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EDITORIAL

Measurement of Procalcitonin in Acute Coronary Syndrome

– Yet Another Prognostic Biomarker? –

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The acute coronary syndromes (ACS) are heterogeneous with respect to pathophysiology, presentation, prognosis, and response to therapy. The clinical spectrum of ACS comprises ST-segment elevation acute myocardial infarction (STEMI), non-ST-segment elevation acute myocardial infarction (NSTEMI), and unstable angina pectoris (UAP). STEMI is caused by acute total coronary occlusion,[1] whereas NSTEMI has been associated with the presence of vulnerable atherosclerotic plaque and subocclusive thrombosis.[2]

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Biomarkers provide potential information regarding normal biological processes, pathological changes, risk stratification, or pharmaceutical responses to a therapeutic intervention. These biomarkers for risk stratification are targeted at the evaluation of myocardial damage, resulting hemodynamic stress and electrical instability, and residual ischemia. Advances in our understanding of the pathophysiology and consequences of ACS have resulted in the development of new biomarkers. In recent years, several novel prognostic biomarkers related to cardiovascular outcome include cardiac troponin, high-sensitivity C-reactive protein (hs-CRP), brain natriuretic peptide (BNP), and N-terminal pro B-type natriuretic peptide (NT-ProBNP).

Inflammation plays a role in the pathophysiology of atherosclerosis. The inflammatory marker CRP is known to be elevated in patients with acute MI and has been shown to predict risk of recurrent events.[3,4] Procalcitonin is introduced as a new marker of inflammation. The original product of the Calc-1 gene is the 141-amino acid chain of pre-procalcitonin, which binds to the endoplasmic reticulum of the C-cells of the thyroid gland with its N terminus, where it is cleaved by an endopeptidase to give rise to procalcitonin. Subsequently, procalcitonin itself is cleaved by a convertase enzyme in calcitonin, katacalcin, and a proteic residue.[5] Normally, the concentration of procalcitonin is undetectable or low in healthy individuals, but in cases of sepsis, marked elevations occur.[6] High serum levels of procalcitonin were first described by Assicot et al in patients with sepsis and infection in 1993.[7] Several studies have reported procalcitonin as a strong marker of inflammation since that first report. Blood concentrations of procalcitonin increase in systemic inflammation and exhibit greater sensitivity and specificity than acute-phase proteins such as CRP.[6]

There is a paucity of data on serum procalcitonin levels across the spectrum of coronary artery disease manifestations. We do not have a consistent base of evidence to guide treatment in response to elevated levels of procalcitonin in this setting. Several studies have shown that procalcitonin levels are increased in ACS patients on admission,[8] but other investigations have demonstrated that plasma procalcitonin concentrations are in the normal range in patients with uncomplicated acute MI.[9,10] Recently, our group evaluated the differences in hs-CRP and procalcitonin level changes occurring during STEMI, NSTEMI and UAP, as well as their correlations with the presence and severity of coronary artery disease (CAD) and the outcomes of patients surviving ACS.[11] We determined that levels of hs-CRP and procalcitonin were increased in patients with ACS but failed to correlate with the severity of coronary disease and early prognosis.[11] We acknowledge that this was a small study with several limitations. Ilhan et al[12] found increased serum levels of procalcitonin and CRP in patients with ACS, and their study indicated a strong correlation between the increases in the levels of CRP and procalcitonin. This study also showed a significant difference between CRP and procalcitonin levels among patients with different cardiologic diagnoses. Remskar et al[10] measured procalcitonin levels in 54 patients with acute MI and determined that procalcitonin levels were increased in patients with acute MI only if associated with severe left heart failure, resuscitation after cardiac arrest or in the presence of bacterial infections. Procalcitonin levels were not increased in patients without complications. In another study, Buratti et al[9] evaluated procalcitonin values, together with interleukin-6 (IL-6), another index of inflammation, in a homogeneous population of patients with acute MI. They reported that, on admission, procalcitonin levels were in the normal range, whereas IL-6 levels were elevated 10-fold. A more recent study by Kafkas et al[8] regarding procalcitonin in acute MI patients evaluated procalcitonin levels on admission. The authors demonstrated that procalcitonin concentrations were elevated on admission and were detectable in serum earlier than CK-MB or troponin I in most patients. The authors suggested that procalcitonin could be considered as a novel sensitive myocardial marker in patients with acute MI. Recently, Picariello et al[13] evaluated levels of procalcitonin on admis-

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sion in patients with cardiogenic shock following STEMI, uncomplicated STEMI, UAP, and NSTEMI. Furthermore, the authors investigated whether procalcitonin levels correlated with CRP concentrations. The authors reported that procalcitonin levels measured on admission were significantly higher in patients with cardiogenic shock following acute MI and did not correlate with those of CRP.[13] Bektas et al[14] evaluated the diagnostic accuracy of the bedside procalcitonin test in detecting MI in patients presenting to the emergency department (ED) with typical chest pain or ischemic symptoms. They showed that the diagnostic accuracy of a point-of-care blood procalcitonin test was lower than that of CK-MB mass, myoglobin, and hs-CRP on admission to the ED and also at the fourth hour post-admission.

In this issue of the Journal, Sinning et al[15] report interesting data on the role of the baseline serum procalcitonin concentration in long-term cardiovascular risk prediction in patients with documented CAD. hs-CRP is the most studied of the markers and several studies also have shown that hs-CRP predicts intermediate or longer-term outcome,[3,4] but data are still lacking regarding a prognostic role of procalcitonin in patients with STEMI and in those with NSTEMI or UAP. In findings similar to our results, Sinning et al[15] demonstrate that patients presenting with ACS on admission showed higher procalcitonin concentrations than did subjects with stable angina pectoris. Their study involved long-term follow-up of 3.6 years. The authors report that increased procalcitonin levels at baseline were related to higher cardiovascular mortality and higher cardiovascular event rate during follow-up, but they did not quantify the increase in CRP. Taken together, these data provide biochemical evidence that a strong inflammatory response identifies high-risk patients with CAD. However, the study has several limitations. The authors performed only baseline measurements and therefore cannot clarify the variability in inflammatory markers during the course of the study. Sequential blood sampling may be needed to investigate the effectiveness of therapeutic strategies and the prognostic role of procalcitonin. When preserved samples are used, data concerning their reliability over time should be kept in mind.

In conclusion, Sinning et al[15] must be congratulated for having reopened the interest in biomarkers for patients with ACS. This is the first study to investigate the role of baseline serum procalcitonin concentration for long-term cardiovascular risk prediction in patients with documented CAD and it provides important long-term prognostic information for such patients. However, further studies are needed to determine the utility of procalcitonin as a diagnostic and prognostic tool in the pathophysiology of ACS.

References

1. DeWood MA, Spores J, Notske R, Mouser LT, Burroughs R, Golden MS, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. *N Engl J Med* 1980; **303:** 897–902.
2. DeWood MA, Stifter WF, Simpson CS, Spores J, Eugster GS, Judge TP, et al. Coronary arteriographic findings soon after non-Q-wave myocardial infarction. *N Engl J Med* 1986; **315:** 417–423.
3. Tommasi S, Carluccio E, Bentivoglio M, Buccolieri M, Mariotti M, Politano M, et al. C-reactive protein as a marker for cardiac ischemic events in the year after a first, uncomplicated myocardial infarction. *Am J Cardiol* 1999; **83:** 1595–1599.
4. Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. *Circulation* 2003; **107:** 363–369.
5. Maruna P, Nedelnıkova K, Gurlich R. Physiology and genetics of procalcitonin. *Physiol Res* 2000; **49**(Suppl 1)**:** S57–S61.
6. Whicher J, Bienvenu J, Monneret G. Procalcitonin as an acute phase marker. *Ann Clin Biochem* 2001; **38:** 483–493.
7. Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, Bohuon C. High serum procalcitonin concentrations in patients with sepsis and infection. *Lancet* 1993; **341:** 515–518.
8. Kafkas N, Venetsanou K, Patsilinakos S, Voudris V, Antonatos D, Kelesidis K, et al. Procalcitonin in acute myocardial infarction. *Acute Card Care* 2008; **10:** 30–36.
9. Buratti T, Ricevuti G, Pechlaner C, Joannidis M, Wiedermann FJ, Gritti D, et al. Plasma levels of procalcitonin and interleukin-6 in IMA. *Inflammation* 2001; **25:** 97–100.
10. Remskar M, Horvat M, Hojker S, Noc M. Procalcitonin in patients with acute myocardial infarction. *Wien Klin Wochenschr* 2002; **114:** 205–210.
11. Senturk T, Cordan J, Baran I, Ozdemir B, Gullulu S, Aydinlar A, et al. Procalcitonin in patients with acute coronary syndrome: Correlation with high-sensitive C-reactive protein, prognosis and severity of coronary artery disease. *Acta Cardiol* 2007; **62:** 135–141.
12. Ilhan F, Akbulut H, Karaca I, Godekmerdan A, Ilkay E, Bulut V. Procalcitonin, c-reactive protein and neopterin levels in patients with coronary atherosclerosis. *Acta Cardiol* 2005; **60:** 361–365.
13. Picariello C, Lazzeri C, Chiostri M, Gensini G, Valente S. Procalcitonin in patients with acute coronary syndromes and cardiogenic shock submitted to percutaneous coronary intervention. *Intern Emerg Med* 2009; **4:** 403–408.
14. Bektas F, Soyuncu S, Gunduz I, Basarici I, Akbas H, Eken C. The value of procalcitonin, a novel inflammatory marker, in the diagnosis of myocardial infarction and evaluation of acute coronary syndrome patients. *J Emerg Med* 2010; Aug 31 [E-pub ahead of print].
15. Sinning CR, Sinning JM, Schulz A, Schnabel RB, Lubos E, Wild PS, et al. Association of serum procalcitonin with cardiovascular prognosis in coronary artery disease: Results from the Athero*Gene* Study. *Circ J* 2011 (in press).