Title: Major Acute Cardiovascular Events in Patients with Inflammatory Bowel Disease

Introduction: Traditional risk factors for coronary artery disease (CAD) are present in 85% of patients presenting with myocardial infarction (MI)[1]. More recently, inflammation and immune mediated diseases have been associated with ischemic heart disease (IHD)[2-5].

Inflammatory Bowel Disease (IBD) is an immune mediated disorder which comprises of ulcerative colitis and Crohn's disease. Estimated prevalence of IBD in the United States in 2004 was 1.4 million people[6]. These patients have an overall increased risk of thrombotic complications with microvascular thrombosis hypothesized to contribute in disease pathogenesis.

Overlap in pathogenesis of these two conditions is seen with sustained activation of immune responses with upregulation of cytokines IL-1 beta, IL-6 and TNF-alpha. Results from a meta-analysis showed increased risk of IHD among IBD patients, although heterogeneity was considerable in overall data[7]. Based on this information, we explored incidence of MACE (Major Adverse Cardiac Event) in this patient population from our health system data-base.

Methods: Propensity scores were estimated for all 15,292 (0.4%) patients with IBD from a total patient pool of 3,917,894 patients to assemble a 1:1 matched cohort balanced for age, gender, race and known cardiovascular risk factors including hypertension, hyperlipidemia, diabetes mellitus and smoking (current and former). ICD-9 and ICD-10 codes were used to identify cardiovascular risk factors and outcomes.

Results: Matched patients (n=30,584) had a mean age of 51 years, with 58% of all being women, and 63% Caucasian. During the median follow up of 4.4 years all-cause mortality was observed in 1.7% and 1.2% of patients from IBD and non-IBD groups respectively (hazard ratio {HR}, 1.31; 95% confidence interval {CI}, 1.08-1.58; p=0.005). Combined outcome for MI or all-cause mortality was noted in 4.1% and 3.4% from IBD and non-IBD groups respectively (HR, 1.16; 95% CI, 1.03-1.30; p=0.014) while HRs for cardiovascular mortality, MI and unstable angina independently were 1.04 (0.74-1.47; p=0.833), 1.05 (0.89-1.23; p=0.591) and 1.10 (0.83-1.46; p=0.524) respectively.

Conclusion: IBD did not show association with MI, unstable angina or cardiovascular mortality when matched for known cardiovascular risk factors, but was associated with increased all-cause mortality and combined end-point of all-cause mortality or MI.

References:

1. Canto JG, Kiefe CI, Rogers WJ, et al. Number of Coronary Heart Disease Risk Factors and Mortality in Patients With First Myocardial Infarction. *JAMA*. 2011;306(19):2120-2127. doi:10.1001/jama.2011.1654.
2. Xiao Z, Pei Z, Yuan M, Li X, Chen S, Xu L. Risk of stroke in patients with inflammatory bowel disease: a systematic review and meta-analysis. J Stroke Cerebrovasc Dis. 2015;24:2774–2780.
3. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med. 2005;352:1685–1695
4. Hansson GK. Atherosclerosis–an immune disease: the Anitschkov lecture 2007. Atherosclerosis. 2009;202:2–10.
5. Dagli N, Poyrazoglu OK, Dagli AF, Sahbaz F, Karaca I, Kobat MA, Bahcecioglu IH. Is inflammatory bowel disease a risk factor for early atherosclerosis? Angiology. 2010;61:198–204.
6. Clinical epidemiology of inflammatory bowel disease: incidence, prevalence, and environmental influences; Loftus, Edward V; Gastroenterology , Volume 126 , Issue 6 , 1504 - 1517
7. Inflammatory Bowel Disease and Risk of Ischemic Heart Disease: An Updated Meta-Analysis of Cohort Studies; Wan Feng, Guangxia Chen, Dawei Cai, Song Zhao, Jiafei Cheng and Hong Shen; Journal of the American Heart Association. 2017;6:e005892, originally published August 2, 201
8. Aniwan S, Pardi DS, Tremaine WJ, Loftus Jr. EV, Increased Risk of Acute Myocardial Infarction and Heart Failure in Patients With Inflammatory Bowel Diseases, Clinical Gastroenterology and Hepatology (2018), doi: 10.1016/j.cgh.2018.04.031