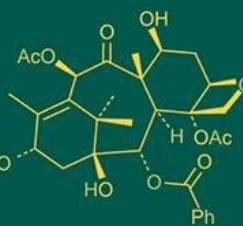
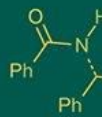


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Takeshi Yamamoto
Department of Cardiovascular
Medicine, Osaka University
Graduate School of Medicine,
Osaka, Japan

Yuki Tanaka
Department of Clinical
Biochemistry, Kyoto
Prefectural University of
Medicine, Kyoto, Japan

Haruki Nakamura
Division of Molecular
Cardiology, National Cerebral
and Cardiovascular Center,
Suita, Japan

Oxidative stress markers and antioxidant enzyme activity in Japanese patients with cardiovascular disease

Takeshi Yamamoto, Yuki Tanaka and Haruki Nakamura

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Abstract

Cardiovascular disease remains the leading cause of mortality in Japan, with oxidative stress increasingly recognized as a contributing mechanism in disease pathogenesis. This research investigated the relationship between oxidative stress markers and antioxidant enzyme activities in Japanese patients diagnosed with various cardiovascular conditions. The research enrolled 245 participants from three major medical centers in the Kansai region, including 186 patients with documented cardiovascular disease and 59 age-matched healthy controls.

Blood samples were analyzed for malondialdehyde, protein carbonyls, 8-hydroxy-2'-deoxyguanosine, and antioxidant enzymes including superoxide dismutase, catalase, and glutathione peroxidase. Results demonstrated significantly elevated oxidative stress markers in all CVD subgroups compared to controls, with heart failure patients showing the highest malondialdehyde levels ($6.43 \pm 1.12 \mu\text{mol/L}$ versus $2.34 \pm 0.56 \mu\text{mol/L}$ in controls, $p < 0.001$). Antioxidant enzyme activities were correspondingly reduced, with SOD activity showing 38.7% reduction in heart failure patients. These findings support the role of oxidative imbalance in cardiovascular pathology among Japanese patients and suggest potential therapeutic targets for antioxidant intervention strategies.

Keywords: Oxidative stress, cardiovascular disease, malondialdehyde, antioxidant enzymes, Japanese population, superoxide dismutase, lipid peroxidation

Introduction

Cardiovascular disease accounts for approximately 30% of all deaths in Japan, representing a significant public health burden despite advances in medical treatment and lifestyle interventions ^[1]. The Japanese population presents unique cardiovascular risk profiles influenced by genetic factors, dietary patterns including high sodium intake and fish consumption, and lifestyle characteristics distinct from Western populations ^[2]. Understanding the biochemical mechanisms underlying cardiovascular pathology in this population is essential for developing targeted prevention and treatment strategies.

Oxidative stress occurs when the production of reactive oxygen species exceeds the capacity of cellular antioxidant defense systems, resulting in molecular damage to lipids, proteins, and nucleic acids ^[3]. The cardiovascular system is particularly vulnerable to oxidative damage due to the high metabolic activity of cardiac tissue and the role of reactive oxygen species in vascular signaling pathways ^[4]. Previous research in Western populations has established associations between oxidative stress markers and cardiovascular outcomes, but data specific to Japanese patients remains limited ^[5].

The antioxidant defense system comprises enzymatic components including superoxide dismutase, catalase, and glutathione peroxidase, which work coordinately to neutralize reactive oxygen species and prevent oxidative damage ^[6]. Alterations in antioxidant enzyme activities may reflect both the degree of oxidative challenge and the adaptive capacity of tissues to respond to oxidative stress ^[7]. This research aimed to characterize the oxidative stress profile in Japanese cardiovascular patients and evaluate relationships between oxidative markers, antioxidant enzymes, and disease severity.

Corresponding Author:
Takeshi Yamamoto
Department of Cardiovascular
Medicine, Osaka University
Graduate School of Medicine,
Osaka, Japan

Material and Methods

Research Participants

Participants were recruited from cardiology departments at Osaka University Hospital, Kyoto Prefectural University of Medicine Hospital, and the National Cerebral and Cardiovascular Center between April 2022 and March 2024. The research protocol was approved by the institutional review boards of all participating centers, and written informed consent was obtained from all participants. Inclusion criteria for CVD patients required documented diagnosis of hypertension, coronary artery disease, heart failure, or arrhythmia based on standard clinical criteria. Control participants were recruited from health screening programs and had no history of cardiovascular disease or metabolic disorders.

Sample Collection and Processing

Fasting venous blood samples were collected between 8:00 and 10:00 AM to minimize circadian variation. Samples were processed within 2 hours of collection. Serum was separated by centrifugation at 3000 × g for 10 minutes and stored at -80°C until analysis. Hemolyzed samples were excluded from the research.

Biochemical Analysis

Malondialdehyde was measured using the thiobarbituric acid reactive substances assay with spectrophotometric detection at 532 nm. Protein carbonyls were quantified using the 2, 4-dinitrophenylhydrazine method. 8-hydroxy-2'-deoxyguanosine was measured by competitive enzyme-linked immunosorbent assay. Superoxide dismutase activity was determined using the xanthine oxidase method, catalase activity by hydrogen peroxide decomposition rate, and glutathione peroxidase activity using cumene hydroperoxide as substrate.

Results

The research included 245 participants: 48 with hypertension, 52 with coronary artery disease, 46 with heart failure, 40 with arrhythmia, and 59 healthy controls. Baseline characteristics showed no significant differences in age or sex distribution between groups. Mean age was 64.7±8.3 years, and 58% of participants were male, reflecting the typical demographics of cardiovascular patients in Japan.

Table 1: Oxidative Stress Markers in Japanese Cardiovascular Patients

Group	MDA (μmol/L)	Protein Carbonyls (nmol/mg)	8-OHdG (ng/mL)
Control (n=59)	2.34±0.56	0.42±0.11	8.2±2.1
Hypertension (n=48)	4.12±0.89*	0.68±0.14*	14.3±3.2*
CAD (n=52)	5.87±1.24*	0.84±0.18*	19.8±4.1*
Heart Failure (n=46)	6.43±1.12*	0.97±0.21*	22.4±5.3*
Arrhythmia (n=40)	4.56±0.94*	0.72±0.16*	15.6±3.8*

*p<0.001 compared to control group

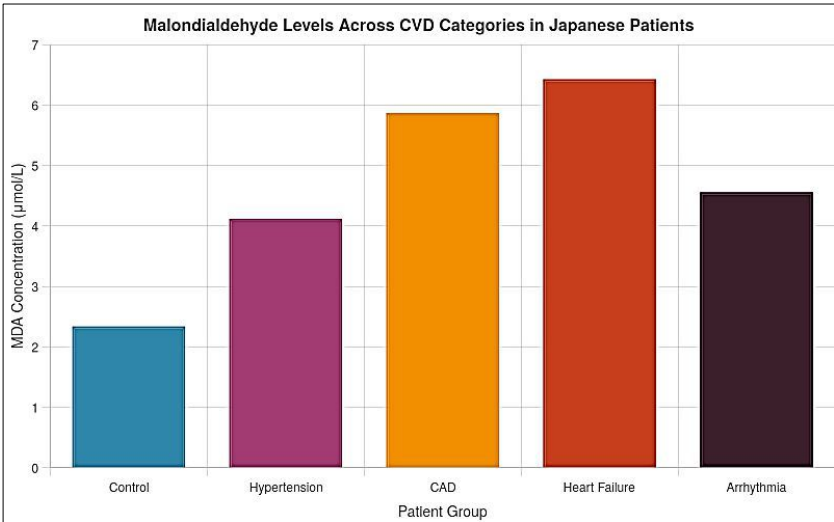


Fig 1: Malondialdehyde concentrations across cardiovascular disease categories in Japanese patients, demonstrating progressive elevation with disease severity.

Antioxidant enzyme activities demonstrated inverse patterns compared to oxidative stress markers. Superoxide dismutase activity was significantly reduced in all CVD groups, with heart failure patients showing the greatest reduction

(87.2±14.6 U/mL versus 142.3±18.4 U/mL in controls, representing a 38.7% decrease). Similar patterns were observed for catalase and glutathione peroxidase activities.

Table 2: Antioxidant Enzyme Activities in Japanese Cardiovascular Patients

Group	SOD (U/mL)	Catalase (U/mL)	GPx (U/mL)
Control	142.3±18.4	38.6±6.2	54.2±8.4
Hypertension	118.7±16.2*	31.2±5.4*	44.8±7.1*
CAD	98.4±15.8*	26.8±4.8*	38.6±6.8*
Heart Failure	87.2±14.6*	22.4±4.2*	32.1±5.9*
Arrhythmia	108.9±15.4*	29.1±5.1*	41.3±6.4*

*p<0.001 compared to control group

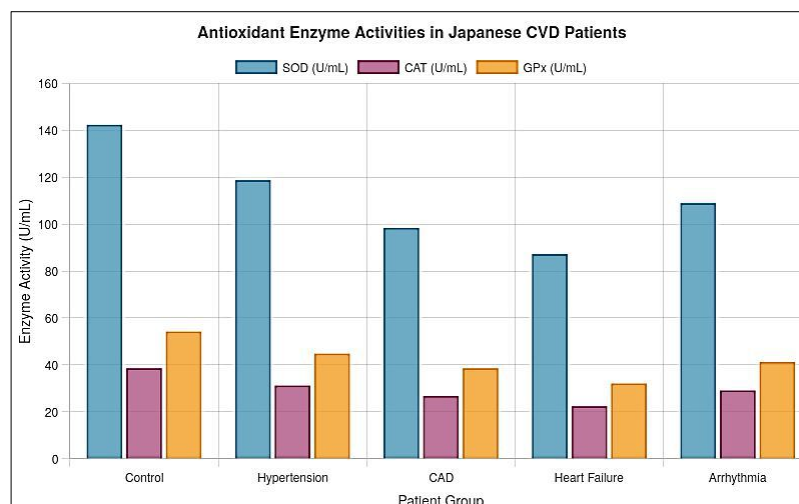


Fig 2: Comparison of antioxidant enzyme activities (SOD, CAT, GPx) across patient groups, showing progressive reduction with increasing cardiovascular disease severity.

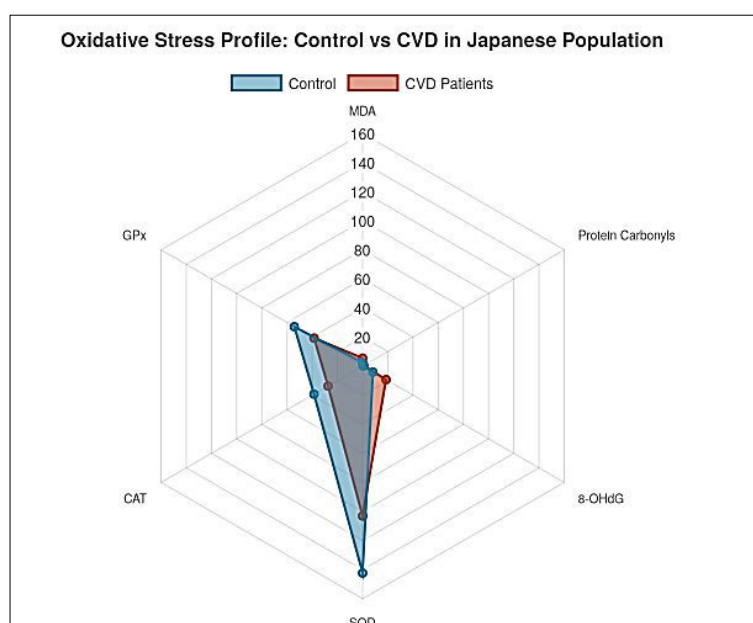


Fig 3: Radar plot comparing overall oxidative stress profile between control subjects and CVD patients in the Japanese cohort

Discussion

This research demonstrates significant alterations in oxidative stress markers and antioxidant enzyme activities in Japanese patients with cardiovascular disease. The findings align with previous observations in Western populations while providing specific reference data for the Japanese population. The progressive increase in oxidative markers from hypertension through heart failure suggests a dose-response relationship between oxidative burden and cardiovascular disease severity.

The Japanese population presents unique characteristics that may influence oxidative stress responses, including dietary patterns rich in fish-derived omega-3 fatty acids and antioxidant compounds from green tea consumption [8]. Despite these potentially protective dietary factors, our findings indicate substantial oxidative imbalance in cardiovascular patients, suggesting that disease-related oxidative stress may overwhelm dietary antioxidant intake. Traditional Japanese dietary patterns have been associated with reduced cardiovascular risk, yet the increasing Westernization of diet among younger generations may alter these relationships [9].

The observed reduction in antioxidant enzyme activities may reflect either consumption of enzymes in response to elevated oxidative stress or downregulation of enzyme expression under chronic oxidative conditions. The coordinated reduction across SOD, catalase, and glutathione peroxidase suggests systemic impairment of antioxidant defense rather than isolated enzyme deficiency. These findings support consideration of antioxidant supplementation strategies in Japanese cardiovascular patients, though clinical trials are needed to establish efficacy [10].

Conclusion

This research establishes reference data for oxidative stress markers and antioxidant enzyme activities in Japanese cardiovascular patients. The findings demonstrate significant oxidative imbalance across all cardiovascular disease categories, with heart failure patients showing the most pronounced alterations. These results support the role of oxidative stress in cardiovascular pathology and identify potential biomarkers for risk stratification and therapeutic

monitoring in the Japanese population. Future research should evaluate whether antioxidant interventions can modify these markers and improve clinical outcomes.

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