Antagonism of miR-33 in Mice Promotes Reverse Cholesterol Transport and Regression of Atherosclerosis


Conclusion: Anti-miR-33 oligonucleotide treatment promotes reverse cholesterol transport and regression of atherosclerosis.

Summary: For every 1% increase in circulating HDL cholesterol (HDL-C), there is a 2% decrease in overall risk for development of coronary artery disease (Wilson PW, Am J Cardiol 1990;66:7A-10A). It has been found in mouse models of atherosclerosis that over expression of apoAI, which increases HDL levels, hinders plaque progression and promotes plaque regression (Plump AS, et al. Proc Natl Acad Sci USA 1994;91:9607-11 and Rong JX, et al. Circulation 2001;104:2447-52). Such evidence has stimulated an interest in therapies to raise HDL levels. Despite the fact HDL raising strategies may be effective therapy for atherosclerosis, the underlying mechanisms that contribute to HDL regulation and its manipulation for therapy remain poorly understood.

Recent advances in lipid metabolism reveal that miR-33, and intronic microRNA within the SREBF 2 gene, suppresses expression of the ABCA1 receptor. Anti-miR-33 treated mice showed reduced plaque size and lipid content. The study demonstrates for the first time that oligonucleotides can penetrate atherosclerotic plaques, reach lesion macrophages, and enhance cholesterol removal. All of this could eventually result in clinically relevant regression of atherosclerosis.

Decreased Kidney Function an Unrecognized and Often Untreated Risk Factor for Secondary Cardiovascular Events After Carotid Surgery


Conclusions: Patients with moderate kidney failure have an increased risk of cardiovascular death and an increased risk of myocardial infarction 5 years after carotid endarterectomy (CEA) compared with patients with normal or mild renal impairment.

Summary: The prevalence of chronic kidney disease (CKD) in the US is currently estimated to be 9.6% of the population (Coreth J, et al. J Am Soc Nephrol 2005;16:180-8) and increasing. Impaired kidney function increases risk of death and hospitalization, and while CKD is irreversible, it is treatable. Angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin II antagonists can delay progression of CKD (Brenner BM, et al. N Engl J Med 2001;345:861-9). This study sought to assess cardiovascular mortality and morbidity following carotid endarterectomy (CEA) in patients with moderate kidney failure and to determine what proportion of patients with moderate kidney failure receive optimal medical treatment or undergo workup of their renal failure prior to CEA.

There were 1085 patients who underwent CEA between 2002 and 2009 who were included in the study. Baseline estimated glomerular filtration rate (eGFR) was assessed, and eGFR of 30-59 was defined as moderate kidney failure. Patients with moderate kidney failure were compared with those with normal or mildly reduced kidney function (eGFR ≥60).

Primary endpoints were cardiovascular death (fatal myocardial infarction, fatal stroke, and ruptured abdominal aortic aneurysm). Secondary endpoints were cardiovascular morbidity. In this study population, 26.3% (n = 288) of the patients had moderate kidney failure. Median follow-up was 2.95 years (0 to 3.0 years). The adjusted hazard ratio for cardiovascular death with moderate kidney failure was 2.22 (1.27-3.89). The adjusted hazard ratio for myocardial infarction with moderate kidney failure was 1.90 (1.04 to 3.47).

There was an increased rate of peripheral interventions or stenting in the patients with moderate kidney failure. Of the patients with moderate kidney failure, 38.3% (105/274) received ACE inhibitors. Only 34.4% had visited a nephrologist and 75% had received statins.

Comment: The short-term risk of moderate kidney failure is largely unrecognized by many surgeons. There are no widespread formal screening programs for moderate kidney failure, but all vascular surgery patients undergo basic metabolic testing and therefore, in essence, are screened for underlying kidney disease. Based on these data, vascular surgeons should consider referral to a nephrologist for any patient they identify with even moderate renal insufficiency.

HDL Promotes Rapid Atherosclerosis Regression in Mice and Alters Inflammatory Properties of Plaque Monocyte-Derived Cells


Conclusion: HDL cholesterol (HDL-C) is in an vivo regulator of inflammatory and inflammatory properties of monocyte-derived cells in mouse atherosclerotic plaques.

Summary: There is an inverse relationship between HDL-C and cardiovascular risk. HDL-C has been shown to be atheroprotective in mouse models of atherosclerosis (Rubin EM. Nature 1991;353:265-7). Infusion of HDL-C into human subjects has been shown to reduce plaque size (Nissen SE. JAMA 2003;290:2992-300). The authors, therefore, postulated HDL-C may be an effective therapy to induce regression of established atherosclerotics. They sought to examine the molecular effects of HDL-C on atheroepithelial plaque cells in vivo utilizing a mouse transplantation model of atherosclerosis (Reis ED, et al. J Vas Surg 2001;34:S41-7).

Plaque bearing aortic arches from apolipoprotein E-deficient (ApoE-/-) mice (low HDL-C, high non-HDL-C) were transplanted into mice with differing levels of HDL-C and non-HDL-C (S7BL6 mice [normal HDL-C, low non-HDL-C]), apoA-/- mice (low HDL-C, low non-HDL-C) or apoE/- mice transgenic for human apoAI (hApoAI/apoE-/-normal HDL-C, high non-HDL-C). In persistently elevated non-HDL-C hApoAI/apoE/- recipients, CD68 cell count decreased in plaques by more than 50% 1 week after transplantation. Little change in CD68 cell content was observed in apoAI/- recipients despite low lipid levels. Immigration and induction of chemokine receptor CCR7 was associated with decreased content of plaque CD68 cells. In CD68 cells laser captured from plaques, normalization of HDL-C levels led to decreased expression of inflammatory markers related to macrophages. No beneficial changes were observed in apoAI/- recipients indicating a requirement for reverse cholesterol transport for beneficial effects of HDL-C.

Meta-Analysis of Postoperative Mortality After Elective Repair of Abdominal Aortic Aneurysms Detected by Screening


Conclusion: Men whose abdominal aortic aneurysms (AAA) are identified through screening have improved early survival following operation compared to men whose AAs are detected incidentally.

Summary: An incidentally detected AAA is an AAA found in the evaluation for another medical problem. AAs detected with screening are detected in patients without an active medical problem. Patients with incidentally detected AAs may be at increased risk for AAA surgery because of greater age, increased comorbidities, or more anatomically complex AAs than those whose AAs are detected through a screening program. The authors thought to compare day mortality of elective AAA surgery in men whose aneurysms were detected incidentally vs those whose were detected by screening. The authors analyzed reports from randomized trials of AAA screening. Reports were identified through a systematic search of MEDLINE. Four relevant trials were identified and were also supplemented with data from the authors home institution. Meta-analysis was performed as fixed effect models. For overall comparisons, the chi-squared test for heterogeneity between the studies was assessed using the x2 test. In the screening studies, there were 25 deaths (2.9%) following elective surgery in men invited for screening (n = 858) compared with 21 deaths in 383 men in the control group (2.3%). The authors undertook a post-hoc meta-analysis of the incidence of perioperative (0 to 30 days) mortality in the study populations. The authors found that overall mortality was not significantly different between the groups. However, when the analysis was restricted to the first 30 days, mortality was significantly lower in the screening group (p = 0.02).