Platelets play important roles in the pathophysiological process of acute coronary syndromes (ACS). Platelet activation, aggregation and thrombus formation secondary to plaque disruption have been implicated as major pathogenic mechanisms underlying ACS. Moreover, activated platelets mediate inflammation through adhesive interaction with leukocytes and endothelial cells, secretion of vasoactive substances and proinflammatory mediators. Indeed antiplatelet drug treatments have decreased mortality and adverse cardiovascular events, which clarifies the importance of platelet activity in ACS. Moreover, residual platelet activity after antiplatelet treatment significantly correlates with the intracoronary thrombus burden and impairment of myocardial perfusion, both of which might predict adverse cardiac events. Thus, evaluating platelet activity is one of the most important keys to managing patients with ACS.

Measuring platelet activity by any of a wide variety of methods (eg, platelet aggregometry, surface expression of adhesion molecules, such as P-selectin, CD40 ligand, and platelet-derived vasoactive substances such as thromboxane A2), has been reported as identifying individuals at increased risk for cardiovascular events. Mean platelet volume, the most commonly used measure of platelets, has been recently established as a potential marker of platelet reactivity. Elevated mean platelet volume is associated with acute myocardial infarction (AMI), mortality following MI, and restenosis following coronary angioplasty. Subjects with very low platelet counts (<50×10^9/L) have higher rates of uncontrolled bleeding whereas those with very high platelet counts (>600×10^9/L) are more likely to develop thrombosis. However, the exact relationship between platelet count and clinical outcome in ACS remains to be elucidated.

In this issue of the Journal, Wu et al clearly demonstrate that a significant relationship between platelet count and clinical outcome was noted in patients with ACS. By meta-analysis of 8 studies comprising 39,324 patients with ACS, these authors show that a higher platelet count at baseline increases the relative risks of mortality and major cardiac adverse events (MACE) during the short and long term. Moreover, they found the relative risks of mortality and MACE were 1.48 and 1.28, respectively, for the upper platelet count. Moreover, the pooled relative risk of longitudinal mortality was 1.024 when platelet count was used as a continuous variable.

In previous platelet studies, a significant relationship between platelet count on admission and mortality or MACE in patients with ACS has been shown. Ly et al showed that elevated platelet count on admission was associated with higher rates of death, congestive heart failure, and reinfarction at 30 days in 10,793 patients with ACS. In multivariate analysis, when compared with platelet count of <200×10^9/L, the composite endpoint of death, congestive heart failure, and reinfarction at 30 days was more likely to occur with elevated platelet counts, with odds ratios of 1.22, 1.37 and 1.71 for admission platelet counts of 201–300×10^9/L, 301–400×10^9/L, and >400×10^9/L, respectively. Similarly, Gibson et al demonstrated a significant relationship between platelet count on admission and reinfarction in 3,491 patients with ST-elevation MI. In multivariate analysis, a high platelet count independently associated with increased rates of reinfarction at 30 days. Nikolsky et al found that angiographic results and outcomes at 30 days and 1 year were stratified by the quartiles of platelet count in 2,082 patients with AMI treated with percutaneous coronary intervention. In multivariate analysis, a higher baseline platelet count was the strongest predictor of 1-year death or reinfarction.

Although the precise mechanism behind the relationship between elevated platelet count and these adverse outcomes in patients with ACS is unknown, a possible explanation is that a higher platelet count directly contributes to thrombosis by providing a larger substrate for thrombus formation. Moreover, platelets mediate inflammation, expressing many types of molecules, including P-selectin, intercellular adhesion molecule 2, toll-like receptors, CD40 and CD40 ligand, that act as immune mediators and contribute to the progression of atherosclerosis. Platelets mediate and amplify the inflammatory response to ACS through adhesive interaction with leukocytes. Elevated platelet counts may reflect increased thrombopoietin levels during MI. Actually, a higher platelet count on admission in patient with ST-elevation MI treated with thrombolysis was associated with the presence of residual angiographic thrombus.

Interestingly, Wu et al demonstrated a U-shaped relationship between platelet count and clinical outcome.
between platelet count and the risk of mortality and MACE. A lower platelet count might correlate with adverse outcomes. McClure et al. found that among 10,984 patients with ACS, 7% developed thrombocytopenia during hospitalization. Thrombocytopenia was defined as a platelet count of <100×10^9/L or a nadir platelet count <50% of the admission value. In multivariate analysis, patients with thrombocytopenia had an increased risk of nonfatal MI. The mechanism for the increased risk of bleeding in thrombocytopenia is clear, but how does a lower platelet count increase the occurrence of death or reinfarction? One possible explanation may be consumption of platelets in a thrombus.

Finally, both elevated and depressed platelet counts are significantly associated with adverse outcomes in patients with ACS. However, there are several reports showing no significant relationship between platelet count and mortality or MACE. Therefore, large-scale prospective, randomized clinical trials are needed to test whether platelet counts obtained from routine testing show greater value in terms of diagnosis, risk stratification, and treatment evaluation in patients with ACS.

**References**