from Iceland, UMI by CMR was associated with a similar rate of death and MACE to RMI on long-term follow-up although the rates for both were lower early on. It is possible that medical and lifestyle interventions applied to the RMI but not the UMI group may have led to the rise in events over time in patients with UMI. The role of interventions to decrease risk in UMI will need evaluation in future trials.

Relationship between left ventricular ejection fraction and mortality after myocardial infarction complicated by heart failure or left ventricular dysfunction. ***Int J Cardiol 2018, ahead of print***

Background: Patients with heart failure and reduced ejection fraction (HFrEF) are at increased risk for death. Hall et al. from the department of Cardiology, Oslo University Hospital, Oslo, Norway, sought to evaluate whether lower LVEF categories impact death rate and specific mode of death. Using data from several heart failure clinical trials (almost 20,000 patients in total), the association between baseline LVEF and type of death was assessed using Cox modeling.

Findings: Over a median follow-up of 1.9 years, 3,419 deaths occurred. The risk of all types of death increased with decreasing LVEF. Using LVEF >35% as reference, patients with LVEF <25% had a significant increased risk of sudden, heart failure, other cardiovascular, and non-cardiovascular deaths (hazard ratio 2.13 [1.53–2.98]), 2.70 [1.83–3.98]), 1.66 [1.14–2.42]), and 1.90 [1.15–3.14], respectively). Furthermore, the distribution pattern for mode of death was similar across different categories of LVEF (<25%, 25–35%, and >35%).

Significance: Patients with HFrEF are at increased risk of death that appears to increase with further worsening of LVEF, and with similar distribution of the different modes of death. In particular, sudden cardiac death accounted for almost a third of all-causes of death in this cohort of patients. Therefore, preventive therapies such as implantable cardiac defibrillators (ICD) on top of optimal medical management seem essential. More interestingly, a third of patients with LVEF >35% also die from sudden cardiac death. While the guideline does not advocate ICD for primary prevention for those with EF >35%, several studies have shown that patients with EF >35% but with significant scar and late Gd enhancement by cardiac magnetic resonance imaging, are indeed at increased risk for sudden cardiac death. Perhaps, additional risk stratification for those with LVEF >35% should be routinely performed in order to better guide treatment options and save lives in a cost-effective manner.