Přehledový článek | Review article

Adipsin as a novel prognostic biomarker for cardiovascular diseases

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SOUHRN

Zvýšený oxidační stres při cévních onemocněních stimuluje sekreci adipokinů z adipocytů. Řada klinických studií prokázala, že hodnoty adipsinu v plazmě poměrně spolehlivě predikují vznik ischemických příhod. Zvýšené hodnoty adipsinu těsně souvisejí s úmrtím z jakýchkoli příčin a s morbiditou. Adipsin je tak novým biomarkerem při sledování rozvoje aterosklerózy. Cílem tohoto přehledu bylo zdůraznit souvislost mezi adipsinem a kardiovaskulárními onemocněními a přínos použití adipsinu v léčbě těchto onemocnění.

ABSTRACT

Increased vascular oxidative stress stimulates the secretion of adipokines from adipocytes. Many clinical studies have demonstrated that plasma adipsin levels are successful in predicting ischemic events. Increased adipsin levels are closely related to all-cause death and morbidity. Therefore, adipsin may be a new biomarker for atherosclerosis. In this review, we aimed to emphasize the association of adipsin with cardiovascular diseases (CVDs) and its beneficial role in the therapeutic field of CVDs.

Introduction

Hypertension, diabetes mellitus (DM), dyslipidemia, and smoking are risk factors of cardiovascular diseases (CVDs).[1] The INTERHEART study showed that hypertension, dyslipidemia, diabetes, smoking, and obesity accounted for approximately 80% of CVDs.[2] Modification of these traditional risk factors provides both primary and secondary protection for CVDs.[3] Despite interventional and medical advances in acute myocardial infarction (AMI), hospital mortality rates are still high due to complications of AMI.[4] One of the adverse events is cardiac arrhythmia, which is an incredibly challenging disease of childhood.[5] Decompensated heart failure (HF) is the other complication that requires hospitalization and, in this case, is defined, high-risk groups.[6] Although HF benefits from medical and device therapy, HF is still a social health problem.[7–9]

The FINMONICA study, the Finnish division of the MONICA project coordinated with the World Health Organization (WHO), covered the provinces of North Karelia and Kuopio in eastern Finland and the surrounding areas of Turku, Loimaa, and Loimaa in southwestern Finland. This study includes hospitalization and mortality records of patients aged 25–64 years with AMI. The FINMONICA AMI Register's mortality findings are consistent with Finland's official CVD mortality statistics.[10]

CRP and other new inflammatory markers may help us properly manage cardiovascular events in AMI patients. The predictive value of CRP is independent of troponin. Aggressive lifestyle changes and preventive medical treatment may regress the increased inflammation in CVD. The early invasive strategy was found beneficial in individuals with high levels of inflammatory biomarkers.[11]

Circulating cytokines/chemokines and growth factors affect endothelial function,[12] and these develop vascular diseases.[13,14] Indeed, vascular diseases are processes involving a series of events such as endothelial dysfunction.[15–17] Hypertension, DM, dyslipidemia, smoking, and aging cause vascular diseases by oxidative stress.[18,19]

The complement system has an active role in the balance of coagulation and fibrinolysis. In contrast, a thrombin-activated fibrinolysis inhibitor neutralizes C3a and

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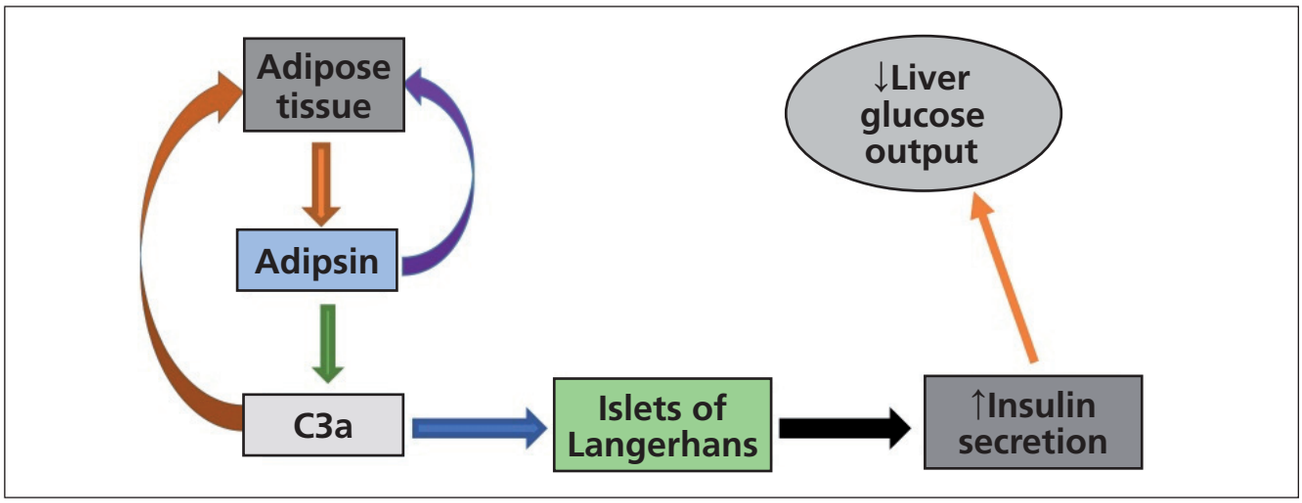

Fig. 1 – The role of adipsin in insulin secretion.

C5a.[20] Thrombin-activated fibrinolysis stimulates the intracellular signal and increases vascular remodeling in endothelial cells and vascular smooth muscle cells. Therefore, thrombin-activated fibrinolysis inhibitor plays a vital role in inflammation by aggregating a series of reactions such as complement system regulation, endothelial dysfunction, etc.[21] Adipsin is an adipocytes-derived biomarker that catalyzes the complement cascades. Adipsin forms fragments such as C3a, C3b, C5a, and C5b with the aid of complementary 3 (C3) convertase.[22] For example, thrombin can be divided directly into C3 and activation fragments and divide C5 into C5a.[23]

The relationship of adipsin with the alternative complement pathway (ACP) provides clues about the etiopathogenesis of CVDs. This review tried to summarize whether adipsin is a valuable prognostic biomarker in CVDs by presenting several studies about the issue.

Adipsin in atherosclerosis pathogenesis

Adipokines, released from adipose tissue, may have a role in the development of coronary artery disease (CAD).[22,23] In a clinical study, plasma adipsin levels predicted ischemic stroke.[24] However, few studies refer about the pathogenesis of adipsin in the atherosclerosis process in the literature. High adipsin levels are closely related to all-cause death and morbidity. Therefore, adipsin may be a potential new biomarker for atherosclerosis. Further analysis is required to support this hypothesis.

Adipsin catalyzes the rate restriction step of ACP, which is secreted from adipocytes, monocytes, and macrophages. Also, adipsin may reflect the metabolic status and insulin resistance (IR) in mice. Adipsin has a close link with IR in obesity.[25] Adipsin is necessary for pancreatic beta-cell function in patients with type 2 diabetes mellitus (DM).[22,26]

Adipokines may be the reason for dyslipidemia and unstable atherosclerotic plaques.[27,28] Adipsin is associated with metabolic disorders.[29] Additionally, adipsin accelerates lipid accumulation and adipocyte differentiation.[30] Therefore, adipsin may lead to instability of atherosclerotic plaques.

Comparison of adipsin with other biomarkers

In the study of Ohtsuki et al., serum levels of adipsin were compared with other biomarkers (BNP and hs-CRP).[31] Higher plasma BNP levels predict poor prognosis in cardiovascular events,[32] and processed BNP forms (N-terminal proBNP) may predict the incidence of revascularization.[33] Besides, high serum hsCRP levels (>1 mg/L) determine future cardiovascular events. However, serum hsCRP levels are also elevated in many non-specific infections.[34] CRP is released mainly from the liver in parallel with cytokine levels.[19] Ohtsuki et al.[31] examined the definitive role of adipose in combination with other biomarkers in CAD. Eventually, the combination of adipsin and BNP predicted adverse events better than alone. This information was also valid for hsCRP. Thus, the combination of adipsin and other biomarkers may guide us in determining CAD. In our opinion, adipsin usage may provide improvements in the clinical practice of CAD.

Contrary to early studies, some studies reported that low adiponectin levels increase the risk of IR and CVD.[35,36] Current findings provide a new perspective on the relationship between adipsin and other adiponectin. The distinction between them is due to the level of participation of the immune system. Future studies will help the understanding of the issue.

Adipsin and other CVDs

Gómez-Banoy et al.[37] thought that the treatment of adipsin/C3a might be a new approach to achieving beta-cell health in type 2 DM. Wang et al.[38] reported that the growth hormone/insulin-like growth factor 1 (GH/IGF-1) axis significantly regulated serum adipsin levels. Adipsin levels were increased in adult growth hormone deficiency cases and associated with glucolipid metabolism disorders. Thus, adipsin may be an early-stage CVD marker.

Brady et al.[39] observed higher adipsin and leptin concentrations in those with back pain. Adipsin was found to be an independent determinant of back pain. Korman et al.[40] revealed higher adipsin levels in systemic sclerosis (SSc) and a close link between pulmonary arterial hypertension (PAH) and adipsin in this population. Adipsin genetic variants may be effective in SSc-PAH. Adipsin potentially might be a new marker of PAH. Also, adipsin may modulate the complement system associated with PAH.

The complement system has a role in the development of inflammation. Adipsin was associated with hs-CRP in polycystic ovary syndrome (PCOS), and adipsin might contribute to the metabolic disorders in PCOS. Despite all this, controversy continues about adipsin in PCOS.[2] Chedraui et al.[41] found that high adipokine levels reflect metabolic syndrome in a postmenopausal woman.

Conclusion

Circulating adipokines may affect endothelial function and cause the development of vascular damage. Given the active role of adipsin in the complement cascade and increased release in adipose tissue, adipsin may be thought to play a potential role in the etiopathogenesis of CVDs. In our opinion, adipsin, along with other biomarkers, maybe an adjunct marker in determining the presence of atherosclerosis. Further studies will clarify this claim.

Conflict of interest

The authors declare that they have no competing interests.

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