Peripheral artery disease is a highly prevalent condition in the United States, and a significant cause of cardiovascular morbidity and all-cause mortality. Although vascular surgical procedures are commonly performed to improve patient survival and quality of life, patients are at heightened risk of adverse perioperative cardiovascular events. Following vascular surgery, patients remain at increased risk of long-term cardiovascular events. Traditional risk factors are limited in their ability to discriminate cardiovascular risk following vascular surgery and are mostly non-modifiable. Pathological and clinical studies consistently demonstrate that platelets are a major culprit in the pathogenesis of atherothrombosis. We propose a novel, reliable, and reproducible measurement of increased platelet activity, thus allowing investigation of this clinically relevant and potentially modifiable cardiovascular risk factor in this very high-risk population.

The study hypothesis is that platelet activity measurements before vascular surgery is independently and significantly associated with 30-day cardiovascular events. We further hypothesize that platelet activity measured postoperatively is independently and significantly associated with long-term cardiovascular events. We will also correlate platelet activity with the genome expression profile to determine molecular mechanisms controlling platelet activity. The long-term goal is to identify a clinically useful assessment of platelet activity for risk stratification that may be used as a diagnostic tool and a target for therapeutic intervention.

The proposed study will be a prospective observational cohort study enrolling 350 subjects before non-emergent open vascular surgery of the lower extremities. Platelet activity will be measured before and after vascular surgery and will be correlated with 30-day and long-term cardiovascular events. The 30-day primary endpoint will be death, myocardial infarction, stroke and troponin I >0.1ng/ml. The long-term primary endpoint will be death, myocardial infarction, or stroke. Secondary endpoints are major bleeding, vascular thrombosis, each individual endpoint, and cardiovascular death. The mechanism of increased platelet activity in patients with peripheral artery disease will be explored; isolated platelet mRNA and microRNA expression profile in 12 patients with increased platelet activity will be compared with 12 patients with normal platelet activity.

This study will provide novel data to address existing gaps in knowledge regarding the association between platelet activity measurements and incident cardiovascular events, and will ascertain whether a unique platelet RNA expression profile exists in peripheral artery disease subjects with increased platelet activity. Data obtained from this study will identify high-risk subjects before vascular surgery using a potentially modifiable risk factor. These data will provide insight into the molecular mechanisms regulating platelet activity and yield novel diagnostic tests for risk stratification and novel therapeutic targets to improve clinical outcomes in patients with peripheral artery disease undergoing vascular surgery.