

PROFILE OF OBESITY AND SMOKING AMONG PATIENTS WITH CORONARY HEART DISEASE AT THE CARDIOLOGY OUTPATIENT CLINIC OF RSD DR. H. SOEMARNO SOSROATMODJO**Yakub Theodorus Angit Yunus Junior¹, Indira Vidiari Juhanna², Nila Wahyuni²***Department of Physiology*

1. Bachelor of Medicine, Faculty of Medicine, Udayana University
2. Department of Physiology, Faculty of Medicine, Udayana University
e-mail: yakubjunior28@gmail.com

ABSTRACT

Background: Coronary heart disease (CHD) remains a major cause of morbidity and mortality in Indonesia and is closely associated with cardiometabolic risk factors such as obesity, smoking, hypertension, and diabetes mellitus. Describing the distribution of these risk factors in specific clinical settings is essential for risk stratification and targeted prevention. **Objective:** This study aims to describe the age profile and cardiometabolic risk factors, including obesity, smoking history, hypertension, and diabetes mellitus among CHD patients attending the Cardiology Clinic of RSD Dr. H. Soemarno Sosroatmodjo from January to June 2025. **Methods:** A retrospective descriptive cross-sectional study was conducted using secondary data from medical records, with total sampling of all eligible CHD patients who met the inclusion and exclusion criteria. Variables assessed were age groups, obesity based on body mass index, smoking history, hypertension defined according to standard clinical criteria, and diabetes mellitus. Data were analyzed using univariate methods and presented as frequencies and percentages. **Results:** Of 139 samples, 129 were eligible for analysis. Most patients were in the elderly age group. Obesity was present in (50.4%) of patients, predominantly class I obesity. Smoking history was identified in (89.9%) of patients. Hypertension and diabetes mellitus were also frequently identified as coexisting conditions, with (24.1%) of patients having established hypertension (grade 1 & 2) and (7.0%) diagnosed with diabetes mellitus. **Conclusion:** The high burden and coexistence of obesity and smoking among CHD patients highlight the importance of integrated cardiometabolic risk assessment and management in clinical practice.

Keywords : Coronary Heart Disease, Obesity, Smoking.**INTRODUCTION**

Coronary Heart Disease (CHD) remains the leading cause of cardiovascular mortality globally¹. The World Health Organization (WHO) identifies cardiovascular diseases as the primary contributor to non-communicable disease deaths, with CHD accounting for a significant portion of this burden.^{1,2} As of late 2024, it is estimated that approximately 250 million people suffer from CHD globally, resulting in around 9 million deaths annually.³ This epidemiological magnitude underscores the critical role of modifiable risk factors in the pathogenesis of coronary atherosclerosis.¹

The pathogenesis of CHD is complex and multifactorial, primarily driven by endothelial dysfunction and chronic inflammation. Among various risk factors, obesity and smoking exert profound deleterious effects through distinct yet synergistic mechanisms.^{1,4} Obesity is not merely a state of excess energy storage but as condition of “adiposopathy” or chronic low-grade inflammation.^{5,6} Hypertrophic adipose tissue functions as a pathologically active endocrine organ that secretes pro-inflammatory cytokines, such as Interleukin-6 (IL-6) and Tumor Necrosis

Factor- α (TNF- α), which induce endothelial dysfunction and promote atherogenesis.^{5,7} This chronic low-grade inflammation, coupled with insulin resistance and dyslipidemia, fosters a pro-thrombotic environment that accelerates plaque accumulation.⁸

Concurrent with metabolic risks, cigarette smoking acts as a potent environmental accelerator of vascular damage.⁹ The toxic components of cigarette smoke, including nicotine and carbon monoxide, induce oxidative stress and direct endothelial injury.^{9,10} is oxidative burden directly scavenges nitric oxide (NO), a crucial molecule for vascular homeostasis, thereby impairing vasodilation and promoting endothelial injury.¹⁰ The synergistic effect of these mechanisms accelerates plaque formation and instability, increasing the risk of acute coronary events.

Despite the well-established link between these risk factors and CHD, regional data regarding their specific prevalence in North Kalimantan remains limited. RSD dr. H. Soemarno Sosroatmodjo, one of the hospitals in North Kalimantan, manages a high volume of CHD cases. However, a detailed clinical profile describing the clustering of obesity, smoking, and comorbidities among these patients has not been adequately documented. Understanding this

local risk factor profile is essential for risk stratification and for developing targeted secondary prevention strategies relevant to the specific demographics of the region.

Therefore, the primary objective of this study is to describe the age profile and determine the prevalence of key cardiometabolic risk factors, specifically obesity, smoking history, hypertension, and diabetes mellitus, among patients with CHD attending the Cardiology Clinic of RSD Dr. H. Soemarno Sosroatmodjo.

MATERIALS AND METHODS

This descriptive observational study utilized a cross-sectional design with a retrospective approach. The study protocol was reviewed and approved by the Research Ethics Commission of the Faculty of Medicine, Udayana University (Ethical Clearance Number: 2084/UN14.2.2.VII.14/LT/2025). The research was conducted in strict adherence to the Declaration of Helsinki regarding patient confidentiality and data privacy.

The study was conducted at the Cardiology Outpatient Clinic of RSD Dr. H. Soemarno Sosroatmodjo, a hospital in Tanjung Selor, North Kalimantan. The study population consisted of all patients clinically diagnosed with CHD recorded in the medical registry from January to June, 2025.

A total sampling technique was employed to recruit participants. The inclusion criteria were: (1) male patients, (2) aged >35 years, and (3) had a confirmed diagnosis of CHD. Patients with incomplete medical records regarding anthropometric measurements (height and weight), smoking history, blood pressure, or glycemic status were excluded from

the study. Out of 139 initially identified records, 129 subjects met the eligibility criteria and were included in the final analysis.

Data extraction was performed using a structured checklist to assess anthropometric indicators and cardiovascular risk factors directly from medical records. Based on age, the study population was stratified into two distinct categories: "Adults", defined as patients aged 36–59 years, and "Elderly", defined as those aged ≥60 years. Body Mass Index (BMI) was calculated based on weight and height, utilizing the International Association for the Study of Obesity (IASO) guidelines for the Asia-Pacific population and categorized as "Obese" if the patient is classified as Obesity Class I (25–29.9 kg/m²) or Obesity Class II (≥30 kg/m²).^{11,12} Smoking history was recorded as "Yes" for patients with any documented history of chronic cigarette consumption. Furthermore, hypertension was categorized as a binary variable, where patients with a recorded systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg were classified as hypertensive.^{13–15} Similarly, DM status was determined based on the definitive physician diagnosis documented in the patient's medical history, reflecting a state of chronic hyperglycemia due to insulin resistance or secretion defects.¹⁶

All gathered data were subjected to a cleaning and coding process to ensure accuracy. Statistical analysis was performed using SPSS software (Statistical Package for the Social Sciences). Univariate analysis was conducted to determine the frequency distribution and percentage of demographic characteristics and cardiometabolic risk factors. Data are presented as descriptive statistics (n, %) to illustrate the prevalence of obesity, smoking, hypertension, and DM.

RESULTS

Table 1. Distribution of subjects by age category

Age characteristic	Frequency	
	N (129)	%
Adult	54	(41.9)
Elderly	75	(58.1)

A total of 129 male patients with confirmed CHD were included in the final analysis. Table 1 demonstrates the demographic distribution demonstrated a predominance of patients in the elderly age group (≥60 years), accounting for

(58,1%) of the total patients, compared to the adult age group (35–59 years). This age profile is consistent with the degenerative nature of atherosclerotic vascular disease.

Table 2. Classification of obesity status based on Asia-Pacific BMI Guidelines

BMI classification	Frequency	
	N (129)	%
Underweight	1	(0.8)
Normal	36	(27.9)
Overweight	27	(20.9)
Obesity class I	53	(41.1)
Obesity class II	12	(9.3)

Analysis of anthropometric data revealed a substantial burden of adiposity within the study population. As shown in Table 2, more than half of the subjects (50.4%) were classified as obese according to the Asia-Pacific classification guidelines. Specifically, Obesity Class I was the most frequent phenotype

observed, comprising 53 patients (41.1%) of the total population, while Obesity Class II was found in 12 patients (9.3%). Only 36 patients (27.9%) presented with a normal BMI. This distribution highlights a significant shift towards metabolic accumulation in this study.

Table 3. Prevalence of Smoking History among CHD Patients

Smoking history	Frequency	
	N (129)	%
Yes	116	(89.9)
No	13	(10.1)

Smoking was identified as the most pervasive modifiable risk factor in this study. Table 3 demonstrates an overwhelming disparity between smokers and non-smokers. With (89.9%) of patients reporting a history of cigarette

consumption, this finding underscores smoking as a primary environmental driver of endothelial injury in this specific male population.

Table 4. Distribution of blood pressure categories

Blood pressure classification	Frequency	
	N (129)	%
Optimal	28	(29.5)
Normal	35	(27.1)
High-normal	25	(19.4)
Hypertension grade 1	21	(16.3)
Hypertension grade 2	10	(7.8)

Regarding blood pressure control, the study stratified patients into detailed categories to capture the full spectrum of hemodynamic risk. As shown in Table 4, less than one-third of the patients (29.5%) presented with optimal blood pressure. A

significant proportion of patients were classified as "High-Normal" (n=25; 19.4%) or established Hypertension (Grade 1 and 2), indicating a widespread loss of vascular compliance and regulation.

Table 5. Prevalence of DM

DM status	Frequency	
	N (129)	%
Yes	9	(7)
No	120	(93)

The assessment of glucose metabolism disorders is summarized in Table 5. A substantial number of patients had a confirmed diagnosis of DM. The presence of this comorbidity

adds a layer of systemic metabolic dysfunction, which is known to accelerate plaque calcification and instability.

Table 6. Distribution of cumulative CHD risk factors per patient

Number of Risk Factors	Frequency	
	N (129)	%
0 Risk factor	5	(3.9)
1 Risk factor	48	(37.2)
2 Risk factors	56	(43.4)
3 Risk factors	19	(14.7)
4 Risk factors	1	(0.8)

Beyond isolated variables, this study analyzed the cumulative burden of risk factors within individual patients. As detailed in Table 6, a significant proportion of the study population was subjected to multiple simultaneous cardiovascular insults. Specifically, (58.1%) of subjects presented with at least two concurrent risk factors. The most prevalent pattern was the dual-risk phenotype (43.4%).

DISCUSSION

Demographic Characteristics based on Age and Gender

The demographic profile of CHD patients in this study was predominantly characterized by elderly individuals (≥ 60 years), accounting for 58.1% of the total sample. This finding aligns with the established understanding of age as a non-modifiable risk factor.¹ Aging is characterized by a systemic reduction in endothelial nitric oxide synthase (eNOS) activity and bioavailability of NO, a crucial vasodilator and anti-atherogenic molecule.^{10,17} Simultaneously, the accumulation of reactive oxygen species (ROS) over decades induces chronic oxidative stress, promoting inflammation and the stiffening of arterial walls.^{17,18} This structural remodeling increases pulse wave velocity and afterload, thereby exacerbating the vulnerability of coronary arteries to atherosclerotic plaque formation and rupture.¹⁸

The study population consisted entirely of male patients as determined by the specific inclusion criteria designed to focus on this high-risk demographic. By focusing exclusively on males, this study eliminates the confounding variable of hormonal protection found in females, allowing for a clearer analysis of metabolic and lifestyle risk factors.

From a physiological perspective, the inherent susceptibility of the male gender is often attributed to the absence of the cardioprotective effects of estrogen. In females, estrogen is understood to enhance endothelial eNOS activity.¹⁹ The lack of this hormonal protection in males renders the vascular endothelium more susceptible to oxidative stress and inflammatory damage earlier in life.²⁰

Obesity

The study identified that over half of the patients (50.4%) were obese, with a predominance of Class I Obesity (41.1%). This prevalence is notably higher compared to previous findings by Syahryan Gibran & Nurulhuda in 2023 at RS Islam Jakarta Cempaka Putih, which reported an obesity rate of (32.9%) among CHD patients.²¹ This observation aligns with the perspective that adipose tissue functions as more than a passive energy depot. In the context of CHD, excess adiposity is increasingly recognized as a pathologically active endocrine organ.^{7,12}

According to established literature, the hypertrophy of adipocytes associated with obesity may alter their secretory profile. This process is suggested to elevate levels of pro-inflammatory cytokines, specifically Tumor Necrosis Factor-alpha (TNF- α) and Interleukin-6 (IL-6), while

potentially suppressing the secretion of adiponectin.^{5,7} Such an imbalance is described as contributing to a milieu of chronic low-grade inflammation, which is a known factor in the acceleration of foam cell formation within the arterial intima.⁷

This chronic inflammation directly impairs vascular homeostasis. Pro-inflammatory cytokines activate the (nuclear factor kappa-light-chain-enhancer of activated B cells) NF- κ B pathway in endothelial cells, leading to the downregulation of endothelial eNOS and a subsequent reduction in NO bioavailability.²² Without sufficient NO, the coronary endothelium loses its ability to maintain vasodilation and resist leukocyte adhesion.¹⁰ Furthermore, the excess free fatty acids (FFAs) released from insulin-resistant adipocytes induce lipotoxicity in non-adipose tissues, including the myocardium and arterial walls, thereby accelerating plaque progression and increasing the susceptibility to acute coronary events.²³

Furthermore, the high prevalence of obesity in this cohort was observed alongside other metabolic comorbidities. The significant proportion of patients with obesity suggests that weight management interventions might need to be prioritized further in the secondary prevention strategies for this population.

Smoking History

The study revealed that a history of smoking was the most prevalent risk factor in the study population, identified in (89.9%) of patients. This prevalence is alarmingly high and significantly exceeds findings from comparable hospital-based studies in Indonesia. For instance, research conducted at RS Islam Jakarta Cempaka Putih reported a smoking prevalence of (51.8%) among CHD patients, while a study at RS Pendidikan Prof. Dr. Chairuddin P. Lubis Medan recorded (69.8%).^{21,24} The exceptionally high rate of smoking in this population suggests that in this specific population, tobacco exposure acts as the primary environmental insult driving the epidemic of coronary atherosclerosis, potentially overshadowing other traditional risk factors.

The mechanistic link between this chronic exposure and coronary pathology is chemically multifaceted. Cigarette smoke introduces a massive load of exogenous ROS, including superoxide anions and hydroxyl radicals, directly into the systemic circulation.⁹ These ROS rapidly react with vascular NO to form peroxynitrite.²⁵ In this dysfunctional state, the eNOS enzyme paradoxically generates more superoxide instead of NO, perpetuating a vicious cycle of oxidative stress and vascular injury.

Furthermore, the toxic components of cigarette smoke, particularly nicotine and carbon monoxide (CO), synergistically accelerate plaque instability.²⁶ Nicotine exerts a potent sympathomimetic effect, increasing heart rate and myocardial oxygen demand while simultaneously imposing hemodynamic shear stress on the arterial wall.²⁷ Concurrently, CO binds to hemoglobin with high affinity to

form carboxyhemoglobin, inducing systemic hypoxia that aggravates endothelial permeability.²⁸ This allows Low-Density Lipoprotein (LDL) to easily penetrate the sub-endothelial space, where it undergoes oxidative modification and is scavenged by macrophages to form foam cells, the hallmark of the vulnerable atherosclerotic plaque.^{29,30}

Hypertension

The study observed that (24.1%) of the patients had a recorded history of hypertension. This prevalence appears lower when compared to findings from similar regional studies, such as those conducted in Sengkang (51.7%), Cilacap (50.4%), and Gorontalo (64.0%).³¹⁻³³ While this discrepancy might reflect differences in population characteristics or methodology.

Despite the lower recorded prevalence, the pathophysiological implications of hypertension in this population remain significant. According to established mechanisms, the continuous hemodynamic shear stress induced by elevated blood pressure mechanically disrupts the endothelial lining, precipitating a loss of barrier function and vascular homeostasis.^{22,34,35} Once the endothelium is injured, it becomes more permeable to LDL and inflammatory cells.³⁶ This condition is worsened by an overactive sympathetic nervous system.³⁷ When combined with low levels of NO, these factors create an environment that promotes inflammation and atherosclerosis.³⁸

Diabetes Mellitus

The study identified a DM prevalence of (7.0%) among the subjects. This figure is markedly lower compared to other regional studies, such as those by Budiawan et al. in Lembean (77.1%) and Usri et al. in Makassar (67.5%).^{39,40} Similar to the findings on hypertension, this lower prevalence might be influenced by effective glycemic control in a secondary care setting potentially masks the diagnosis in retrospective data reviews.

However, even at this lower prevalence, the presence of DM carries significant pathophysiological weight. Hyperglycemia is described as a critical factor in the non-enzymatic glycation of proteins, leading to the formation of Advanced Glycation End-products (AGEs).^{41,42} Furthermore, AGEs bind to their specific receptors (RAGE) on endothelial cells, triggering a signaling cascade that activates Nicotinamide Adenine Dinucleotide Phosphate (NADPH) oxidase.^{43,44} This enzyme is a major producer of superoxide anions, which rapidly scavenge NO to form peroxynitrite.⁴⁴

The resulting depletion of NO impairs endothelium-dependent vasodilation and promotes a pro-thrombotic state. Additionally, hyperglycemia activates Protein Kinase C (PKC), which upregulates the expression of vasoconstrictor endothelin-1 and adhesion molecules (VCAM-1, ICAM-1).^{45,46} This facilitates the recruitment of monocytes into the sub-endothelial space, where they transform into foam

cells.^{29,47} Consequently, the presence of diabetes remains a clinically critical finding, as the resulting metabolic dysfunction provides a persistent stimulus for vascular inflammation and plaque instability, directly contributing to the pathogenesis of coronary artery occlusion

CONCLUSION AND SUGGESTION

Based on the results and discussion, this study concludes that the male CHD population at RSD Dr. H. Soemarno Sosroatmodjo is characterized by a severe burden of modifiable risk factors, forming a phenotype of "Metabolic-Oxidative Syndrome." The pathology is overwhelmingly driven by the synergistic toxicity of chronic smoking (89.9%), which serves as the primary source of oxidative vascular injury, and obesity (50.4%), which contributes to systemic chronic inflammation. Furthermore, the majority of patients presented with a clustering of multiple risk factors (2 concurrent insults), confirming that endothelial dysfunction in this setting is multi-factorial. These findings indicate that secondary prevention efforts in this region have been suboptimal, allowing risk factors to accumulate unchecked until the onset of clinical events.

Based on the high prevalence of modifiable risk factors identified, it is recommended that clinical management at RSD Dr. H. Soemarno Sosroatmodjo shifts from symptomatic treatment to aggressive upstream intervention, prioritizing mandatory smoking cessation programs and rigorous metabolic screening for all CHD patients. Institutional policy should support this by establishing an integrated secondary prevention unit focused on long-term lifestyle modification to prevent recurrent cardiac events. Furthermore, future research should expand the scope to include female participants and incorporate serological biomarkers of inflammation (e.g., hs-CRP) and oxidative stress to provide direct biomolecular evidence of the mechanisms driving disease progression in this population.

STUDY LIMITATIONS

Several limitations inherent to this study must be acknowledged. This study relied on clinical surrogates (such as BMI and smoking history) to infer metabolic risk and oxidative stress. Due to resource constraints, direct serological biomarkers of inflammation (e.g., hs-CRP, TNF- α , IL-6) and oxidative damage (e.g., oxidized LDL, plasma cotinine) were not measured. Consequently, the mechanistic links discussed, such as endothelial inflammation and ROS generation, are based on theoretical extrapolation from established literature rather than direct biomolecular evidence from the subjects.

The use of secondary data from medical records introduces the potential for information bias. As noted in the discussion regarding hypertension and diabetes, the recorded prevalence may underestimate the true biological burden due to the "treatment paradox," where controlled

clinical parameters in patients on secondary prevention therapy mask baseline severity. Finally, the intentional restriction of the study population to male patients, while necessary to eliminate hormonal confounding, limits the generalizability of these findings to female patients, who may exhibit distinct risk factor profiles.

REFERENCES

1. Brown JC, Gerhardt TE, Kwon E. Risk Factors for Coronary Artery Disease. *Risk Factors Coron Artery Dis* [Internet]. 2023 Jan 23 [cited 2024 Dec 1];1:1–219. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK554410/>
2. Muharram FR, Multazam CECZ, Mustofa A, Socha W, Andrianto, Martini S, et al. The 30 Years of Shifting in The Indonesian Cardiovascular Burden—Analysis of The Global Burden of Disease Study. *J Epidemiol Glob Health* [Internet]. 2024 Mar 1 [cited 2024 Nov 17];14(1):193–212. Available from: <https://link.springer.com/article/10.1007/s44197-024-00187-8>
3. British Heart Foundation. Global Heart & Circulatory Diseases Factsheet. *Br Hear Found* [Internet]. 2024;(Januari):1–12. Available from: <https://www.bhf.org.uk/-/media/files/for-professionals/research/heart-statistics/bhf-cvd-statistics-global-factsheet.pdf?rev=169125b6b7e2474985f8a0c419ba9676&hash=79BA5336A597F7180A0B8898F5C2ADEB>
4. Nugiaswari PP, Laksmi NMD, Ferdiyanthi APH, Adiputra KY, Jagannatha GNP. Evaluation of Cardiac Autonomic Control During Six-Minute Walk Test in Obese Among Medical Faculty Students of Udayana University. *E-Jurnal Med Udayana* [Internet]. 2025 Jun 4 [cited 2025 Dec 30];14(6):9–15. Available from: <https://ejournal4.unud.ac.id/index.php/medika/article/view/651>
5. Henning RJ. Obesity and Obesity-Induced Inflammatory Disease Contribute to Atherosclerosis: A Review of the Pathophysiology and Treatment of Obesity. *Am J Cardiovasc Dis* [Internet]. 2021 [cited 2023 Jun 30];11(4):504. Available from: <https://pubmed.ncbi.nlm.nih.gov/articles/PMC8449192/>
6. Perone F, Pingitore A, Conte E, Halasz G, Ambrosetti M, Peruzzi M, et al. Obesity and Cardiovascular Risk: Systematic Intervention Is the Key for Prevention. *Healthcare* [Internet]. 2023 Mar 1 [cited 2025 Dec 29];11(6):902. Available from: <https://pubmed.ncbi.nlm.nih.gov/articles/PMC10048800/>
7. Khafagy R, Dash S. Obesity and Cardiovascular Disease: The Emerging Role of Inflammation. *Front Cardiovasc Med*. 2021;8(October):1–10.
8. Nussbaumerova B, Rosolova H. Obesity and Dyslipidemia. *Curr Atheroscler Rep* [Internet]. 2023 Dec 1 [cited 2025 Dec 29];25(12):947–55. Available from: <https://pubmed.ncbi.nlm.nih.gov/37979064/>
9. Salehi N, Janjani P, Tadbiri H, Rozbahani M, Jalilian M. Effect of Cigarette Smoking on Coronary Arteries and Pattern and Severity of Coronary Artery Disease: A Review. *J Int Med Res* [Internet]. 2021 Dec 1 [cited 2024 Dec 1];49(12). Available from: <https://pubmed.ncbi.nlm.nih.gov/34855538/>
10. Doulias PT, Tenopoulou M. Endothelial Nitric Oxide Synthase-Derived Nitric Oxide in the Regulation of Metabolism. *F1000Research* [Internet]. 2020 [cited 2023 Jun 30];9. Available from: <https://pubmed.ncbi.nlm.nih.gov/33042519/>
11. Okawa Y, Mitsuhashi T, Tsuda T. The Asia-Pacific Body Mass Index Classification and New-Onset Chronic Kidney Disease in Non-Diabetic Japanese Adults: A Community-Based Longitudinal Study from 1998 to 2023. *Biomedicine* [Internet]. 2025 Feb 1 [cited 2025 Dec 30];13(2):373. Available from: <https://pubmed.ncbi.nlm.nih.gov/articles/PMC11853003/>
12. Lin X, Li H. Obesity: Epidemiology, Pathophysiology, and Therapeutics. *Front Endocrinol (Lausanne)*. 2021 Sep 6;12:706978.
13. Kemenkes RI. Kandungan Rokok yang Berbahaya Bagi Kesehatan [Internet]. Kementerian Kesehatan Republik Indonesia. 2022 [cited 2023 Jun 20]. Available from: https://yankes.kemkes.go.id/view_artikel/406/kandungan-rokok-yang-berbahaya-bagi-kesehatan
14. PERHI, Perhimpunan Dokter Hipertensi Indonesia. Konsensus Penatalaksanaan Hipertensi 2021: Update Konsensus PERHI 2019. *I-HefcardCom* [Internet]. 2021;118. Available from: http://www.inash.or.id/upload/event/event_Update_konsensus_2019123191.pdf
15. Seravalle G, Grassi G. Essential Hypertension. *Prim Auton Nerv Syst* Fourth Ed [Internet]. 2023 Jul 20 [cited 2025 Nov 9];467–70. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK539859/>
16. PERKENI. Pedoman Pengelolaan Dan Pencegahan Diabetes Melitus Tipe 2 Di Indonesia 2024 Perkumpulan Endokrinologi Indonesia. 2024;1–126.
17. Picos A, Seoane N, Campos-Toimil M, Viña D. Vascular Senescence and Aging: Mechanisms, Clinical Implications, and Therapeutic Prospects. *Biogerontology* 2025 263 [Internet]. 2025 May 26 [cited 2025 Dec 29];26(3):118–. Available from: <https://link.springer.com/article/10.1007/s10522-025-10256-5>

18. Herzog MJ, Müller P, Lechner K, Stiebler M, Arndt P, Kunz M, et al. Arterial Stiffness and Vascular Aging: Mechanisms, Prevention, and Therapy. *Signal Transduct Target Ther* 2025 101 [Internet]. 2025 Sep 1 [cited 2025 Dec 29];10(1):282-. Available from: <https://www.nature.com/articles/s41392-025-02346-0>
19. Niță AR, Knock GA, Heads RJ. Signalling Mechanisms in the Cardiovascular Protective Effects of Estrogen: With A Focus on Rapid/Membrane Signalling. *Curr Res Physiol*. 2021 Jan 1;4:103–18.
20. Robert J. Sex Differences in Vascular Endothelial Cells. *Atherosclerosis*. 2023 Nov 1;384:117278.
21. Syahryan Gibran M, Nurulhuda U. Hubungan Obesitas dengan Kejadian Penyakit Jantung Koroner. *JHCN J Heal Cardiovasc Nurs*. 2023;3(2):57–62.
22. Theofilis P, Sagris M, Oikonomou E, Antonopoulos AS, Siasos G, Tsioufis C, et al. Inflammatory Mechanisms Contributing to Endothelial Dysfunction. *Biomedicines* [Internet]. 2021 Jul 1 [cited 2025 Dec 29];9(7). Available from: <https://pubmed.ncbi.nlm.nih.gov/34356845/>
23. Reardon CA, Shibata R, Akasaki Y, Den Hartigh LJ, Chait A. Adipose Tissue Distribution, Inflammation and Its Metabolic Consequences, Including Diabetes and Cardiovascular Disease. *Front Cardiovasc Med* [Internet]. 2020 Feb 25 [cited 2025 Dec 29];7:22. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7052117/>
24. Sembiring A, Lubis R. Faktor-Faktor yang Berhubungan dengan Kejadian Penyakit Jantung Koroner di Rumah Sakit Pendidikan Prof. dr. Chairuddin P. Lubis Medan Tahun 2025. *J Ilmu Kedokt dan Kesehat Indones*. 2025;5(2):506–22.
25. Daiber A, Kröller-Schön S, Oelze M, Hahad O, Li H, Schulz R, et al. Oxidative Stress and Inflammation Contribute to Traffic Noise-Induced Vascular and Cerebral Dysfunction via Uncoupling of Nitric Oxide Synthases. 2020 Jul 1 [cited 2025 Dec 29];34:101506. Available from: <https://pubmed.ncbi.nlm.nih.gov/32371009/>
26. Ishida M, Sakai C, Kobayashi Y, Ishida T. Cigarette Smoking and Atherosclerotic Cardiovascular Disease. *J Atheroscler Thromb* [Internet]. 2024 [cited 2024 Dec 11];31(3):189–200. Available from: <https://pubmed.ncbi.nlm.nih.gov/38220184/>
27. Klein LW. Pathophysiologic Mechanisms of Tobacco Smoke Producing Atherosclerosis. *Curr Cardiol Rev* [Internet]. 2022 Apr 12 [cited 2025 Dec 29];18(6):e110422203389. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9893148/>
28. Zazzeron L, Franco W, Anderson R. Carbon Monoxide Poisoning and Phototherapy. *Nitric Oxide*. 2024 May 1;146:31–6.
29. Jebari-Benslaiman S, Galicia-García U, Larrea-Sebal A, Olaetxea JR, Alloza I, Vandenbroeck K, et al. Pathophysiology of Atherosclerosis. *Int J Mol Sci* [Internet]. 2022 Mar 1 [cited 2024 Dec 4];23(6). Available from: <https://pubmed.ncbi.nlm.nih.gov/35328769/>
30. Shaya GE, Leucker TM, Jones SR, Martin SS, Toth PP. Coronary Heart Disease Risk: Low-Density Lipoprotein and Beyond. *Trends Cardiovasc Med* [Internet]. 2022 May 1 [cited 2024 Dec 1];32(4):181–94. Available from: <https://pubmed.ncbi.nlm.nih.gov/33872757/>
31. Seppo MPRA. Overview of Heart and Vascular Disease Patients at Lamaddukelleng Sengkang Hospital in 2023. *An Idea Heal J* [Internet]. 2025 Feb 22 [cited 2025 Nov 9];5(02):151–7. Available from: <https://www.ihj.ideajournal.id/index.php/IHJ/article/view/430>
32. Tri Kumala Swandari M, Nur Fauziah A, Pertiwi Y, Farmasi F. Karakteristik Pasien Jantung Koroner dengan Komorbid di Rumah Sakit X Cilacap Periode 2019-2020. *Parapemikir J Ilm Farm* [Internet]. 2022 Aug 29 [cited 2025 Nov 9];11(3):211–5. Available from: <https://ejournal.poltekharber.ac.id/index.php/parapemikir/article/view/3614>
33. Ammarie SAU, Wahidji V, Pateda SM, Purwanto R, Dungga EF. Gambaran Faktor Risiko pada Penderita Penyakit Jantung Koroner di RSUD Prof. Dr. H. Aloe Saboe Kota Gorontalo Tahun 2020-2021. *Jambura Axon Med* [Internet]. 2024 Dec 22 [cited 2025 Nov 10];1(1):24–34. Available from: <https://ejurnal.ung.ac.id/index.php/axon/article/view/29249>
34. Gallo G, Volpe M, Savoia C. Endothelial Dysfunction in Hypertension: Current Concepts and Clinical Implications. *Front Med* [Internet]. 2022 Jan 20 [cited 2025 Nov 9];8. Available from: <https://pubmed.ncbi.nlm.nih.gov/35127755/>
35. Cheng CK, Wang N, Wang L, Huang Y. Biophysical and Biochemical Roles of Shear Stress on Endothelium: A Revisit and New Insights. *Circ Res* [Internet]. 2025 Mar 28 [cited 2025 Nov 9];136(7):752–72. Available from: <https://www.ahajournals.org/doi/10.1161/CIRCRES.AHA.124.325685>
36. Alexander Y, Osto E, Schmidt-Trucksäss A, Shechter M, Trifunovic D, Duncker DJ, et al. Endothelial Function in Cardiovascular Medicine: A Consensus Paper of the European Society of Cardiology Working Groups on Atherosclerosis and Vascular Biology, Aorta and Peripheral Vascular Diseases, Coronary Pathophysiology and

- Microcirculation, and Thr. Cardiovasc Res [Internet]. 2020 Jan 1 [cited 2025 Dec 29];117(1):29. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7797212/>
37. DeLalio LJ, Sved AF, Stocker SD. Sympathetic Nervous System Contributions to Hypertension: Updates and Therapeutic Relevance. *Can J Cardiol* [Internet]. 2020 May 1 [cited 2025 Dec 29];36(5):712. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7534536/>
38. Baig MS, Markin AM, Poznyak A V, Av P, Nk S, Kartuesov AG, et al. Hypertension as a Risk Factor for Atherosclerosis: Cardiovascular Risk Assessment. *Front Cardiovasc Med* [Internet]. 2022 Aug 22 [cited 2025 Dec 29];9:959285. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9441708/>
39. Budiawan H, Johanis K, Palenewen LA, Djeramu O, Manaung V. Determinasi Faktor Risiko Penyakit Jantung Koroner di Rumah Sakit Umum Hermana Lembean. *J Keperawatan* [Internet]. 2025 Aug 31 [cited 2025 Nov 10];13(02):246–53. Available from: <https://ejournal.unsrat.ac.id/v3/index.php/jkp/article/view/63849>
40. Afifah Usri N, Wisudawan K, Nurmadilla N, Irmayanti. Karakteristik Faktor Risiko Pasien Penyakit Jantung Koroner di Rumah Sakit Ibnu Sina Makassar Tahun 2020. *Fakumi Med J J Mhs Kedokt* [Internet]. 2022 Oct 1 [cited 2025 Nov 10];2(9):619–29. Available from: <https://fmj.fk.umi.ac.id/index.php/fmj/article/view/117>
41. Ritchie RH, Abel ED. Basic Mechanisms of Diabetic Heart Disease. *Circ Res* [Internet]. 2020 May 22 [cited 2025 Nov 10];126(11):1501–25. Available from: <https://www.ahajournals.org/doi/10.1161/CIRCRES.AHA.120.315913>
42. Khalid M, Petroianu G, Adem A. Advanced Glycation End Products and Diabetes Mellitus: Mechanisms and Perspectives. *Biomol* 2022, Vol 12, Page 542 [Internet]. 2022 Apr 4 [cited 2025 Nov 13];12(4):542. Available from: <https://www.mdpi.com/2218-273X/12/4/542/htm>
43. Wang B, Jiang T, Qi Y, Luo S, Xia Y, Lang B, et al. AGE-RAGE Axis and Cardiovascular Diseases: Pathophysiologic Mechanisms and Prospects for Clinical Applications. *Cardiovasc Drugs Ther* 2024 [Internet]. 2024 Nov 5 [cited 2025 Nov 13];1–18. Available from: <https://link.springer.com/article/10.1007/s10557-024-07639-0>
44. Reynaert NL, Vanfleteren LEGW, Perkins TN, Reynaert NL, Vanfleteren LEGW, Perkins TN. The AGE-RAGE Axis and the Pathophysiology of Multimorbidity in COPD. *J Clin Med* 2023, Vol 12, [Internet]. 2023 May 9 [cited 2025 Dec 29];12(10). Available from: <https://www.mdpi.com/2077-0383/12/10/3366>
45. González P, Lozano P, Ros G, Solano F, González P, Lozano P, et al. Hyperglycemia and Oxidative Stress: An Integral, Updated and Critical Overview of Their Metabolic Interconnections. *Int J Mol Sci* 2023, Vol 24, [Internet]. 2023 May 27 [cited 2025 Dec 29];24(11). Available from: <https://www.mdpi.com/1422-0067/24/11/9352>
46. Qin P, He C, Ye P, Li Q, Cai C, Li Y. PKC δ Regulates the Vascular Biology in Diabetic Atherosclerosis. *Cell Commun Signal* 2023 211 [Internet]. 2023 Nov 16 [cited 2025 Dec 29];21(1):330-. Available from: <https://link.springer.com/article/10.1186/s12964-023-01361-4>
47. Shahjehan RD, Sharma S, Bhutta BS. Coronary Artery Disease. *Med Nurs*. 2024 Oct 9;110–4.

