Review Article

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Omentin: A Novel Biomarker in Cardiovascular Disease

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Abstract

Omentin-1 is a novel adipokine that is highly expressed in visceral adipose tissue. Omentin-1, has appeared to show cardioprotective nature in several studies. The aim of this study was to review the existing literature from clinical studies on the role played by omentin-1 in the context of cardiovascular disorders. A total of 14 articles were finalized from the 1158 articles that were screened using the search terms "omentin AND cardiovascular disease". Omentin-1 is found in lower concentrations in diseased individuals (CAD or risk factors of CAD), and the concomitant presence of CAD and metabolic syndrome or diabetes further suppresses omentin-1 concentration indicating that omentin-1 is an important regulatory molecule in pathways key to the development of cardiovascular disease. Omentin -1 was found to have a moderate correlation with inflammatory biomarkers. Omentin-1 levels were found to predict CAD severity even when adjusted for multiple risk factors. Lower levels of omentin-1 were also found to have a five times higher risk of cardiovascular events in patients with heart failure. The main limitations existing in the literature are the lack of well designed prospective cohort studies that explore the utility of omentin-1 in CVD and the inter study variability in the concentration of omentin-1 across several studies. Much translational work needs to be carried out before omentin-1 measurement becomes an important tool in clinical medicine.

Keywords: Omentin-1, cardiovascular disease, risk, biomarker, diabetes, metabolic syndrome

Introduction

Cardiovascular Disease is the No.1 killer in Western Populations [1], and the major metabolic conditions of obesity, diabetes, and metabolic syndrome significantly drive the cardiovascular epidemic [2]. The current lifestyles practices including eating a fat-rich diet, sedentary living, and low-exercise exacerbate these conditions [3]. The dysregulation of ectopic fat in viceral adipose tissue is the cause of many adverse metabolic events. Obesity, diabetes, vascular disorders, and metabolic syndrome, conditions that are risk factors for cardiovascular disease are all associated with dysregulated adipose tissue. Pathological changes during these conditions trigger the release of certain factors called "Adipokines" from the white adipose tissue. The white adipose tissue has been found to affect a number of bodily functions such as energy regulation, glucose and lipid metabolism, thermogenesis, neuroendocrine function, reproduction, immunity and most relevantly cardiovascular function. Adipokines mediate these functions by different signaling pathways and chemical mediators. Adipokines have good-bad; Yin-Yang behavior with some of them being cardio protective by promoting endothelial function, angiogenesis and reducing hypertension, atherosclerosis and inflammation while some others performing functions that aggravate these very

processes [4]. Leptin and Adiponectin are the two best known and widely studied adipokines discovered in the mid 1990's. Subsequent research led to the discovery of newer adipokines such as chemerin, omentin, apelin, vaspin, visfatin whose exact roles and function is still under scrutiny [3].

Omentin-1 is a novel adipokine initially discovered in intestinal Paneth cells, was first called intellectin-1 and intestinal lactoferrin receptor [5]. Its subsequent discovery in endothelial cells gave it the name endothelial lactin [6]. Later, Omentin-1 identified in omental fat c-DNA library, was found to be scarce in subcutaneous adipose tissue but highly expressed in visceral adipose tissue. Omentin-1 however is also expressed in other tissues such as endothelial cells, human epicardial fat, thymus, small intestine, colon, reticulocytes, ovary, lungs and placenta [7]. Animal studies investigating the role of omentin-1 have found that supplementing omentin-1 via adenoviral vectors or via systemic administration greatly decreased infarct size in I/R murine model. Omentin-1 was found to prevent myocardial apoptosis via AMPK and Akt signaling pathways in these animal models however it is likely that other pathways may also be involved [8]. In humans, there are two homologous forms of omentin, omentin-1 and omentin-2, with the former being the major circulating form [9]. Omentin-1 is secreted predominantly in epicardial adipose tissue (EAT). Since the EAT is not separated from the myocardium by the fascia, the secreted omentin-1 greatly influences cardiac function [10, 11].

The role of Omentin-1 has been investigated in a wide spectrum of disorders. "Omentin-1 deficiency" has been found in a variety of medical conditions including diabetes, obesity, and metabolic syndrome [9, 11, 12]. Shibata et al found that Omentin-1 levels were decreased in patients with CAD compared to controls thereby indicating that this may prove to be a cardiovascular risk factor [13]. Diminished levels of the biomarker were also found by Katoaka and colleagues in the setting of acute myocardial infarction. Their study suggested that those with higher omentin levels at 7 days after coronary stenting had greater myocardial salvage at 6 months [8]. Considering the pooled evidence from these studies, omentin's role seems to largely cardio-protective, and that its expression is upregulated as a response to injury.

Studies on adipokines have been pursued with fervor since they seem to link obesity, metabolic syndrome and diabetes. Omentin-1, a novel adipokine seems to be a cardiovascular risk marker and studies show its cardioprotective nature. The aim of this study was to review the existing literature from clinical studies on the role played by omentin-1 in the context of cardiovascular disorders.

Methodology

We performed an electronic search using databases such as MEDLINE, Science Direct, Springer, Scopus, Google Scholar and Cochrane Library from inception until August 14th 2014 in the English Language. We used the search terms: "Omentin-1 in Cardiovascular Disease", "Omentin-1 in Heart", "Omentin-1 in Ischemic Heart Disease", "Omentin-1 in Heart Failure" and "Omentin-1 in Coronary Artery Disease." We included studies that investigated the role of Omentin-1 in Diabetes Mellitus, Hypertention, Obesity, Metabolic Syndrome, Coronary artery Disease, Myocardial Infarction, and Acute Coronary Syndrome. All studies conducted in populations without CV risk factors or those that did not investigate cardiovascular aspects or endpoints were excluded. We also excluded basic science studies such as invitro studies, RNA expression studies, genetic studies and animal studies. We excluded reviews, posters and conference articles. References of the final set of articles were also scrutinized to ensure no relevant articles were missed. Three investigators independently performed the literature search after which they jointly screened the articles for inclusion based on full-text review. Disagreements were resolved by consensus.

Results

A total of 1158 articles were retrieved from MEDLINE, Science Direct, Springer, Scopus and Google Scholar from which 16 original studies were included in the systematic review. Most of the studies were conducted in Asian populations, with 7 studies were from China, 2 from Japan, and 2 from South Korea. Three studies were conducted in Middle Eastern population, with 2 from Turkey and one from Egypt. Furthermore, 2 studies by the same group were conducted in Greek population, and one collaborative study between Belgium. The Netherlands and Germany was conducted in German population. The populations explored included those with heart disease (HF/CAD/ACS/SAP), those with risk factors of heart disease such as Metabolic Syndrome and Diabetes (Table 1). The years of publication of these studies run from 2011 till date. Omentin-1 was measured using a simple ELISA assay. Since most studies were cross-

sectional in nature, determining the causal link leading to omentin-1 deficiency hasn't yet been explored. Furthermore, the cross-sectional study design did not permit the analysis of the prognostic value of Omentin-1. However, most studies explore the relationship between omentin-1 and inflammatory markers (CRP, IL-8 and IL-6), BMI, waist circumference, HDL cholesterol and insulin resistance (or conversely insulin sensitivity). A weak to moderate correlation was observed between omentin-1 and inflammatory biomarkers.

These studies observe that lower omentin-1 levels inversely correlate with all of the above factors except HDL cholesterol. Studies suggest that Omentin-1 predicts CAD severity even when adjusted with multiple risk factors in multivariate linear regression analysis. It also is inversely associated with CIMT, a reflection of subclinical atherosclerosis. One of them observed that lower omentin-1 level exacts a 5 times higher risk of cardiovascular events in HF patients. Another study found that omentin-1 predicts CAD severity using CAI in MetS patients.

Fig. 1: Flow Chart of the systematic review

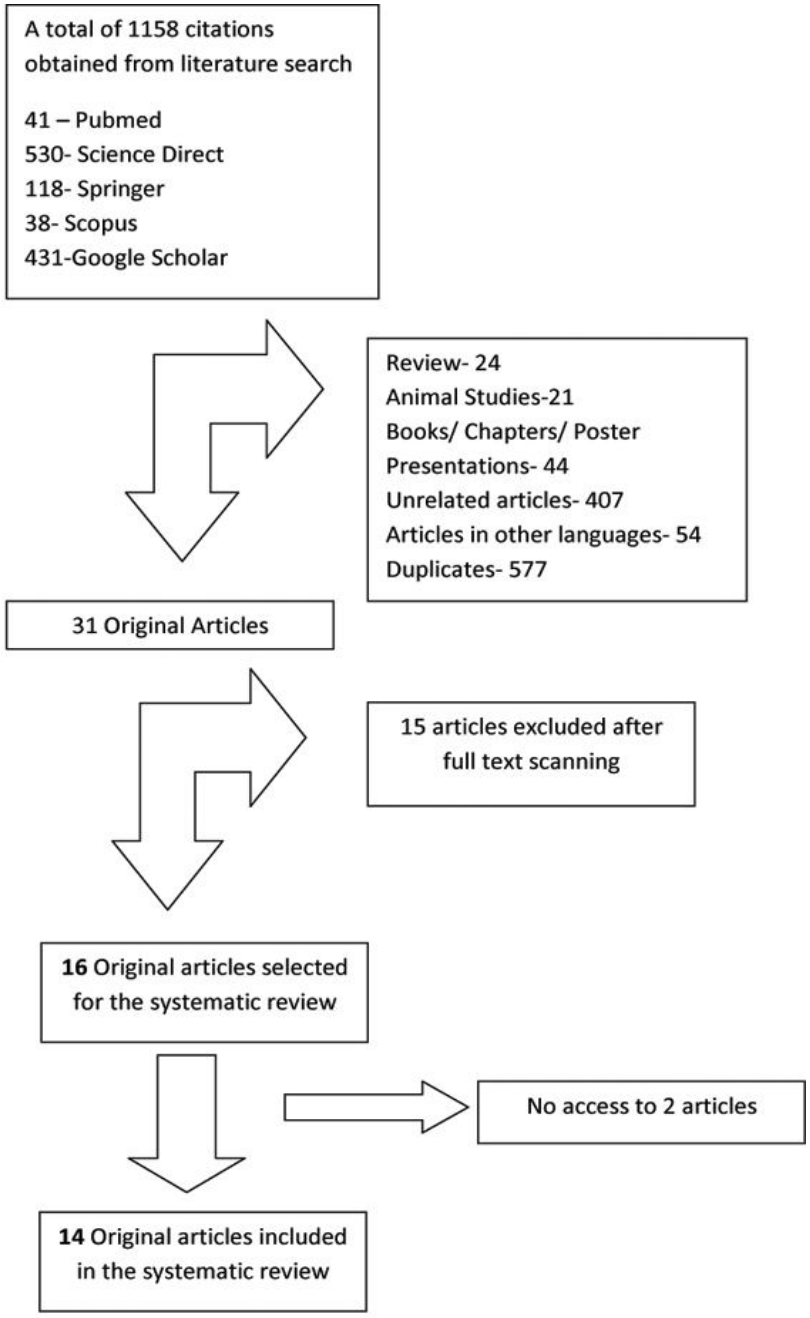

Table 1: Baseline Characteristics of the studies included in the systematic review

Author	N	Age	BMI	Gender (Male, %)	Type of Study	Assay Method, Manufacturer	Omentin-1 levels	Purpose
Shibata et al. 2011	78- Males with =75% stenosis of at least 1 major coronary as conformed by CAG 61- Matched Controls	Cases: 63.6±8.2 Controls: 61.3±5.1	Cases: 24.4±3.8 Controls: 22.9±2.5	100	Case-Control	ELISA, Bio Vendor, NC, USA	Cases: 102.8±69.0 Controls: 442.4±131.2	To investigate whether circulating omentin associates with the prevalence of coronary artery disease (CAD).
Kadoglou et al. 2013	300- Established carotid Atherosclerosis 73- Controls	Cases: 68 ±8, Controls: 65 ± 11	Cases: 27.14 ± 3.79 Controls: 27.44 ± 3.88	69%- Cases 71%- Controls	Cross-Sectional	ELISA, Enzo Life Sciences, Farmingdale, NY, USA	Cases: 518.61 ± 191.10 Controls: 815.3 ± 185.32	To investigate the relationship of omentin-1 serum levels with the presence and the ultrasonographically quantified severity of established carotid atherosclerosis.
Narumi et al. 2014	Heart Failure: 136, Control: 20	Case: 72 ± 12, Controls: 65 ± 16	Cases: 21.7 ± 3.9 Controls: 23.3 ± 3.4	56%- Cases, 55%- Controls	Prospective Cohort	ELISA, Immuno-Biological Laboratories CO., Ltd., Gunma, Japan)	Cases: 305 (35–473) Controls: 494 (351–630)	To clarify the impact of serum omentin-1 levels on cardiac prognosis in patients with HF.
Greulich et al. 2014	Controls (n = 14) DM2-patients (n = 78)	Control: 54.56±7.1 Case: 56.56±5.6	Control: 27.06±2.5 Case: 28.76±3.5**	100%- Men	Cross-Sectional	ELISA, USCN Life Science Inc, Cologne, Germany	(Median)Cases: 313 Controls: 426 ng/m	To examine whether omentin-1 expression and secretion in various adipose tissue depots, including EAT, pericardial, and subcutaneous adipose tissue, is altered in patients with DM2. To evaluate whether omentin-1 levels were associated with metabolic and cardiac parameters in men with

Wang et al. 2014	59- CHD patinets; 31 age- and sex-matched healthy controls	Controls: 75.85±8.99 CHD 73.90± 8.39	Controls: 22.32± 2.61 CHD: 24.05±2.92	Controls: 65%, Cases: 61%	Cross-sectional study	ELISA, Wellbiotechnology Company, Changsha	Controls: 717.63±229.11 ng/L, Cases" 1 115.49±361.41 ng/L,	To investigate the alteration of plasma levels of omentin-1 and visfatin in elderly patients with coronary heart disease (CHD) and heart failure.
Zhong et al. 2011	ACS (n=127) SAP (n=28) Control (n=52)	ACS: 61.85±12.05 SAP: 60.61±15.02 Controls: 59.81±9.88	ACS: 25.52±3.35 SAP: 24.71±3.74 Controls: 25.73±3.14	ACS: 70.87 SAP: 53.57 Controls: 73.08	Cross-sectional study	ELISA, Cusabio Biotech Corporation, USA	ACS: 113.08±61.43 SAP: 155.41±66.89 Controls: 254.00 (72.98) (for controls IQR)	To investigate whether serum omentin-1 levels were independently related to the incidence of CAD
Liu et al. 2011	MetS + AS: 30 MetS-AS: 30 Controls: 30	MetS + AS MetS-AS	MetS + AS 59.93 ± 9.44 MetS-AS : 54.73 ± 11.91 Controls 54.03 ± 9.43	MetS + AS: 53% MetS-AS : 57% Controls: 43%	Cross-sectional study	ELISA, B&G	MetS + AS: 10.66 ± 3.41 MetS- AS: 23.48 ± 5.87 Controls: 34.58 ± 4.23*	To investigate the role of omentin-1 in atherosclerosis
Yoo et al. 2011	Normal glucose tolerance: 30 Type 2 diabetes without carotid plaque: 30 Type 2 diabetes with carotid plaque: 30	Normal glucose tolerance: 54.07 ± 8.14 Type 2 diabetes without carotid plaque 53.1 ± 6.81 Type 2 diabetes with carotid plaque 56.47 ± 6.04	Normal glucose tolerance: 23.99 ± 2.88 Type 2 diabetes without carotid plaque 23.89 ± 2.29 Type 2 diabetes with carotid plaque 24.18 ± 2.11 0.895	Normal glucose tolerance: 40 Type 2 diabetes without carotid plaque: 33 Type 2 diabetes with carotid plaque: 50	Cross-sectional design.	ELISA, Apotech, Axxora, Nottingham, UK	NA	To determine the relationship of circulating omentin-1 levels with atherosclerosis, as measured by carotid IMT and baPWV, in subjects with type 2 diabetes and controls To determine the exact correlation of circulating level of omentin-1 with baPWV and carotid IMT in type 2 diabetes after adjustment with other cardiovascular risk factors and detailed drug history that could affect vascular function.

Yoo et al. 2013	type 2 diabetes mellitus: 120	58.3 ± 8.6	24.1 (22.8,26.4)	60	Prospective Cohort	ELISA, Biovender Laboratory Medicine Inc., Modrice, Czech Republic	446.7 ± 168.5	To clarify the influence of changes in levels of circulating omentin-1 on the progression of arterial stiffness in subjects with type 2 diabetes mellitus.
								To examine whether baseline circulating omentin-1 levels could predict arterial stiffening after a period of 1 year.
Kadoglou et al. 2014	AMI group=78, Healthy Controls= 32	AMI: 66.2 ±14.4 Controls: 63.1 ±9	AMI: 28.86 ±3.80 Controls: 28.96±4. 56	AMI: 81% Controls: 78%	Prospective Cohort	ELISA, Enzo Life Sciences, Farmingdale, New York, USA	NA	To assess the omentin-1 levels in patients with AMI at admission and at 6 months follow-up compared with individuals without angiographically proven CAD.
								To investigate the relation of novel adipokines with CAD extension and other cardiovascular risk factors.
Onur et al. 2013	Post Menopausal women with CAD n =110 Post Menopausal women Control group n= 83	CAD group = 68.2 ± 10.2 Control= 66.2 ±11.9	-	0% Males	Cross-sectional design	BioVendor Research and Diagnostic Products, Modrine, Czech Republic	CAD group: 247.5± 127.4 Non- CAD group: 506 ± 246.	To investigate the possible association between serum omentin levels and CAD and its severity in postmenopausal women.

Sengul et al. 2013	Stage 3–4 CKD: 55 Healthy Controls: 30	Stage 3–4 CKD : 48.7±13.2 Healthy Controls 43.6±8.9	Stage 3–4 CKD : 2 9.1± 6.9 Healthy Controls 27.3±4.7	Stage 3–4 CKD: 40 Healthy Controls: 30%	Cross-sectional study	BIOVENDOR R&D, Czech Republic	Stage 3–4 CKD: 183.5 ±75.5 Healthy Controls 150.7±53.6	To examine the hypothesis that omentin-1 levels are reduced in CKD patients, not on dialysis are inversely associated with carotid AS, which is mediated by inflammation
El-Mesallamy et al. 2011	Control: 15 T2DM: 53 T2DM + IHD: 22	Control: 52.6 ±3 T2DM: 58 ±1 T2DM + IHD: 59 ±1	Control: 26 ± 0.5 T2DM: 31 ± 0.8 T2DM + IHD: 28 ± 0.3	Control: 93 % T2DM: 66% T2DM + IHD: 82%	Cross-sectional study	AviBion (Orgenium, Vantaa, Finland	Control: 27.4 ±2.5 T2DM: 19.7 ± 1 T2DM + IHD: 18.5 ±1.6	To study the correlation between omentin-1 and chemerin and between each of them with other variables, such as interleukin (IL)-6 and insulin resistance, as well as other metabolic and anthropometric variables.
Shang et al. 2011	Controls:46 MetS patients without CAD: 68 MetS patients with CAD: 107	Controls: 62.56 ± 9.35 MetS patients without CAD: 62.51 ± 8.66 MetS patients with CAD: 64.41 ± 8.14	Controls: 23.36 ± 2.59 MetS patients without CAD: 24.55 ± 2.79 MetS patients with CAD: 25.11 ± 2.52	Controls: 56.5% MetS patients without CAD: 51.47% MetS patients with CAD: 60.75%			Controls: 31.31 [range 22.84–42.26] ng/mL MetS patients without CAD: 22.07 [range 16.25–26.89] MetS patients with CAD: 12.88 [range 10.26–16.20]	The current study was designed to clarify the relationship between serum omentin-1 levels and the presence and angiographic severity of CAD in patients with MetS.

Discussion

Omentin-1 is found in lower concentrations in diseased individuals (CAD or risk factors of CAD), and the concomitant presence of CAD and MetS or DM further suppresses omentin-1 concentration indicating that omentin-1 is an important regulatory molecule in pathways key to the development of cardiovascular disease. Omentin-1, an adipokine secreted in the visceral and epicardial adipose tissue is found at low levels in coronary artery disease patients compared to controls without CAD or risk factors of CAD. Consistent with these findings, Zhong and coworkers found that omentin-1 is found to linearly increase in patients with Acute Coronary Syndrome (ACS), Stable Angina Pectoris (SAP) and controls [14] while Wang et al., found that omentin-1 is significantly higher in healthy controls, compared to SAP and Unstable Angina (UA) patients [15]. However, omentin-1 levels were numerically higher in UA patients compared with SAP patients but this difference did not emerge to be statistically significant. It is possible that since the study wasn't adequately powered, they could not observe a significant change in levels between the two conditions. Therefore, it remains to be investigated if omentin-1 levels are truly different in UA and SAP. In another independent study, at a cut-off level of 16.34ng / mL as assessed by ROC, Omentin-1 was able to differentiate patients with and without CAD [12]. El-Messallamy et al., in their study consisting of 75 T2DM subjects found that omentin-1 levels were lowest in obese patients with T2DM and known ischemic heart disease, compared to the rest of the cohort [16], suggesting that activation of a host of inflammatory pathways in these populations gravely affects omentin concentrations.

Inflammation is central to all phases of atherosclerosis. It has been shown that inflammatory biomarkers play a major role in the development and progression of heart disease. Inflammation plays a key role in plaque destabilization resulting in the production of inflammatory cytokines and apoptosis of vascular cells (17). Diabetes and hypertension, powerful risk factors for Coronary Artery Disease (CAD), are regarded as low grade inflammatory processes. Therefore the studies have also assessed omentin-1 in the context of diabetes and observed correlation indices with blood pressure. Omentin-1 was found to negatively correlate with inflammatory biomarkers, glucose, insulin resistance, and systolic blood pressure (SBP) and positive correlation was observed between omentin-1 and insulin sensitivity [11, 13, 15, 16, 18]. IL-6, a pro-inflammatory cytokine has been pathogenically implicated in CAD [19]. IL-6 and omentin-1 are produced in the vascular fraction of cells [20], and a negative correlation was found between the two biomarkers in a number of studies [14, 16, 21]. Furthermore, other pro-inflammatory markers such as IL-18 and CRP [22-24] were also found to negatively correlate with omentin-1 levels. Recent studies have found that omentin-1 significantly attenuates CRP and TNF á induced NF-êB activation, suggesting a plausible anti-inflammatory role of omentin-1[25]. Additionally, omentin-1 was observed to be decreased in other inflammatory conditions such as Crohns Disease, Rheumatoid Arthritis, Diabetes and Polycystic Ovary Disease (PCOD) [7, 25–27]. Taking this together, it appears that pro-inflammatory states suppress omentin-1 levels, and the events resulting in such an interaction must be explored.

A strong motivation to explore the association between omentin-1 and diabetes is the fact that omentin-1 gene is located in the 1q22-q23 chromosomal region. This region has been linked to diabetes type II in several populations indicating the probability that omentin-1 gene may be the candidate gene for diabetes susceptibility in humans (28). In-vitro studies in human adipocytes have shown that omentin-1 promotes insulin stimulated glucose uptake and Akt phosphorylation [29]. In fact, at lower omentin-1 levels, lower insulin stimulated glucose uptake was observed in insulin sensitive tissues, resulting in insulin resistance observed in T2DM patients. In T2DM patients, omentin-1 was found to be negatively correlated with insulin resistance. In-vitro data shows that in human omental AT transplants, insulin and glucose decrease mRNA expression, protein levels and secretion of omentin-1 into conditioned media. Furthermore, prolonged insulin-glucose infusion inducing hyper insulinemia reduced circulating omentin-1 levels [25]. Given that most studies suggest Insulin and Omentin-1 as anti-inflammatory agents, it seems absurd that insulin suppresses omentin-1 production. However, exvivo and in-vitro data suggest that insulin could be pro-inflammatory. Therefore, there is a requirement to clarify the relationship between insulin and omentin-1[30].

Additionally, omentin-1 was found to negatively correlate with BMI, visceral fat volume, waist circumference and positively correlate with HDL cholesterol [18]. Several inflammatory factors are produced by the adipose tissue that directly or indirectly regulate systemic and vascular inflammatory processes. High BMI, visceral fat volume and waist circumference are factors representative of high adipose tissue mass. This

suggests that obesity negatively regulates omentin-1 expression. Substantiating this, Zhong et al. found that weight loss increased serum omentin-1 levels [14]. Another study found that weight loss induced by a hypo-calorific diet increased omentin-1 levels, along with a parallel increase in insulin sensitivity [31]. Pro-inflammatory cytokines are increased with increasing adiposity, and studies have indicated that a negative correlation is observed between omentin-1 and some of these cytokines as discussed above. This is suggestive of the fact that omentin-1 plays a key role in adiposity induced inflammation.

Deposition of plaque in the carotid artery is indicative of the occurrence of the atherosclerotic process. Suppressed levels of omentin-1 were found in post carotid revascularization patients with high grade stenosis compared to those with low grade stenosis and controls. Furthermore, omentin-1 was found to be associated with Gray Scale Matrix (GSM) score and carotid related symptoms, with patients manifesting symptoms having a further reduction in omentin-1 levels compared to asymptomatic individuals [24]. The authors suggest that this could perhaps mean that omentin-1 associated regulatory mechanisms exert a stronger influence during plaque rupture than plaque development. Role of Omentin-1 in plaque development was expounded by Duan and coworkers who showed that the biomarker prevented osteoblastic differentiation of calcifying vascular smooth muscle cells through the phosphatidylinositol 3-kinase (PI3K) D Akt signalling pathway (32). It was further suggested that omentin-1 inhibited arterial calcification in viscerally obese subjects. Carotid intima media thickness (CIMT) and presence of plaque are markers of cardiovascular disease with the former a measure of early atherosclerosis, while the latter being a measure of degree of atherosclerosis. CIMT is also associated with stiffness and strain and reflects arterial function decline, which precedes structure change and plaque deposition. Omentin-1 levels were also found to be predictive of arterial stiffness as measured by CIMT in T2DM patients by Yoo et al. Furthermore, it was also found that those that experienced arterial stiffening had a greater increase in omentin-1 levels at one year, possibly reflecting Omentin-1's attempt but inability to prevent exacerbation of arterial stiffness [33]. Similar findings were observed by Liu and Shang et al. who found that presence of metabolic syndrome and concomitant CAD further suppresses omentin-1 levels, with the biomarker showing an inverse relationship between Coronary Atherosclerosis Index (CAI) and CIMT, exhibiting its role in the development of coronary disease [12, 18]. Since previous research shows that insulin and glucose decreased omentin-1 mRNA expression significantly, it is possible that omentin-1 decelerates atherosclerosis progression by optimizing glucose metabolism [18]. The events leading up to change in arterial function to plaque deposition, plaque rupture, and progression of CAD to MI and finally HF, are all marked by gradual decline in endothelial function and a host of inflammatory events drive the process. Furthermore, greater stiffness results in increase in systolic blood pressure and subsequent damage to the arterial wall, endothelial injury and atherosclerosis. Consistent with this, omentin-1 levels were found to be inversely correlated with SBP [15]. The decreased levels of omentin-1 in subjects with cardiovascular disease or the risk factors of the disease suggest that omentin-1 could be involved in the inhibition of vascular endothelial inflammation and endothelial dysfunction both which are markers of early atherosclerotic disease. In addition to this, inhibition of TNFα and COX-2 expression by omentin-1 are characteristic of anti-atherosclerotic activity of omentin-1 by modulating the vascular endothelial inflammatory state [34]. Subsequently, omentin-1 has been found to be a novel marker of endothelial dysfunction. Thirdly, omentin-1 may be involved in NOS derived endothelium dependent relaxation thereby exerting its influence on lowering BP [35].

Omentin-1's influence on cardiac function in DM2 patients was explored by Gruelich et al., where increase in omentin-1 levels correlated with the improvement in diastolic function [11). Molecules produced in the EAT directly affect cardiac function, (since the EAT is not separated from the myocardium by the fascia) and omentin-1 has been found to be highly expressed in the EAT [10]. Furthermore, when adult rat cardiomyocytes were exposed to EAT from DM2 individuals, recombinant omentin-1 was found to protect against cardiomyocyte contractile dysfunction and insulin resistance induced by the EAT released factors suggesting that perhaps omentin-1 acts as a scavenger of harmful factors [11]. Two prospective studies conducted in MI and HF cohorts found decreased levels of omentin-1 in diseased individuals compared to control individuals without cardiovascular disease [22, 23]. Over the 6 months of follow up of MI patients, the omentin-1 levels improved indicating a recovering myocardium. Similarly in the prospective study in HF patients, omentin-1

displayed its prognostic capability by furnishing a 5 times higher risk of cardiovascular events to those with lower levels compared to those with higher levels of omentin-1. It is also worth noting that omentin-1 levels were lowest in those with NYHA class IV compared to class III and II [22].

Limitations

While a number of studies have explored the role between omentin-1 in patient populations with CAD and/or with risk factors of CAD, the area still calls for extensive research to determine certain key characteristics of omentin-1. Firstly, omentin-1 levels in healthy populations remains to be determined. Omentin-1 levels in the control populations in the studies considered for this review range from 31.31ng/mL to 815.3ng/mL. Furthermore, the influence of age, gender and other basic demographic characteristics on omentin-1 levels must be determined. Secondly, the factors that govern omentin-1 synthesis must be determined, so should the effects of exogenous omentin-1 on cardiovascular function be determined. Thirdly and importantly, omentin-1 levels must be examined in large studies, in a prospective study design. The cross-sectional natures of most of the studies considered in this review pose as a hindrance to analyze the causality.

Conclusion

Omentin-1 is an adipokine secreted by the stromal vascular cells and is expressed in the heart, lung, ovary as well as the placenta. The suppression in the expression of omentin-1 in pro-inflammatory states, along with data from in-vivo and in-vitro studies suggests that omentin-1 is an anti-inflammatory molecule. The concomitant presence of CAD and risk factors of CAD further suppress omentin-1 levels suggesting that the triggering of multiple inflammatory events negatively affect omentin-1 concentration and drive omentin-1 deficiency. The immediate need in omentin-1 research is to define normal concentrations of this biomarker. Furthermore, it is required to conduct several large scale prospective studies in cardiovascular disease populations to determine both the causality driving omentin-1 deficiency and its possible prognostic value.

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