

# Can resistin be used as a biomarker in coronary artery disease: A review

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## Abstract

Resistin was first discovered as a mediator of insulin resistance and obesity in rodents but the effects of resistin on human is still been investigated. It is mostly associated with inflammation in humans. Several publications suggest its relationship with cardiovascular diseases and many systemic disorders. In this review we focused on resistin and coronary artery disease.

## Resistin as a peptide

Resistin was discovered in 2001 in rodent experiments and taken its name from its relationship with insulin resistance. Human resistin is a cysteine-rich peptide consisting of 108 amino acid sequences at a weight of 12.5 kDa. Human and rodent resistin are 59% similar in amino acid level [1]. The presence of different promoter regions of rodent and human resistin genes suggests differences in tissue distribution, function, and regulatory mechanisms [1,2]. In humans resistin is secreted from peripheral blood mononuclear cells, macrophages and bone marrow cells [3,4].

Several studies have shown that serum resistin concentration is increased in obese and diabetic patients [5-7]. Resistin has also been associated with atherosclerosis and cardiovascular disease development, nonalcoholic fatty liver disease, rheumatologic diseases, malign tumors, asthma, inflammatory bowel disease and chronic renal failure [8,9].

## Resistin and coronary artery disease relationship

The first important study showing the relationship between atherosclerosis and resistin was performed by Reilly et al. [10] in 2005. In this study, there was a relationship between increased resistin level and coronary calcium score. Afterwards, several studies investigating the presence or severity of coronary artery disease (CAD) and resistin relationship were performed. In a study conducted by Ohmori et al. [11], it was found that as the number of vessels with more than 50% stenosis increases, the resistin level also increases. Wang et al. [12] grouped 220 patients as control group, stable angina pectoris group and acute coronary syndrome group and performed coronary angiography. Resistin levels were higher in the acute coronary syndrome group than the other groups, while no significant difference was found between the control group and the stable angina pectoris group. Also results of this study showed that as the number of coronary arteries with more than 50% stenosis increases, the level of resistin also increases.

In a follow-up study of patients with percutaneous coronary intervention, resistin levels were found to be independent predictors of MACE (major adverse cardiac events), but there was no relationship between stent restenosis and resistin levels in the same study [13]. Another study in diabetic patients found an association between resistin levels and stent restenosis [14].

In a study conducted by Chu et al. [15], resistin levels have been significantly increased at 24 hours and remained higher for 1 week at patients with acute coronary syndrome when compared to control group. This increase was found to be higher in myocardial infarction patients than unstable angina pectoris patients. In another study conducted by Lubos et al. [16], resistin levels were found to be higher in unstable angina, ST elevation and non-ST elevation myocardial infarction compared to stable angina patients. It was found that there was a relationship between the resistin level and the incidence of cardiovascular death after 2.6 years of follow-up. Another study comparing unstable angina patients with stable angina and control group found that patients with unstable angina had a higher level of resistin. There was no significant difference in resistin levels in patients with stable angina and the control group [17].

In a study conducted by Zhang et al. [18], 980 patients with CAD were followed for an average of 6.1 years. In this follow-up, patients with the highest quartile of resistin levels were found to have the highest risk of heart failure and mortality. In a study conducted by Wu et al. [19], 108 patients with Ejection fraction (EF) <50% were followed for an average of 776 days. In this study, mortality was found to be higher in the group with high resistin level. In another study, a statistical association of resistin levels with MACCE (major adverse cerebrovascular and cardiac events) was found in patients with multivessel disease over a year's follow-up [20].

There are also a number of studies showing no relationship between resistin and CAD. Yaturu et al. [21] shows the relationship between inflammatory process and resistin in CAD patients. This study compared the patient group with 57 CAD and 45 control patients. The diagnosis of CAD was based on the myocardial infarction history, myocardial perfusion scintigraphy or coronary angiography results. In this study, there was no significant difference in resistin levels in patients

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with and without CAD. In this study, resistin levels were strongly correlated with inflammatory markers such as TNF- $\alpha$  and CRP. Hoelfe et al. [22] evaluated resistin levels in 547 patients who underwent coronary angiography for stable CAD assessment and patients were followed up for 4 years for major cardiac event frequency. In this study, resistin was not associated with coronary artery stenosis. Also resistin had no relationship for future vascular events according to results of 4-year follow-up. In this study resistin was also significantly correlated with CRP levels. Another study evaluated 128 stable angina pectoris patients according to coronary angiography results. This study grouped patients according to their CAD severity. This study also showed no relationship between resistin levels and presence or severity of CAD [23]. In a study conducted by Pischon et al. [24] on female patients, 185 patients with coronary artery disease and control group consisting of 227 patients were compared with each other. At initial analysis there was a significant relationship between resistin level and coronary artery disease but after adjustments for CRP, the association was no longer significant. LURIC (The Ludwigshafen Risk and Cardiovascular Health Study) study [25] evaluated 1162 patients according to their coronary angiography results. CAD is defined as having  $\geq 20\%$  lesion in at least one coronary artery. According to the result of angiography, 911 patients were taken into the CAD group and 251 patients were defined in the non-CAD group. When resistin levels were examined, there was no significant difference between the groups. There was no significant difference in resistin levels between the groups when the coronary artery stenosis limit was  $\geq 50\%$ . There was also no relationship in terms of resistin levels when acute coronary syndrome and stable angina patients were compared.

## Conclusion

There are several studies investigating resistin, atherosclerosis, and coronary artery disease. There are both positive resulted studies and negative ones. It is noteworthy that, in studies showing the association, the relationship is often more prominent in acute coronary syndromes. There are also studies showing that resistin levels are higher in patients with stable coronary artery disease, as well as studies showing that they are similar to normal populations. Furthermore, when analysis is done considering CRP values, the association of resistin often disappears in coronary artery disease patients. This suggests that the inflammation parameters and resistin are strongly related. More work needs to be done to clarify this issue and the effect of inflammation parameters should be considered in future studies.

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