Letters to the Editor

The effect of adiponectin on the results of coronary interventions in patients with acute coronary syndromes: Primary phenomenon or epiphenomena?

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Since its description in 1966, adiponectin, a family member of adipocytokines, appears to be the most promising one studied to date with a potential impact on the development of therapeutic strategies in the field of cardiovascular disease [1]. However, the potential usefulness of different adipocytokines in the field of cardiovascular medicine and their value in our “every-day” clinical practice are still uncertain.

We read with great interest the article titled “Time-dependent changes of plasma adiponectin concentration in relation to coronary microcirculatory function in patients with acute myocardial infarction (MI) treated by primary percutaneous coronary intervention” by Trifunovic D et al. [2]. They have analyzed plasma adiponectin kinetics in patients with ST-segment elevation myocardial infarction (STEMI) without heart failure treated by primary percutaneous coronary intervention (pPCI) and its association with coronary flow reserve (CFR). It has been concluded that low plasma adiponectin concentrations are strongly associated with impaired coronary microcirculatory function in patients with their first anterior STEMI treated by pPCI, especially during the early post-pPCI period.

Higher adiponectin concentrations correlate with a lower risk of first MI and chronic coronary heart disease. However, there are also studies indicating the possibility that adiponectin has differing prognostic implications depending upon the type of cardiovascular disease and its severity. Higher adiponectin levels have been associated with an increased risk of future adverse cardiovascular events in patients with symptomatic coronary artery disease or acute coronary syndromes [3]. In other words, depending on the clinical settings of patients, both higher and lower levels of adiponectin have been considered as a predictor of increased risk of future adverse cardiovascular events.

We would like to discuss two aspects of the study by Trifunovic et al. to understand more clearly the relationship between adiponectin levels and the clinical course of acute STEMI patients.

Firstly, it could have been more useful if the authors could quantify the extent of myocardial necrosis with more sensitive measures, although no correlation was noted between adiponectin and other markers of myocardial damage, namely troponin (Tn) I and creatine kinase (CK)-MB. However, TnI and CK-MB levels were considerably high, although not statistically significant, in patients with CFR < 2. The relatively low number of study subjects could be responsible for this. On the other hand, infarct size determined by means of scintigraphy is known to correlate better with 1-year mortality than any other biomarker [4]. Patients with impaired CFR had higher Killip class on admission, and larger left ventricles with lower ejection fractions as compared to patients with preserved CFR, all of which indicate that a greater extent of myocardium is more likely to be affected in this patient subset. Observation of higher admission white blood cell and neutrophil counts and higher highsensitivity C-reactive protein levels in patients with CFR < 2 lend further support to this.

In the present study, left ventricular ejection fraction values and adiponectin levels were found to be independent predictors of recovery of CFR. If the myocardial injury and developing scar area had been quantified by more sensitive methods, in which direction would they influence the independent predictive value of adiponectin levels for recovery of CFR? In other words, the question of whether the adiponectin levels are merely an indicator or an active regulator of recovery of CFR has not been clearly answered, as pointed out partly by the authors of this study. It seems that this is an interesting subject, which needs to be evaluated in detail.

The second point that we would like to discuss is when and which cut-off value of adiponectin levels should be used in predicting cardiovascular events. In the current study, the adiponectin values obtained at the second day of acute MI (≤4.04 mg/mL) best predict the worse outcome regarding recovery of CFR. However, in another study, an admission adiponectin level of ≤3.8 mg/mL has been reported as the best cut-off to predict major adverse clinical events in males after STEMI, whereas an adiponectin level of ≤4.7 mg/mL at day 7 after STEMI has been found to be the best cut-off in predicting left ventricular remodeling in another study [5].

In conclusion, adiponectin levels show dynamic changes during the course of acute coronary syndromes. The question of when and which cut-off value is the worthiest remains unresolved. Adiponectin levels measured after the beginning of STEMI may be more valuable in predicting worse cardiovascular outcomes as compared to the admission adiponectin levels. However, this needs to be evaluated in large-scale studies, as admission levels of any biochemical marker would be more useful in the guidance of the initial therapy than the assessments in the later stages of the disease.

Conflict of interest

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References


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Author’s reply

We thank Professor Amasyali and Professor Kilic for their interest in our paper “Time-dependent changes of plasma adiponectin concentration in relation to coronary microcirculatory function in patients with acute myocardial infarction (MI) treated by primary percutaneous coronary intervention (pPCI)” recently published by the Journal of Cardiology. They discussed two aspects of our work.

First, we have the impression that the primary end point of our study, the recovery of coronary microcirculatory function (CMF) assessed as coronary flow reserve (CFR), is misread as the size of the infarction. CMF in ST-elevation MI (STEMI) patients after pPCI is indeed closely related to the quantity of myocardial damage, but is not its surrogate. Impaired CMF after pPCI is a complex phenomenon [1] and we focused on analysis of its predictors. Although we found white blood cell and neutrophil count, blood glucose and Killip class on admission and peak troponin I as significant univariate predictors of impaired CFR, in multivariate analysis (i.e. after adjustment for these variables), low adiponectin concentrations remained an independent predictor of impaired CFR in three separate models. These data suggest a strong relationship between low adiponectin concentration and impaired CMF, independently from other covariates. Since this is not an interventional study, causal or non-causal connection between impaired CMF and low plasma adiponectin cannot be presumed.

The second question was the cut-off value of adiponectin concentration for predicting poor outcome in STEMI and the optimal sampling time. We confirmed dynamic changes of adiponectin concentration during the first week in STEMI patients. Adiponectin’s predictive value and its cut-off depend on the endpoint selection. Comparing ours with the results of other authors, we believe that minimal adiponectin concentration (i.e. lower limit) of around 4 μg/ml is important, whenever it is reached (i.e. on admission or 48 h after pPCI). The lower limit of 4 μg/ml of adiponectin concentration on the 2nd day after pPCI was found as the best predictor of impaired CFR in our study. It is close to the 3.8 μg/ml of adiponectin concentration found on admission as best predictor of major adverse clinical events in males after STEMI [2]. Shibata et al. [3] found adiponectin <4.7 μg/ml at day 7 after STEMI as the best cut-off to predict left ventricular remodeling. These cut-offs should be compared with caution, since they predict comparable but not identical endpoints.

Large-scale studies are always welcome, although our study had enough statistical power to test the predefined hypothesis.

In our opinion the major breakthrough would be to test whether early application of the recombinant adiponectin in STEMI patents prior to or soon after pPCI would have an impact on coronary microcirculation and final infarct size, since there are positive data from animal models [4]. To the best of our knowledge, to date there are no such data.

References


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