Oxidative Stress and Inflammation Are Associated with Coexistent Severe Multivessel Coronary Artery Stenosis and Right Carotid Artery Severe Stenosis in Elderly Patients

Xia Li, Dianxuan Guo, Youdong Hu, and Ying Chen

Department of Geriatrics, The Affiliated Huaian Hospital of Xuzhou Medical University, Huaian 223002, China

Correspondence should be addressed to Xia Li; xial_li@qq.com

Received 16 August 2021; Revised 29 November 2021; Accepted 1 December 2021; Published 22 December 2021

Academic Editor: Jeferson Luis Franco

Copyright © 2021 Xia Li et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Oxidative stress and inflammatory response are the main pathogenic pathways in atherosclerosis stenosis. This study is aimed at evaluating the roles of oxidative stress and inflammatory response in coexistent right carotid artery severe stenosis and severe multivessel coronary artery stenosis in elderly patients. Circulating levels of total oxidant status (TOS), lipid hydroperoxide (LHP), 8-isoprostane (8-IP), malondialdehyde (MDA), monocyte chemotactic protein-4 (MCP-4), amyloid A (AA), high-sensitivity C-reactive protein (hs-CRP), and tumor necrosis factor-α (TNF-α) were measured by standardised laboratory test methods. Markers of oxidative stress and inflammatory response: levels of TOS, LHP, 8-IP, MDA, MCP-4, AA, hs-CRP, and TNF-α, were increased \((P < 0.001)\) in elderly patient. These results suggested that oxidative stress and inflammatory response may be involved in carotid artery severe stenosis and severe multivessel coronary artery stenosis and measuring oxidative stress and inflammation biomarkers may also be a promising step in the development of an effective method for monitoring the severity of right carotid artery stenosis and multivessel coronary artery stenosis in elderly patients.

1. Introduction

Oxidative stress is related to intracranial carotid artery atherosclerosis, and the elevated cerebrovascular oxidative stress reduces cerebrovascular superoxide dismutase activity and promotes cerebrovascular oxidative injuries and intracranial carotid artery atherosclerosis [1, 2]. The vascular inflammatory response is associated with the development and progression of atherosclerotic plaques in the human aorta, carotid, cerebral, and coronary arteries [3]. The intracranial artery atherosclerosis is the most common cause of cerebral ischemic stroke [4].

Total oxidant status (TOS) is a marker of oxidative stress. High level of TOS inhibits expression of antioxidant enzymes and is associated with oxidant/antioxidant imbalance [5] and oxidant-antioxidant imbalance is involved in the development of atherosclerosis [6]. Lipid hydroperoxide (LHP) is a biomarker of oxidative stress. Histopathological studies show significant elevation in LHP induces the progression of oxidative damage [7] and accelerates the development and progression of atherosclerosis [8]. Increased 8-isoprostane (8-IP) as an oxidative damage biomarker induces oxidative stress and plays a key role in the progression of atherosclerosis [9, 10] and is further related to CAD and the extent of coronary stenosis [9]. High level of malondialdehyde (MDA) as reliable biomarker of oxidative stress induces oxidative stress and contributes to the imbalance between oxidant and antioxidant status and promotes the progression of atherosclerosis [11, 12]. Monocyte chemotactic protein-4 (MCP-4) as a proinflammatory molecular plays a key in atherogenesis. MCP-4 is expressed in the artery atherosclerotic lesions in patients with atherosclerotic coronary arteries and is involved in the atherosclerotic inflammatory process [13]. Amyloid A (AA) as an indicator of inflammatory response plays a key role in acute and chronic inflammatory response [14], and atherosclerosis is a chronic inflammatory response related to increased expression of AA in humans [15]. High-sensitivity C-reactive protein (hs-CRP) is a marker of systemic inflammatory response and inflammatory response plays an important role in the development and progression of atherosclerosis [16].
role in atherosclerosis initiation and progression [16]. The pathogenic activity of proinflammatory cytokine tumor necrosis factor-α (TNF-α) promotes inflammatory response and plays a pivotal role in the progression of in atherosclerotic cardiovascular diseases [17]. This study is aimed at evaluating the relationships among oxidative stress and inflammation markers as well as carotid and coronary artery severe stenosis to test the contribution of oxidative stress and inflammation to coexistent right carotid artery severe stenosis and severe multivessel coronary artery stenosis in patients.

2. Material and Methods

2.1. Patient Selection. From 3 January 2014 to 25 December 2018, our research included the patients with carotid artery stenosis and carotid artery stenosis+coronary artery stenosis in different aged groups. The inclusion criteria adopted in the present research were (1) the patients aged 65 to 86 years old and (2) the patients with right common carotid artery stenosis (RCCAS), right external carotid artery stenosis (RECAS), right internal carotid artery stenosis (RICAS), and RCCAS+RECAS+RICAS+coronary artery stenosis. The research was approved by the Xuzhou Medical University and the University Human Research Ethics Committee according to the relevant laws of China, and the written informed consents were obtained for all participants according to the Revised Declaration of Helsinki. The patients with one or more of the following criteria were excluded: (1) acute and chronic brain infarction, (2) acute myocardial infarction, (3) upper limb artery stenosis or occlusion, (4) lower extremity arterial stenosis or occlusion, (5) coronary artery occlusion, (6) malignant tumors, (7) using antiphlogistic drugs, and (8) using antioxidants.

2.2. Research Protocol. The healthy individuals defined as without any illnesses [18] were included in the control (CON) group (n=61) and patients without carotid stenosis defined as arterial intimal hyperplasia [19] were included in the without carotid stenosis group (n=56). The numbers of patients with RCCAS, RECAS, RICAS, RCCAS+RECAS +RICAS, and RCCAS+RECAS+RICAS+coronary artery stenosis were 167, 162, 167, 165, and 155, respectively. The patients with RCCAS were included in mild right common carotid artery stenosis (MI-RCCAS) defined as the stenosis diameter <50% [20] group (n=59), moderate right common carotid artery stenosis (MO-RCCAS) defined as the stenosis 50-69% [20] group (n=55), and severe right common carotid artery stenosis (SE-RCCAS) defined as the stenosis 70-99% [20] group (n=53). The patients with RECAS were included in the mild right external carotid artery stenosis (MI-RECAS) group (n=54), moderate right external carotid artery stenosis (MO-RECAS) group (n=51), and severe right external carotid artery stenosis (SE-RECAS) group (n=57). The patients with RICAS were included in the mild right internal carotid artery stenosis (MI-RICAS) group (n=57), moderate right internal carotid artery stenosis (MO-RICAS) group (n=54), and severe right internal carotid artery stenosis (SE-RICAS) group (n=56). The numbers of patients with SE-RCCAS+SE-RECAS, SE-RCCAS+SE-RICAS, and SE-RCCAS+SE-RECAS+SE-RICAS were 58, 55 and 52, respectively. The numbers of patients with SE-RCCAS+severe one-vessel coronary stenosis (SOVCS), SE-RECAS+severe two-vessel coronary stenosis (STVCS), and SE-RICAS+severe multivessel coronary stenosis (SMVCS) were 51, 50, and 54, respectively. Severe coronary stenosis was defined as ≥70% narrowing [21].

2.3. Evaluations of Carotid Stenosis and Coronary Artery Stenosis. The assessment of carotid stenosis was measured with computed tomography angiography and Color Doppler ultrasonography [22]. Coronary artery stenosis was determined on both stress and rest coronary computed tomography angiography images [23] The evidence was assessed independently by three experienced interventional cardiologists.

2.4. Measurements of the Levels of TOS, LHP, 8-IP, and MDA. Fasting venous blood samples were collected into blood test tubes, and the serum was separated from blood samples by centrifugating at 1500 g for 15 min at 4°C, and the blood serum samples were stored frozen at -80°C until further TOS analysis [24]. The evaluations of LHP in the patients’ plasma were performed by using ferrous oxidation in xylene orange assays in conjunction with triphenylphosphine, and the results were expressed as μmol/L [25]. Blood plasma samples were collected and centrifuged at 6000g for 15 minutes at 4°C and stored frozen immediately at -80°C until further 8-IP analysis. Concentrations of 8-IP analyses were determined by using enzyme immunooassay (ELISA), and all results were expressed as pg/mL [26]. The concentration of MDA was measured by using ELISA, which was performed by using a commercial ELISA kit for the measurements of the levels of MDA (DL Naturegene Life Sciences, Inc., USA). All serum samples were stored frozen at -80°C until analysis. Reading of the results was measured at 456 nm on a plate reader (STAT FAX 2100, Awareness technology Inc., USA). The concentrations of MDA were expressed in nmol/L [27].

2.5. Measurements of the Levels of MCP-4, AA, hs-CRP, and TNF-α. After overnight fasting, the venous blood samples were collected and frozen immediately at -80°C until further use. The levels of serum MCP-4 were measured by ELISA assays (R&D Systems, Minneapolis, MN, USA) according to the manufacturer’s instruction [28]. The serum samples were collected and frozen immediately and kept at -80°C until further processing. AA in serum was quantified by using ELISA kit from Human AA Assay Kit (Invitrogen Life Technologies, Carlsbad, CA, USA) according to the instruction of the kit [29]. Blood plasma samples were collected from participants after overnight fasting and were stored frozen at -80°C until use. The hs-CRP in plasma was determined by turbidometric assay and ELISA method (ELISA kit, Calbiotech Inc., Spring Valley, CA, USA) [30]. Venous serum blood samples were collected after overnight fasting and were stored frozen in aliquots at -80°C until further processing. Sensitive ELISA sandwich immunoassay (Immundiagnostik AG,
3. Results

3.1. The Participant Baseline Characteristics. The characteristics of individuals participating were very similar among different study groups (Table 1). All participants in study groups were well-matched without significant differences in gender, age, coronary artery disease (CAD) defined as coronary arteries with stenosis ≥ 50% in a major epicardial coronary arteries [32], hypertension defined as blood pressure higher than 130/80 mmHg [33], diabetes mellitus defined as fasting plasma glucose ≥ 126 mg/dL (7 mmol/L) [34], history of stroke defined as intracranial ischemia and hemorrhage [35], current smoking defined as ≥ 20 pack-years and > 20 joint-years, respectively [36], current drinking defined as any alcoholic drinking and alcoholic binge drinking as consuming five or more drinks on one or more occasions, both in the past two months [37], regular exercise defined as any kind of favorite recreational or sport and physical activity other than simply walking more than three days a week for at least twenty minutes [38], myocardial infarction defined as sudden ischemic necrosis of myocardial tissue [39], dizziness defined as persistent subjective unsteadiness [40], memory impairment defined as delayed word recall test score < 4 and poor cognitive function by mini-mental state examination score < 25 [41], amaurosis fugax defined as transient monocular vision loss secondary to the retinal ischemia [42], cognitive impairment defined as impairment of ≥ 2 cognitive tests [43], and angina pectoris defined as pain, pressure, or discomfort in the chest [44].

3.2. Levels of TOS, LHP, 8-IP, MDA, MCP-4, AA, hs-CRP, and TNF-α in Elderly Patients with MI-RCCAS, MO-RCCAS, and SE-RCCAS. The levels of TOS, LHP, 8-IP, MDA, MCP-4, AA, hs-CRP, and TNF-α were increased significantly in the SE-RCCAS group when compared with the MI-RCCAS and MO-RCCAS groups, respectively (P < 0.001). It is likely that the increased levels of oxidative stress and proinflammatory response may play a key role in the development of right common carotid artery stenosis (Table 2).

3.3. Oxidative Stress and Proinflammatory Response Were Associated with MI-RECAS, MO-RECAS, and SE-RECAS in Elderly Patients. The levels of TOS, LHP, 8-IP, MDA, MCP-4, AA, hs-CRP, and TNF-α were increased significantly in the SE-RECAS group compared to the MI-RECAS and MO-RECAS groups, respectively (P < 0.001). Thus, inhibition of oxidative stress and proinflammatory response in elderly patients with right external carotid artery stenosis may be beneficial (Table 3).

3.4. Biomarker Levels of Proinflammation and Oxidative Stress in Elderly Patients with MI-RECAS, MO-RECAS, and SE-RECAS. Levels of TOS, LHP, 8-IP, MDA, MCP-4, AA, hs-CRP, and TNF-α were increased significantly in the SE-RECAS group compared to the MI-RECAS and MO-RECAS groups, respectively (P < 0.001) (Table 4). Our study demonstrated that high levels of pro-inflammation and oxidative stress may be related to RICAS.

3.5. Levels of Proinflammation and Oxidative Stress in Elderly Patients with SE-RCCAS+SE-RECAS, SE-RCCAS+SE-RECAS, and SE-RCCAS+SE-RICAS. The levels of TOS, LHP, 8-IP, MDA, MCP-4, AA, hs-CRP, and TNF-α were increased significantly in the SE-RCCAS+SE-RECAS+SE-RICAS group compared to the SE-RCCAS+SE-RECAS and SE-RCCAS+SE-RICAS groups, respectively (P < 0.001). Our study demonstrated that the interplay of oxidative stress and inflammation may promote the development of carotid artery severe stenosis in patients (Table 5).

3.6. The Levels of Proinflammation and Oxidative Stress in Elderly Patients with SE-RCCAS+SOVCS, SE-RECAS+STVCS, and SE-RICAS+SMVCS. The levels of TOS, LHP, 8-IP, MDA, MCP-4, AA, hs-CRP, and TNF-α were increased significantly in the SE-RICAS+SMVCS group compared to the SE-RCCAS+SOVCS and SE-RECAS+STVCS groups, respectively (P < 0.001) (Table 6). We also observed that the expression of markers of inflammation and oxidative stress was responsible for carotid artery severe stenosis and severe coronary artery stenosis. Increased oxidative stress and inflammation may cause the initiation and progression of carotid artery severe stenosis and severe coronary artery stenosis (Table 6).

3.7. Incidences of Carotid Artery Severe Stenosis and Severe Coronary Artery Stenosis in Elderly Patients. The incidences of SE-RAS+SMVCS in 81-86 years old age group were
Table 1: Baseline characteristics of patients with RCCAS, RECAS, RICAS, RCCAS+RECAS+RICAS, and RCCAS+RECAS+RICAS+coronary artery lesions.

|                      | CON (n = 61) | No carotid stenosis (n = 56) | RCCAS (n = 167) | RECAS (n = 162) | RICAS (n = 167) | RCCAS+RECAS+RICAS (n = 165) | RCCAS+RECAS+RICAS+coronary artery stenosis (n = 155) | P value |
|----------------------|--------------|-------------------------------|-----------------|-----------------|-----------------|-----------------------------|-----------------------------------------------|---------|
| Gender               |              |                               |                 |                 |                 |                             |                                               |         |
| Male, n (%)          | 31 (51)      | 29 (52)                       | 83 (49)         | 82 (51)         | 83 (49)         | 82 (49)                     | 79 (51)                                       | 0.41    |
| Female, n (%)        | 30 (49)      | 27 (48)                       | 84 (51)         | 80 (49)         | 84 (51)         | 83 (51)                     | 76 (49)                                       | 0.43    |
| Age (years)          | 65.1 ± 13.0  | 65.8 ± 13.2                   | 64.2 ± 13.4     | 65.1 ± 14.0     | 63.8 ± 14.4     | 62.2 ± 15.1                | 76.6 ± 15.3                                   | 0.32    |
| CAD, n (%)           | 0            | 17 (30)                       | 83 (49)         | 81 (50)         | 84 (50)         | 82 (49)                     | 77 (50)                                       | 0.41    |
| Hypertension, n (%)  | 0            | 15 (27)                       | 35 (21)         | 54 (33)         | 60 (35)         | 54 (32)                     | 47 (30)                                       | 0.07    |
| Diabetes mellitus, n (%) | 0       | 10 (18)                       | 33 (19)         | 30 (18)         | 33 (20)         | 32 (19)                     | 30 (19)                                       | 0.12    |
| History of stroke, n (%) | 0       | 0                             | 9 (5)           | 8 (5)           | 7 (4)           | 8 (4)                       | 9 (5)                                          | 0.06    |
| Current smoking, n (%) | 0       | 6 (11)                        | 42 (25)         | 29 (17)         | 40 (23)         | 29 (17)                     | 40 (25)                                       | 0.07    |
| Current drinking, n (%) | 0       | 0                             | 9 (5)           | 11 (7)          | 9 (4)           | 12 (7)                      | 9 (5)                                          | 0.06    |
| Regular exercise, n (%) | 0       | 5 (8)                         | 4 (7)           | 7 (4)           | 5 (3)           | 6 (3)                       | 4 (2)                                          | 0.17    |
| Myocardial infarction, n (%) | 0       | 0                             | 0               | 0               | 0               | 0                           | 11 (7)                                         | 0.14    |
| Dizziness, n (%)     | 0            | 0                             | 6 (3)           | 3 (1)           | 4 (2)           | 7 (4)                       | 4 (2)                                          | 0.10    |
| Memory impairment, n (%) | 0       | 0                             | 25 (15)         | 21 (13)         | 17 (10)         | 20 (12)                     | 9 (6)                                          | 0.27    |
| Amaurosis fugax, n (%) | 0       | 0                             | 16 (9)          | 13 (8)          | 12 (7)          | 11 (6)                      | 10 (6)                                         | 0.16    |
| Cognitive impairment, n (%) | 0       | 0                             | 10 (5)          | 7 (4)           | 6 (3)           | 8 (4)                       | 7 (4)                                          | 0.09    |
| Angina pectoris, n (%) | 0       | 0                             | 0               | 0               | 0               | 0                           | 20 (13)                                        | 0.14    |

CON: control; RCCAS: right common carotid artery stenosis; RECAS: right external carotid artery stenosis; RICAS: right internal carotid artery stenosis; CAD: coronary artery disease.
**Table 2: Levels of biomarkers in patients with RCCAS.**

|               | CON (n = 61) | No carotid stenosis (n = 56) | MI-RCCAS (n = 59) | MO-RCCAS (n = 55) | SE-RCCAS (n = 53) |
|---------------|--------------|------------------------------|-------------------|-------------------|-------------------|
| TOS (μmol H₂O₂ Eq/L) | 7.3 ± 0.7    | 7.4 ± 0.7                    | 7.8 ± 1.5*        | 8.3 ± 0.8**       | 9.1 ± 0.9***     |
| LHP (μmol/L)   | 5.8 ± 0.6    | 5.9 ± 0.6                    | 6.7 ± 0.7*        | 7.9 ± 0.8**       | 8.7 ± 0.9***     |
| 8-IP (pg/mL)   | 45.2 ± 4.5   | 45.0 ± 4.4                   | 56.2 ± 5.6*       | 68.8 ± 6.9**      | 77.4 ± 7.6***    |
| MDA (nmol/L)   | 1.7 ± 0.3    | 1.6 ± 0.2                    | 2.8 ± 0.3*        | 3.6 ± 0.4**       | 4.5 ± 0.5***     |
| MCP-4 (ng/mL)  | 41.9 ± 4.2   | 42.0 ± 4.1                   | 49.7 ± 5.0*       | 58.5 ± 5.9**      | 66.3 ± 6.6**     |
| AA (mg/L)      | 35.2 ± 3.5   | 36.1 ± 3.6                   | 44.2 ± 4.3*       | 57.0 ± 5.6**      | 65.2 ± 6.5***    |
| hs-CRP (mg/L)  | 2.7 ± 0.3    | 2.6 ± 0.4                    | 3.9 ± 0.4*        | 5.6 ± 0.6**       | 6.5 ± 0.7***     |
| TNF-α (ng/L)   | 20.1 ± 2.0   | 21.3 ± 2.1                   | 29.4 ± 2.9*       | 45.7 ± 4.6**      | 50.6 ± 5.1***    |

RCCAS: right common carotid artery stenosis; CON: control; MI-RCCAS: mild right common carotid artery stenosis; MO-RCCAS: moderate right common carotid artery stenosis; SE-RCCAS: severe right common carotid artery stenosis; TOS: total oxidant status; LHP: lipid hydroperoxide; 8-IP: 8-isoprostane; MDA: malondialdehyde; MCP-4: monocyte chemotactic protein-4; AA: amyloid A; hs-CRP: high-sensitivity C-reactive protein; TNF-α: tumor necrosis factor-α. *P < 0.05 (CON group/no carotid stenosis group). **P < 0.01 (MI-RCCAS group/MO-RCCAS group). ***P < 0.001 (MO-RCCAS group/SE-RCCAS group). Group comparisons (CON group/no carotid stenosis group/MI-RCCAS group/MO-RCCAS group/SE-RCCAS group) were made using ANOVA, P < 0.001.

**Table 3: Levels of biomarkers in patients with RECAS.**

|               | CON (n = 61) | No carotid stenosis (n = 56) | MI-RECAS (n = 54) | MO-RECAS (n = 51) | SE-RECAS (n = 57) |
|---------------|--------------|------------------------------|-------------------|-------------------|-------------------|
| TOS (μmol H₂O₂ Eq/L) | 7.3 ± 0.7    | 7.4 ± 0.7                    | 8.9 ± 0.9*        | 10.0 ± 1.2**      | 12.1 ± 1.3***    |
| LHP (μmol/L)   | 5.8 ± 0.6    | 5.9 ± 0.6                    | 7.0 ± 0.7*        | 8.5 ± 0.9**       | 9.7 ± 2.3***     |
| 8-IP (pg/mL)   | 45.2 ± 4.5   | 45.0 ± 4.4                   | 59.7 ± 6.0*       | 65.2 ± 6.4**      | 82.0 ± 7.8***    |
| MDA (nmol/L)   | 1.7 ± 0.3    | 1.6 ± 0.2                    | 3.8 ± 0.5*        | 4.9 ± 0.6**       | 7.2 ± 0.8***     |
| MCP-4 (ng/mL)  | 41.9 ± 4.2   | 42.0 ± 4.2                   | 59.6 ± 6.0*       | 78.5 ± 7.9**      | 96.3 ± 8.9***    |
| AA (mg/L)      | 35.2 ± 3.5   | 36.1 ± 3.6                   | 54.1 ± 5.3*       | 75.0 ± 7.3**      | 96.2 ± 8.7***    |
| hs-CRP (mg/L)  | 2.7 ± 0.3    | 2.6 ± 0.3                    | 4.4 ± 0.5*        | 6.9 ± 0.6**       | 8.5 ± 0.7***     |
| TNF-α (ng/L)   | 20.1 ± 2.0   | 21.3 ± 2.1                   | 40.4 ± 3.9*       | 69.7 ± 7.0**      | 88.6 ± 9.1***    |

RECAS: right external carotid artery stenosis; CON: control; MI-RECAS: mild right external carotid artery stenosis; MO-RECAS: moderate right external carotid artery stenosis; SE-RECAS: severe right external carotid artery stenosis; TOS: total oxidant status; LHP: lipid hydroperoxide; 8-IP: 8-isoprostane; MDA: malondialdehyde; MCP-4: monocyte chemotactic protein-4; AA: amyloid A; hs-CRP: high-sensitivity C-reactive protein; TNF-α: tumor necrosis factor-α. *P < 0.05 (CON group/no carotid stenosis group). **P < 0.01 (MI-RECAS group/MO-RECAS group). ***P < 0.001 (MO-RECAS group/SE-RECAS group). Group comparisons (CON group/no carotid stenosis group/MI-RECAS group/MO-RECAS group/SE-RECAS group) were made using ANOVA, P < 0.001.

**Table 4: Levels of biomarkers in patients with RICAS.**

|               | CON (n = 61) | No carotid stenosis (n = 56) | MI-RICAS (n = 57) | MO-RICAS (n = 54) | SE-RICAS (n = 56) |
|---------------|--------------|------------------------------|-------------------|-------------------|-------------------|
| TOS (μmol H₂O₂ Eq/L) | 7.3 ± 0.7    | 7.4 ± 0.7                    | 13.7 ± 1.4*       | 18.0 ± 2.0**      | 26.9 ± 3.0***    |
| LHP (μmol/L)   | 5.8 ± 0.6    | 5.9 ± 0.6                    | 7.9 ± 0.7*        | 11.5 ± 1.2**      | 12.7 ± 1.4***    |
| 8-IP (pg/mL)   | 45.2 ± 4.5   | 45.0 ± 4.4                   | 69.7 ± 7.0*       | 95.0 ± 9.2**      | 106.4 ± 10.3***  |
| MDA (nmol/L)   | 1.7 ± 0.3    | 1.6 ± 0.2                    | 3.8 ± 0.4*        | 6.5 ± 1.3**       | 9.2 ± 1.2***     |
| MCP-4 (ng/mL)  | 41.9 ± 4.2   | 42.0 ± 4.2                   | 69.7 ± 7.0*       | 88.5 ± 8.2**      | 116.3 ± 11.6***  |
| AA (mg/L)      | 35.2 ± 3.5   | 36.1 ± 3.6                   | 54.1 ± 5.9*       | 85.0 ± 9.0**      | 109.2 ± 10.3***  |
| hs-CRP (mg/L)  | 2.7 ± 0.3    | 2.6 ± 0.3                    | 5.2 ± 0.5*        | 7.9 ± 0.8**       | 11.0 ± 1.1***    |
| TNF-α (ng/L)   | 20.1 ± 2.0   | 21.3 ± 2.1                   | 50.4 ± 5.3*       | 79.7 ± 8.0**      | 98.6 ± 9.2***    |

RICAS: right internal carotid artery stenosis; CON: control; MI-RICAS: mild right internal carotid artery stenosis; MO-RICAS: moderate right internal carotid artery stenosis; SE-RICAS: severe right internal carotid artery stenosis; TOS: total oxidant status; LHP: lipid hydroperoxide; 8-IP: 8-isoprostane; MDA: malondialdehyde; MCP-4: monocyte chemotactic protein-4; AA: amyloid A; hs-CRP: high-sensitivity C-reactive protein; TNF-α: tumor necrosis factor-α. *P < 0.05 (CON group/no carotid stenosis group). **P < 0.01 (MI-RICAS group/MO-RICAS group). ***P < 0.001 (MO-RICAS group/SE-RICAS group). Group comparisons (CON group/no carotid stenosis group/MI-RICAS group/MO-RICAS group/SE-RICAS group) were made using ANOVA, P < 0.001.
higher than 65-70 and 75-80 years old age groups. These results showed that SE-RAS+SMVCS occurred more frequently in 81-86 years old age group than in 65-70 and 75-80 years old age groups (Table 7).

### 3.8. Multiple Regression Analysis to Calculate and Confirm the Statistical Significance of Variables for Carotid and Coronary Artery Stenosis

By multiple regression analyses, TOS, LHP, 8-IP, MDA, MCP-4, AA, hs-CRP, and TNF-α were found to be independent risk predictors of worsening of carotid and coronary artery lesions after adjustment for gender, age, CAD, hypertension, diabetes mellitus, history of stroke, current smoking, current drinking, regular exercise, myocardial infarction, dizziness, delayed memory, amaurosis fugax, and angina pectoris in elderly patients. All P values of less than 0.05 were regarded as statistically significant (Table 8).

### 4. Discussion

The increased TOS as oxidative stress marker leads to oxidative stress, resulting from an imbalance of reactive oxygen species-antioxidants [45]. Oxidative stress causes oxidative damage in vascular endothelium, leading to vascular endothelial cell dysfunction and cardiovascular diseases and plays a key role in the progression and development of atherosclerosis [46]. High levels of LHP are related to an imbalance between generation and removal of free radicals, promoting oxidative vascular damages, vascular dysfunction, oxidative damage to cell proteins, cell membrane, and cellular

---

#### Table 5: Levels of biomarkers in patients with carotid artery severe stenosis.

|                  | CON (n = 61) | No carotid stenosis (n = 56) | SE-RCCAS+SE-RECAS (n = 58) | SE-RCCAS+SE-RICAS (n = 55) | SE-RCCAS+SE-RECAS+SE-RICAS (n = 52) |
|------------------|-------------|------------------------------|----------------------------|---------------------------|----------------------------------|
| TOS (μmol H₂O₂ Eq/L) | 7.3 ± 0.7   | 7.4 ± 0.7                    | 17.3 ± 1.6*                | 33.9 ± 2.4**              | 46.9 ± 3.6***                    |
| LHP (μmol/L)     | 5.8 ± 0.6   | 5.9 ± 0.6                    | 11.7 ± 1.2*                | 18.3 ± 1.6**              | 24.7 ± 2.3***                    |
| 8-IP (pg/mL)     | 45.2 ± 4.5  | 45.0 ± 4.4                   | 73.7 ± 7.3*                | 115.0 ± 10.5**            | 146.4 ± 13.6***                  |
| MDA (nmol/L)     | 1.7 ± 0.3   | 1.6 ± 0.2                    | 4.0 ± 0.4*                 | 7.5 ± 0.6**               | 10.2 ± 0.9***                    |
| MCP-4 (ng/mL)    | 41.9 ± 4.2  | 42.0 ± 4.2                   | 79.7 ± 6.8*                | 138.5 ± 12.8**            | 176.3 ± 16.4**                   |
| AA (mg/L)        | 35.2 ± 3.5  | 36.1 ± 3.6                   | 60.9 ± 5.9*                | 86.0 ± 7.6**              | 110.2 ± 10.1***                  |
| hs-CRP (mg/L)    | 2.7 ± 0.3   | 2.6 ± 0.3                    | 5.4 ± 0.4*                 | 8.4 ± 0.6**               | 12.0 ± 0.9***                    |
| TNF-α (ng/L)     | 20.1 ± 2.0  | 21.3 ± 2.1                   | 49.4 ± 3.9*                | 79.7 ± 6.5**              | 118.6 ± 10.8***                  |

**CON**: control; **SE-RCCAS**: severe right common carotid artery stenosis; **SE-RECAS**: severe right external carotid artery stenosis; **SE-RICAS**: severe right internal carotid artery stenosis; **TOS**: total oxidant status; **LHP**: lipid hydroperoxide; **8-IP**: 8-isoprostan; **MDA**: malondialdehyde; **MCP-4**: monocyte chemotactic protein-4; **AA**: amyloid A; **hs-CRP**: high-sensitivity C-reactive protein; **TNF-α**: tumor necrosis factor-α. *P < 0.001 (no carotid stenosis group/SE-RCCAS+SE-RECAS group). **P < 0.001 (SE-RCCAS+SE-RECAS group/SE-RCCAS+SE-RICAS group). ***P < 0.001 (SE-RCCAS+SE-RECAS+SE-RICAS group/SE-RCCAS+SE-RECAS+SE-RICAS group). Group comparisons (CON group/no carotid stenosis group/SE-RCCAS+SE-RECAS+SE-RICAS group) were made using ANOVA, P < 0.001.

#### Table 6: Levels of biomarkers in patients with carotid artery severe stenosis and severe coronary artery stenosis.

|                  | CON (n = 61) | No carotid stenosis (n = 56) | SE-RCCAS+SOVCS (n = 51) | SE-RECAS+STVCS (n = 50) | SE-RCCAS+SMVCS (n = 54) |
|------------------|-------------|------------------------------|--------------------------|-------------------------|------------------------|
| TOS (μmol H₂O₂ Eq/L) | 7.3 ± 0.7   | 7.4 ± 0.7                    | 18.6 ± 1.5*              | 39.0 ± 3.6**            | 48.9 ± 4.5***          |
| LHP (μmol/L)     | 5.8 ± 0.6   | 5.9 ± 0.6                    | 12.0 ± 0.9*              | 19.5 ± 2.0**            | 28.6 ± 3.1***          |
| 8-IP (pg/mL)     | 45.2 ± 4.5  | 45.0 ± 4.4                   | 83.9 ± 7.2*              | 135.0 ± 12.5**          | 159.4 ± 14.8**         |
| MDA (nmol/L)     | 1.7 ± 0.3   | 1.6 ± 0.2                    | 5.8 ± 0.4*               | 9.0 ± 0.7**             | 11.3 ± 1.2**           |
| MCP-4 (ng/mL)    | 41.9 ± 4.2  | 42.0 ± 4.2                   | 87.9 ± 7.9*              | 149.5 ± 13.2**          | 190.3 ± 18.6**         |
| AA (mg/L)        | 35.2 ± 3.5  | 36.1 ± 3.6                   | 64.1 ± 5.4*              | 86.0 ± 7.4**            | 120.2 ± 11.3**         |
| hs-CRP (mg/L)    | 2.7 ± 0.3   | 2.6 ± 0.3                    | 5.9 ± 0.5*               | 10.4 ± 0.9**            | 14.5 ± 1.3**           |
| TNF-α (ng/L)     | 20.1 ± 2.0  | 21.3 ± 2.1                   | 53.4 ± 5.2*              | 99.7 ± 10.1**           | 140.6 ± 13.0**         |

**CON**: control; **SE-RCCAS**: severe right common carotid artery stenosis; **SE-RECAS**: severe right external carotid artery stenosis; **SOVCS**: severe one-vessel coronary stenosis; **STVCS**: severe two-vessel coronary stenosis; **SMVCS**: severe multivessel coronary stenosis; **TOS**: total oxidant status; **LHP**: lipid hydroperoxide; **8-IP**: 8-isoprostan; **MDA**: malondialdehyde; **MCP-4**: monocyte chemotactic protein-4; **AA**: amyloid A; **hs-CRP**: high-sensitivity C-reactive protein; **TNF-α**: tumor necrosis factor-α. *P < 0.001 (no carotid stenosis group/SE-RCCAS+SOVCS group). **P < 0.001 (SE-RCCAS+SOVCS group/SE-RECAS+STVCS group). ***P < 0.001 (SE-RCCAS+SOVCS group/SE-RCCAS+SMVCS group). Group comparisons (CON group/no carotid stenosis group/SE-RCCAS+SOVCS group/SE-RECAS+STVCS group/SE-RCCAS+SMVCS group) were made using ANOVA, P < 0.001.
comparisons (65-70 age group/75-80 age group/81-86 age group) were made using ANOVA, P<0.05. AA gene is related to carotid artery intimal mRNA is detected in atherosclerotic plaques in human membrane receptors promoting the generation of oxidative stress and interplay with cell MDA is formed during the lipid peroxidation, leading to initiation and the development of atherosclerosis [49]. MDA as a biomarker of oxidative stress is involved in the oxidative stress as indicator of oxidative stress status [48]. considered one of the most sensitive and reliable biomarker of through cyclooxygenase-independent mechanisms, is con- acids [47], 8-IP, a prostaglandin-like substance produced through cyclooxygenase-independent mechanisms, is considered one of the most sensitive and reliable biomarker of oxidative stress as indicator of oxidative stress status [48]. MDA as a biomarker of oxidative stress is involved in the initiation and the development of atherosclerosis [49]. MDA is formed during the lipid peroxidation, leading to generation of oxidative stress and interplay with cell membrane receptors promoting the inflammatory procession and arterial plaque ruptures [50]. We showed levels of oxidative stress (TOS, LHP, 8-IP, and MDA) were increased in elderly patients with coexistent right carotid artery severe stenosis and severe multivessel coronary artery stenosis. Our study indicated that the increased levels of oxidative stress showed significant correlation with carotid artery severe stenosis and severe multivessel coronary artery stenosis in elderly patients and demonstrated that the oxidative stress may promote the development and progression of carotid artery severe stenosis and severe multivessel coronary artery stenosis in elderly patients. This indicated that high oxidative stress level played key role in worse prognosis of carotid artery stenosis and multivessel coronary artery stenosis in these patients.

MCP-4 is related to low-density lipoprotein-cholesterol and an independent prognostic predictor of elevated carotid arterial intima-media thickness. MCP-4 plays a role in atherosclerosis by increasing the circulating levels of the macrophage inflammatory protein-1 beta and is the main atherosclerosis and inflammatory biomarkers [51, 52]. AA mRNA is detected in atherosclerotic plaques in human arteries, and AA gene is related to carotid artery intimal media thickness. Inflammatory response is central to AA pathophysiology and development of atherosclerosis [15], and inflammatory response is the important component of atherosclerotic plaques. AA as an inflammatory marker is associated with inflammatory response and atherosclerosis, and the persistently increased AA level is involved in acute and chronic inflammatory injuries. The hs-CRP promotes inflammatory response in the progression of atherosclerosis and plays an important role in atherosclerosis [53]. TNF-α significantly increases the vascular endothelial inflammatory response and atherosclerosis through nuclear factor kappa-B signaling. Atherosclerosis is an inflammatory process of the artery walls and TNF-α as a proinflammatory cytokine triggers nuclear factor kappa-B inflammatory pathway and is involved in an accelerated development of vascular endothelial inflammation and atherosclerosis [54]. We identified relevant inflammatory biomarkers (MCP-4, AA, hs-CRP, and TNF-α) of severe carotid artery stenosis and coronary artery stenosis and toxicological effects of inflammatory response on carotid artery stenosis and multivessel coronary artery stenosis in elderly patients. Oxidative stress is a key factor that triggers inflammatory response [55], and therefore, the high levels of oxidative stress and inflammatory response may simultaneously resulted in the progression of carotid artery stenosis and coronary artery stenosis in elderly patients. Increased oxidative stress promotes inflammatory response, and the complex interplay between oxidative stress and inflammatory response plays a key role in the pathogenesis of disease [55]. The elevation of intracellular oxidative stress levels and the upregulation of the expression of proinflammatory genes lead to a series of cellular and molecular events (serious cellular toxicity and apoptosis) [56]. Inflammatory response directly causes cellular toxicity, apoptosis, and necrosis through oxidative stress, and interplay of oxidative stress and inflammatory response leads to the activation of oxidative stress and the increased levels of pro-inflammatory mediators such as TNF-α [56] and interleukin-15 as an inflammatory cytokine independently associated with CAD and carotid intima-media thickness, suggesting a main role of IL-15 in the atherosclerosis process [57]. Clinical trials have revealed crosstalk between oxidative stress and inflammatory response is closely associated with atherosclerosis, and this close link is also supported by reports on aggravated proinflammatory phenotype or over-generation of reactive oxygen species [58]. In this study, we assessed the relationships between oxidative stress, inflammatory response, and right carotid artery severe stenosis as well as severe multivessel coronary artery stenosis

### Table 7: The incidences of severe right carotid stenosis and coronary artery stenosis.

| Age groups (years) | MI-RCS (n = 170) | MO-RCS (n = 160) | SE-RAS (n = 166) | SE-RAS+SMVCS (n = 106) |
|--------------------|-----------------|-----------------|-----------------|------------------------|
| 65-70, n (%)       | 80 (47.0)       | 70 (41.7)       | 40 (24.0)       | 22 (20.7)              |
| 75-80, n (%)       | 60 (34.2)*      | 50 (33.2)*      | 50 (33.1)*      | 31 (32.2)*             |
| 81-86, n (%)       | 30 (18.6)**     | 40 (25.0)**     | 76 (42.7)**     | 53 (47.0)**            |

MI-RCS: mild right carotid stenosis; MO-RCS: moderate right carotid stenosis; SE-RAS: severe right carotid stenosis; SE-RAS+SMVCS: severe right carotid stenosis+severe multivessel coronary stenosis. *P < 0.05 (65-70 age group/75-80 age group). **P < 0.05 (75-80 age group/81-86 age group). Group comparisons (65-70 age group/75-80 age group/81-86 age group) were made using ANOVA, P < 0.05.

### Table 8: Multiple regression analysis to evaluate risk predictors for carotid and coronary artery stenosis.

| TOS    | 5.30 | 1.45-18.65 | 0.002 |
|--------|------|------------|-------|
| LHP    | 3.19 | 1.32-2.97  | 0.01  |
| 8-IP   | 2.50 | 1.30-3.14  | 0.04  |
| MDA    | 4.78 | 1.46-19.86 | 0.001 |
| MCP-4  | 2.36 | 1.35-4.20  | 0.03  |
| AA     | 3.07 | 1.31-2.99  | 0.04  |
| Hs-CRP | 4.92 | 1.62-12.05 | 0.001 |
| TNF-α  | 5.81 | 1.49-19.83 | 0.001 |

TOS: total oxidant status; LHP: lipid hydroperoxide; 8-IP: 8-isoprostane; MDA: malondialdehyde; MCP-4: monocyte chemotactic protein-4; AA: amyloid A; hs-CRP: high-sensitivity C-reactive protein; TNF-α: tumor necrosis factor-α.
in elderly patients. We found that elderly patients with carotid and coronary artery severe stenosis had higher levels of oxidative stress and inflammatory response in our studies. We also found that oxidative stress and inflammatory response were associated with right carotid artery severe stenosis and severe multivessel coronary artery stenosis in elderly patients. Moreover, we found that 81 to 86 years old patients suffered from coexistent severe multivessel coronary artery stenosis and right carotid artery severe stenosis more easily. The association among oxidative stress, inflammatory response, and carotid as well as coronary artery severe stenosis provided evidences for the potential mechanisms of carotid and coronary artery severe stenosis in elderly patients. The mechanisms could be considered that continuous high levels of oxidative stress were involved in the initiation and progression of carotid and coronary artery severe stenosis; the expressions of inflammatory mediators played an important role in carotid and coronary artery severe stenosis; the oxidative stress regulated inflammatory processes and initiated a process of inflammatory response [57], indicating that the interplay between oxidative stress and inflammatory response further accelerated development and progression of carotid and coronary artery severe stenosis in elderly patients.

Right carotid artery severe stenosis leads to cerebral circulatory insufficiency, intracerebral steal phenomenon [59], reduction of blood flow of the right cerebral hemisphere, hemichorea [60], transient ischemic attacks, and strokes [61], and the rates of concurrent carotid artery stenosis and CAD are elevating gradually day by day. CAD patients who are undergoing percutaneous coronary intervention have severe carotid artery stenosis and the majority of patients with carotid artery severe stenosis have complex CAD [62]. The severe multivessel coronary artery stenosis as a risk factor is related to severe carotid artery stenosis [62]. Patients with concurrent carotid and coronary artery severe stenosis are demonstrated to have a more severe atherosclerosis involving multiple arteries [62]. Therefore, it is very important clinically for studying concurrent right carotid artery severe stenosis and severe multivessel coronary artery stenosis in elderly patients.

5. Limitations

The findings from our research had several limitations. The lifestyle in elderly patients with coronary artery and carotid artery severe stenosis was not evaluated in the present study and life style factors including body mass index, nutrition condition, dietary habits, and exercise may influence the coronary and carotid atherosclerosis through oxidative stress and inflammation. Our data were also limited in lacking assessment of the effects of drinking patterns (none to moderate drinking, nonproblematic heavy drinking, and problem drinking) on blood biomarkers of oxidative stress and inflammatory mediators in elderly patients with severe coronary and carotid stenosis. Another limitation was lack of research data on the changes of oxidative stress and inflammation markers in active and passive smoking that could have better clarified the relationships among oxidative stress, inflammation, the progression of coronary atherosclerosis, and severe carotid atherosclerosis. Besides, there was no information available regarding the impacts of comorbidities (e.g., type 2 diabetes mellitus, hypertension, and angina pectoris) on oxidative stress and inflammation in elderly patients with severe coronary and carotid stenosis. It would have more information if we could examine the detailed histopathological characterizations of atherosclerotic plaques in the coronary and carotid arteries.

6. Conclusions

This research shows that high levels of TOS, LHP, 8-IP, MDA, MCP-4, AA, hs-CRP, and TNF-α are associated with severe coronary and carotid stenosis suggesting a possible roles of oxidative stress and inflammatory mediators in the development of coronary and carotid atherosclerosis. Further research with larger sample sizes and adequate follow up period will be required to better understand the mechanisms of severe coronary and carotid atherosclerosis in elderly patients.

Data Availability

All relevant data are within this research paper. All data used to support the findings of the research are available from the corresponding author on reasonable. No additional data are available.

Conflicts of Interest

The authors declare that they have no competing interests regarding the publication of this article.

Authors’ Contributions

X.L. wrote the main manuscript text. D.G. collected the research data. Y.H. analysed the research data. Y.C. discussed the results of the research. All the authors listed have read and approved the final manuscript and agreed to the submission of our manuscript to Oxid Med Cell Longev.

References

[1] C. Song and X. Zhao, “Uric acid promotes oxidative stress and enhances vascular endothelial cell apoptosis in rats with middle cerebral artery occlusion,” Bioscience Reports, vol. 38, no. 3, 2018.
[2] L. Guan, X. Geng, C. Stone et al., “PM2.5 exposure induces systemic inflammation and oxidative stress in an intracranial atherosclerosis rat model,” Environmental Toxicology, vol. 34, no. 4, pp. 530–538, 2019.
[3] R. Shirai, K. Sato, T. Yamashita et al., “Neopterin counters vascular inflammation and atherosclerosis,” Journal of the American Heart Association, vol. 7, no. 3, article e007359, 2018.
[4] J. Li, K. Li, and X. Chen, “Inflammation-regulatory microRNAs: valuable targets for intracranial atherosclerosis,” Journal of Neuroscience Research, vol. 97, no. 10, pp. 1242–1252, 2019.
[5] A. Skutnik-Radziszewska, M. Maciejczyk, K. Fejfer et al., "Salivary Antioxidants and Oxidative Stress in Psoriatic Patients: Can Salivary Total Oxidant Status and Oxidative Status Index Be a Plaque Psoriasis Biomarker?", *Oxidative Medicine and Cellular Longevity*, vol. 2020, Article ID 9086024, 12 pages, 2020.

[6] Y. Shokri, A. Variji, M. Nosrati et al., "Importance of paraoxonase 1 (PON1) as an antioxidant and antiatherogenic enzyme in the cardiovascular complications of type 2 diabetes: genotypic and phenotypic evaluation," *Diabetes Research and Clinical Practice*, vol. 161, article 108067, 2020.

[7] D. Patel, S. Desai, T. Gajaria, R. Devkar, and A. V. Ramachandran, "Coriandrum sativum L. seed extract mitigates lipotoxicity in RAW 264.7 cells and prevents atherogenic changes in rats," *EXCLI Journal*, vol. 12, pp. 313–334, 2013.

[8] G. Garg, S. Singh, A. K. Singh, and S. I. Rizvi, "Whey protein concentrate supplementation protects rat brain against aging-induced oxidative stress and neurodegeneration," *Applied Physiology Nutrition and Metabolism*, vol. 43, no. 5, pp. 437–444, 2018.

[9] B. Wang, J. Pan, L. Wang, H. Zhu, R. Yu, and Y. Zou, "Associations of plasma 8-isoprostane levels with the presence and extent of coronary stenosis in patients with coronary artery disease," *Atherosclerosis*, vol. 184, no. 2, pp. 425–430, 2006.

[10] G. Zhou, J. Wu, C. Gu et al., "Prorenin independently causes hypertension and renal and cardiac fibrosis in cyp1a1-prorenin transgenic rats," *Clinical Science (Lond)*, vol. 132, no. 12, pp. 1345–1363, 2018.

[11] N. Briklića Bottegaro, J. Gotić, J. Šuran et al., "Effect of prolonged submaximal exercise on serum oxidative stress biomarkers (d-ROMs, MDA, BAP) and oxidative stress index in endurance horses," *BMC Veterinary Research*, vol. 14, no. 1, p. 216, 2018.

[12] M. V. Samsonov, A. Y. Khapchay, A. V. Vorontnikov et al., "Impact of atherosclerosis- and diabetes-related dicarbonyls on vascular endothelial permeability: a comparative assessment," *Oxidative Medicine and Cellular Longevity*, vol. 2017, Article ID 1625130, 10 pages, 2017.

[13] I. Hashimoto, J. Wada, A. Hida et al., "Elevated serum monocyte chemoattractant protein-4 and chronic inflammation in overweight subjects," *Obesity (Silver Spring)*, vol. 14, no. 5, pp. 799–811, 2006.

[14] Y. Zhang, J. Zhang, H. Sheng, H. Li, and R. Wang, "Acute phase reactant serum amyloid A in inflammation and other diseases," *Advances in Chemical Medicine*, vol. 90, pp. 25–80, 2012.

[15] G. S. Getz, P. A. Krishack, and C. A. Reardon, "Serum amyloid A and atherosclerosis," *Current Opinion in Lipidology*, vol. 27, no. 5, pp. 531–535, 2016.

[16] D. A. Swastini, I. A. D. Wiryantini, N. L. P. Aristiuti, and A. Muliantara, "Atherosclerosis prediction with high sensitivity C-reactive protein (hs-CRP) and related risk factor in patient with dyslipidemia," *Open Access Macedonian Journal of Medical Sciences*, vol. 7, no. 22, pp. 3887–3890, 2019.

[17] H. Ait-Outella, P. Libby, and A. Tegdui, "Anticytokine immune therapy and atherothrombotic cardiovascular risk," *Arteriosclerosis, Thrombosis, and Vascular Biology*, vol. 39, no. 8, pp. 1510–1519, 2019.

[18] T. Zakharkina, E. Heinzel, R. A. Koczilla et al., "Analysis of the airway microbiota of healthy individuals and patients with chronic obstructive pulmonary disease by T-RFLP and clone sequencing," *PLoS One*, vol. 8, no. 7, article e68302, 2013.

[19] O. Ntholohang, R. McDonagh, S. Nicholson, F. Brett, D. Bradley, and J. Harbison, "Is intimal hyperplasia associated with cranial arterial stenosis in cannabis-associated cerebral infarction?", *International Journal of Stroke*, vol. 10, no. 6, pp. E56–E59, 2015.

[20] K. M. Wanamaker, R. J. Moraca, D. Nitzberg, and G. J. Magovern Jr., "Contemporary incidence and risk factors for carotid artery disease in patients referred for coronary artery bypass surgery," *Journal of Cardiothoracic Surgery*, vol. 7, no. 1, p. 78, 2012.

[21] A. E. Carmona-Rubio, A. M. Lee, S. Puchner, B. Ghoshhajra, and U. C. Sharma, "A review of adherence to the guidelines for coronary CT angiography quantitative stenosis grading thresholds in published research," *Postgraduate Medicine*, vol. 127, no. 2, pp. 194–201, 2015.

[22] N. Rustempasic and M. Gengo, "Assessment of carotid stenosis with CT angiography and color Doppler ultrasonography," *Medical Archives*, vol. 73, no. 5, pp. 321–325, 2019.

[23] H. Y. Kim, H. S. Yong, E. J. Kim, E. Y. Kang, and B. K. Seo, "Value of transluminal attenuation gradient of stress CCTA for diagnosis of haemodynamically significant coronary artery stenosis using wide-area detector CT in patients with coronary artery disease: comparison with stress perfusion CMR," *Cardiovascular Journal of Africa*, vol. 29, no. 1, pp. 16–21, 2018.

[24] F. C. Eraldemir, N. Uren, T. Kum et al., "Association of serum paraoxonase 1 activities, polymorphisms and oxidative stress in breast cancer patients with type 2 diabetes mellitus," *Journal of Medical Biochemistry*, vol. 38, no. 3, pp. 368–375, 2019.

[25] M. Adamczyk-Sowa, P. Sowa, J. Adamczyk et al., "Effect of melatonin supplementation on plasma lipid hydroperoxides, homocysteine concentration and chronic fatigue syndrome in multiple sclerosis patients treated with interferons-beta and mitoxantrone," *Journal of Physiology and Pharmacology*, vol. 67, no. 2, pp. 235–242, 2016.

[26] B. Peters, C. Ballmann, T. Quindry et al., "Experimental woodsmoke exposure during exercise and blood oxidative stress," *Occupational and Environmental Medicine*, vol. 60, no. 12, pp. 1073–1081, 2018.

[27] S. Rašić, D. Rebić, S. Hasić, I. Rašić, and M. Delić Šarac, "Influence of Malondialdehyde and Matrix Metalloproteinase-9 on Progression of Carotid Atherosclerosis in Chronic Renal Disease with Cardiometabolic Syndrome," *Mediators of Inflammation*, vol. 2015, Article ID 614357, 8 pages, 2015.

[28] A. Moen, A. L. Lind, M. Thulin et al., "Inflammatory serum protein profiling of patients with lumbar radicular pain one year after disc herniation," *International Journal of Inflammation*, vol. 2016, Article ID 3874964, 8 pages, 2016.

[29] E. Couderc, F. Morel, P. Levillain et al., "Interleukin-17A-induced production of acute serum amyloid A by keratinocytes contributes to psoriasis pathogenesis," *PLoS One*, vol. 12, no. 7, article e0181486, 2017.

[30] J. J. Hu, J. J. Urbanic, L. D. Case et al., "Association between inflammatory biomarker C-reactive protein and radiotherapy-induced early adverse skin reactions in a multi-racial/ethnic breast cancer population," *Journal of Oncology*, vol. 36, no. 24, pp. 2473–2482, 2018.

[31] A. E. Yanni, G. Agrogiannis, C. Gkekas, and D. Perrea, "Clusterin/apolipoprotein J immunolocalization on carotid artery is affected by TNF-alpha, cigarette smoking and anti-platelet treatment," *Lipids in Health and Disease*, vol. 13, no. 1, p. 70, 2014.

[32] J. E. Tamis-Holland, H. Jneid, H. R. Reynolds et al., "Contemporary diagnosis and management of patients with myocardial infarction in the absence of obstructive coronary..."
artery disease: a scientific statement from the American Heart Association,” *Circulation*, vol. 139, no. 18, pp. e891–e908, 2019.

[33] P. López-Jaramillo, J. López-López, M. F. Forero-Trillos et al., “Will the new figures from the AHA/ACC guidelines on the definition and treatment of hypertension in Latin America have an impact?,” *Hipertension Y Riesgo Vascular*, vol. 37, no. 1, pp. 33–38, 2020.

[34] W. V. Bobo, W. O. Cooper, C. M. Stein et al., “Positive predictive value of a case definition for diabetes mellitus using automated administrative health data in children and youth exposed to antipsychotic drugs or control medications: a Tennessee Medicaid study,” *BMC Medical Research Methodology*, vol. 12, no. 1, p. 128, 2012.

[35] R. L. Sacco, S. E. Kasner, J. P. Broderick et al., “An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association,” *Stroke*, vol. 44, no. 7, pp. 2064–2089, 2013.

[36] W. C. Tan, J. Bourbeau, S. D. Aaron et al., “The effects of marijuana smoking on lung function in older people,” *European Respiratory Journal*, vol. 54, no. 6, p. 1900826, 2019.

[37] R. Huang, S. Y. Ho, M. P. Wang, W. S. Lo, and T. H. Lam, “Socio-demographic risk factors of alcohol drinking in Hong Kong adolescents,” *Journal of Epidemiolical Community Health*, vol. 70, no. 4, pp. 374–379, 2016.

[38] M. Maddah, Z. Akbarian, S. Shoyooie, M. Rostamnejad, and X. Q. Ma, C. Q. Jiang, L. Xu et al., “The development of cognitive and emotional impairement after a minor stroke: a longitudinal study,” *Acta Neurologica Scandinavica*, vol. 140, no. 4, pp. 281–289, 2019.

[39] R. A. Kloner and B. Chaitman, “Angina and its management,” *Journal of Cardiovascular Pharmacology*, vol. 22, no. 3, pp. 199–209, 2017.

[40] E. Romuk, C. Wojciechowska, W. Jache et al., “Comparison of oxidative stress parameters in heart failure patients depending on ischaemic or nonischaemic aetiology,” *Oxidative Medicine and Cellular Longevity*, vol. 2019, Article ID 7156038, 13 pages, 2019.

[41] M. Aslan, U. Duzenli, R. Esen, and Y. U. Soyoral, “Serum pro-lidase enzyme activity in obese subjects and its relationship with oxidative stress markers,” *Clinica Chimica Acta*, vol. 473, pp. 186–190, 2017.

[42] B. Y. Aju, R. Rajalakshmi, and S. Mini, “Protective role of *Moringa oleifera* leaf extract on cardiac antioxidant status and lipid peroxidation in streptozotocin induced diabetic rats,” *Heliyon*, vol. 5, no. 12, article e02935, 2019.

[43] J. Kauppi, J. Räsänen, E. Sihvo et al., “Increased Oxidative Stress in the Proximal Stomach of Patients with Barrett’s Esophagus and Adenocarcinoma of the Esophagus and Esophagegastric Junction,” *Translational Oncology*, vol. 9, no. 4, pp. 336–339, 2016.

[44] E. McNair, M. Qureshi, K. Prasad, and C. Pearce, “Atherosclerosis and the hypercholesterolemic AGE-RAGE axis,” *International Journal of Angiology*, vol. 25, no. 2, pp. 110–116, 2016.

[45] R. Sri-Amad, N. Huipao, P. Prasertsi, and T. Roengrit, “Aortic pulse wave velocity, ankle-brachial index, and Malondialdehyde in older adults with or without metabolic syndrome,” *Pulse (Basel)*, vol. 8, no. 1–2, pp. 31–39, 2020.

[46] A. Gentili, M. S. Zaibi, S. Y. Alomar et al., “Circulating levels of the adipokines monocyte chemotactic protein-4 (MCP-4), macrophage inflammatory protein-1β (MIP-1β), and eotaxin-3 in Severe obesity and following bariatric surgery,” *Hormone and Metabolic Research*, vol. 48, no. 12, pp. 847–853, 2016.

[47] M. J. Junger, B. C. ter Meulen, T. van Osch, H. C. Weinstein, and R. Ostelo, “Inflammatory biomarkers in patients with sciatica: a systematic review,” *BMJ Musculoskeletal Disorders*, vol. 20, no. 1, p. 156, 2019.

[48] Y. Li, C. G. Zhang, X. H. Wang, and D. H. Liu, “Progression of atherosclerosis in ApoE-knockout mice fed on a high-fat diet,” *European Review for Medical and Pharmacological Sciences*, vol. 20, no. 18, pp. 3863–3867, 2016.

[49] W. Gao, H. Liu, J. Yuan et al., “Exosomes derived from mature dendritic cells increase endothelial inflammation and atherosclerosis via membrane TNF-α mediated NF-κB pathway,” *Journal of Cellular and Molecular Medicine*, vol. 20, no. 12, pp. 2318–2327, 2016.

[50] T. McGarry, M. Biniecka, D. J. Veale, and U. Fearon, “Hypoxia, oxidative stress and inflammation,” *Free Radical Biology and Medicine*, vol. 125, pp. 15–24, 2018.

[51] P. Khanna, C. Ong, B. H. Bay, and G. H. Bae, “Nanotoxicity: an interplay of oxidative stress, inflammation and cell death,” *Nanomaterials (Basel)*, vol. 5, no. 3, pp. 1163–1180, 2015.

[52] G. Tarantino, V. Citro, C. Balsano, and D. Capone, “Age and interleukin-15 levels are independently associated with intima-media thickness in obesity-related NALFD patients,” *Frontiers in Medicine*, vol. 8, article 634962, 2021.

[53] S. Steven, K. Frenis, M. Oelze et al., “Vascular inflammatory and oxidative stress: major triggers for cardiovascular disease,” *Oxidative Medicine and Cellular Longevity*, vol. 2019, Article ID 7092151, 26 pages, 2019.

[54] L. Stefanczyk, K. Szymczyk, K. Stefanicznyk, and M. Polgju, “The presence of a right aortic arch associated with severe stenosis of the right common carotid artery and steal phenomenon,” *Rinshō Shinkeigaku*, vol. 59, no. 8, pp. 509–514, 2019.

[55] L. Rangel-Castilla, E. I. Levy, and A. H. Siddiqui, “Direct cerebral carotid stenting and angioplasty of right internal carotid artery and brachiocephalic artery ostial stenoses with flow reversal: 2-dimensional operative video,” *Operative Neurosurgery (Hagerstown)*, vol. 16, no. 2, pp. 269–270, 2019.

[56] D. Adhikary, R. I. Ranjan, S. Mandal, M. Hawlader, D. K. Mitra, and A. B. Adhikary, “Prevalence of carotid artery stenosis in ischaemic heart disease patients in Bangladesh,” *SAGE Open Medicine*, vol. 7, pp. 1–5, 2019.