Role of Postoperative Inflammation in Reverse Cholesterol Transport and Atherogenesis

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Background: Atherosclerosis is a disease characterized by the build-up of lipid-rich plaques in the walls of blood vessels. In patients undergoing surgery, atherosclerosis is a recognized risk factor for major postoperative cardiovascular complications, which each year affect >10 million patients worldwide. While a strong link between chronic inflammation and atherosclerosis has been established, little is known about how atherosclerotic plaques are affected by the acute inflammation induced by surgical procedures. Previously, an aggravation of atherosclerosis has been observed in mice postoperatively, yet the underlying mechanisms of this relationship remain unknown. Generally, the balance between amelioration and aggravation within atherosclerotic plaques relies on controlling inflammation and removing fatty deposits, both of which are orchestrated by immune cells. These cells can transfer lipids onto High-Density Lipoproteins (HDL) for transport to and excretion by the digestive system, a process known as Reverse Cholesterol Transport (RCT). Acute inflammation compromises RCT due to the interaction of HDL with inflammatory proteins.
Hypothesis: Postoperative inflammation alters the HDL proteome, impairing lipid removal from atherosclerotic plaques and leading to disease aggravation.
Results: Atherosclerosis-prone mice ($ApoE^{-/-}$) were fed a high-fat diet for 8 weeks, before undergoing abdominal surgery, or anesthesia only (control). To assess RCT, radiolabelled cholesterol-loaded macrophages were injected at the time of surgery. Radioactive measurements of plasma, liver, bile, and feces were obtained 24 and 48 hours postoperatively, revealing that RCT is profoundly impaired at both time points. In a separate cohort, we observed a significant increase in the necrotic area of atherosclerotic plaques 15 days postoperatively, a measure linked to plaque instability.
Conclusion: Our results identify postoperative dysfunctions in RCT and histological changes to atherosclerotic plaques associated with worsening disease. This highlights the need to further define how surgical inflammation affects athero-protective mechanisms, to set foundational knowledge that could influence perioperative care guidelines.