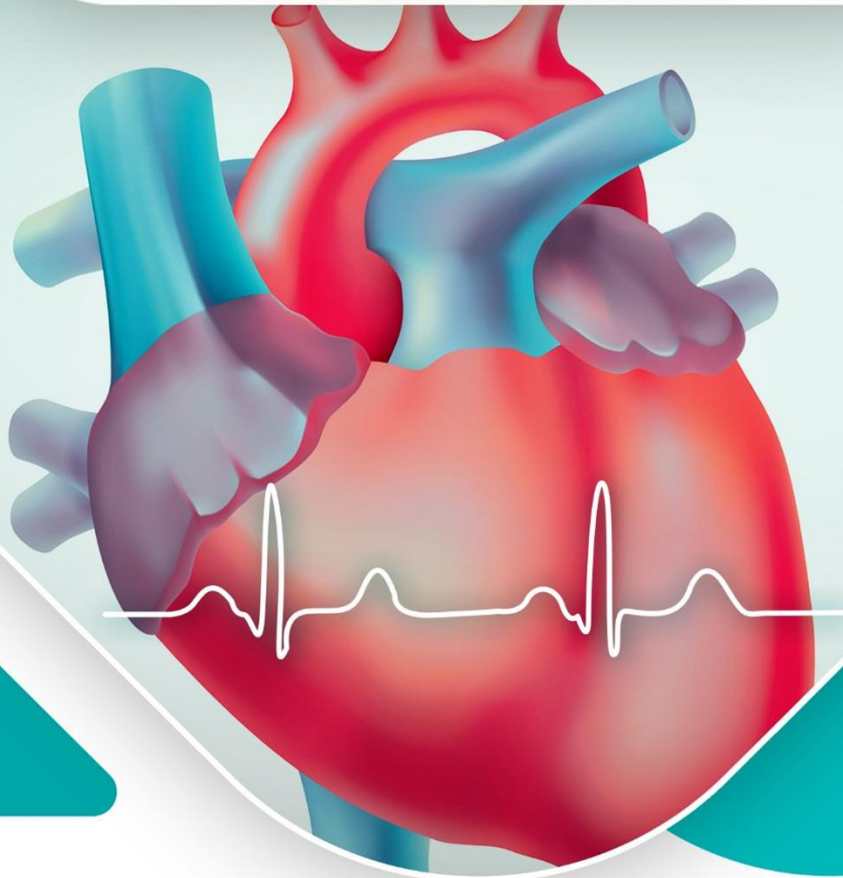




DIGITAL
30th As*o*iha
Annual Scientific Meeting of Indonesian Heart Association



15-23 Oktober 2021



PROCEEDING BOOK

Editors:

Sunu Budhi Raharjo, MD, PhD
Hary Sakti Muliawan, MD, PhD
Dian Zamroni, MD
Ario Soeryo Koencoro, MD

Proofreaders:

Ray Wijaya, MD, M. Res
Annisa Firdausi, S.Si

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Phone	021-5681149
Fax	021-5684220
Email	secretariat@inaheart.org
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INDONESIAN HEART ASSOCIATION PRESIDENT FOREWORD



Greeting colleague,

Greeting colleague,

It was a great pleasure for me to welcome you all to the 30th Annual Scientific Meeting of the Indonesian Heart Association (ASMIHA). The meeting has become one of the most significant cardiology events this year. The forum is jointly organized by The 2nd Indonesian Society of Cardiovascular Imaging Annual Meeting (ISCI) and The 3rd Indonesian Annual Congress of Congenital Heart Disease (INACHD), 15–23 October 2021.

This meeting was disseminated the latest research results and findings to discuss with experts, academia, medical practitioners and also a researcher. A backward-looking since 2003, *Cardiology Update* has changed the name became ASMIHA, we see the participation in this meeting has increased significantly over the years. In 2021, as we celebrate the 30th year of ASMIHA, the organizing committee would to enrich knowledge-sharing forum and stimulate advanced research findings. Indonesian Heart Association and Organizing Committee of 30th ASMIHA looks forward to provide an opportunity for participants to revisit key takeaways from the experts through this proceeding The 30th ASMIHA.

We would like to express our sincere appreciation to all experts for their invaluable support for this meeting. We sincerely hope that the Proceeding will be a useful reference for all readers to expand their knowledge and push ahead with advanced research findings.

Isman Firdaus, MD, PhD

President of Indonesian Heart Association

30th ASMIHA CONGRESS CHAIRPERSON FOREWORD



Greeting colleague,

On behalf of the 30th Annual Scientific Meeting of Indonesian Heart Association (ASMIHA) Committee, we would like to acknowledge all parties who have taken part and participated in this event. The 30th ASMIHA 2021 was successfully held in-conjunction with the 2nd Indonesian Society of Cardiovascular Imaging (ISCI) Annual Meeting and the 3rd Indonesian Annual Congress of Congenital Heart Disease (INACHD). Months of preparation involving hundreds of experts around the world, various international cardiovascular and medical societies, and joined by thousands of participants has once again proven the prestige of ASMIHA, originally known as 'Cardiology Update', as the biggest cardiovascular conference in Indonesia since 1989.

This program is formulated to accommodate participants from different backgrounds ranging from medical students until sub-specialists. The limitation to congregate set by COVID-19 pandemic was put aside by adapting the format of this event into a digitalized platform. Furthermore, in doing so, the committee believes a wider selection of topics can be presented that is accessible to participants joining from all over the world.

As the final project, we have prepared a proceeding compilation of the topics presented in ASMIHA 2021. Thank you to all faculties for their time, effort, and expertise in the creation of this proceeding. Hopefully, it may extend our reach in sharing the knowledge that was gathered to all regions in Indonesia and even globally. See you on the event next year!

Ario Soeryo Kuncoro, MD

Congress Chairperson of the 30th ASMIHA

CHAIRPERSON OF 30th ASMIHA SCIENTIFIC COMMITTEE FOREWORD



Dear colleague,

The 30th ASMIHA was successfully held for 9 days from 15th until 23rd October 2021. A virtual gathering of many cardiologists and medical practitioners from various expertise to share their insights and experiences. With more than 90 symposium and workshop sessions prepared, we hope the whole experience was as eventful for you as it was for the committee formulating them.

Through this proceeding, we would like to share some of the issues that were discussed. The proceeding comprised more than 100 topics from 20 chapters ranging from basic clinical examination to the recent study of COVID-19 pandemic impacts on cardiovascular health. Thank you to all colleagues, and especially the proceeding committee, for their time and effort that helped this proceeding to be published. We believe the medical field will always evolve and thus, the committee welcomes any suggestion and feedback to improve it even further.

Once again, thank you for all your participation and support. We hope this event will keep contributing to the development of the cardiovascular field in Indonesia.

Dian Zamroni, MD

Chairperson of 30th ASMIHA Scientific Committee

CHAIRPERSON OF 30th ASMIHA PROCEEDING BOOK FOREWORD



Greeting colleagues,

First of all, I am so grateful to Allah SWT for giving us the ability to finish the Proceeding of 30th ASMIHA 2021 within a short period of preparation. The sole purpose of this proceeding is to spread knowledge to a greater extent and longer period. Presentation in a scientific meeting, such as this 30th ASMIHA is one form of knowledge sharing. Unfortunately, this format was limited to participants who attended the meeting or who recorded the presentation. Therefore, we provide another platform where experts from various fields may impart their wisdom and experiences with others. As life-long learners, medical practitioners must keep being updated with the many developments that have been agreed upon or is under researched.

Over 20 chapters and 100 topics were being discussed in-depth by experts in their respective field. Hopefully, the readers may find some interesting issues that piqued their curiosity and by doing so, we are hopeful that more scientific questions and research may take place after this conference aimed to optimize patients' experience.

I personally would like to show my appreciation to all committee, authors, and contributors that has made this proceeding possible. To never stop learning and asking questions is the way to keep improving ourselves, as knowledge increases by sharing and not by saving them.

Sunu Budhi Raharjo, MD, PhD

Editor-in-Chief of 30th ASMIHA Proceeding Book

ORGANIZING COMMITTEE

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Promotion and Publication

Suci Indriani, MD
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Vito Anggarino Damay, MD

Registration, IT, and Website

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Exhibition

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Coordinator YIA, Free Paper and Poster Session

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Idar Mappangara, MD, PhD
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Johanes Nugroho Eko Putranto, MD, PhD
Dyah Wulan Anggrahini, MD, PhD
Hary Sakti Muliawan, MD, PhD

Coordinator Workshop

Siska S. Danny, MD

LIST OF CONTRIBUTORS

Abdul Hakim Alkatiri, MD

Department of Cardiology
Faculty of Medicine
Hassanudin University
Cardiac Centre Wahidin Sudirohusodo
General Hospital
Makassar

Abdul Halim Raynaldo, MD

Department of Cardiology and
Vascular Medicine
Universitas Sumatera Utara
Haji Adam Malik General Hospital
Medan

Aditya Agita Sembiring, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Agus Subagyo, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University
of Airlangga
Dr. Soetomo General Hospital
Surabaya

Ali Nafiah Nasution, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University
of North Sumatera
H. Adam Malik General Hospital
Medan

Amiliana M. Soesanto, MD, PhD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Andre Ketaren, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University
of North Sumatera
H. Adam Malik General Hospital
Medan

Anggoro Budi Hartopo, MD, PhD

Department of Cardiology and Vascular
Medicine
Faculty of Medicine Gadjah Mada
University
Sardjito Central General Hospital
Yogyakarta

Anna Fuji Rahimah, MD

Department of Cardiology and
Vascular Medicine
Faculty of Medicine University of
Brawijaya
Dr. Saiful Anwar General Hospital
Malang

Anna Ulfah Rahajoe, MD

Department of Cardiology and
Vascular Medicine Faculty of Medicine,
Universitas Indonesia
National Cardiovascular Center,
Harapan Kita - Jakarta, Indonesia

Antonia Anna Lukito, MD, PhD

Departement of Cardiology
and Vascular Medicine
Faculty of Medicine
University Pelita Harapan
Siloam Hospital Lippo Village
Banten

A.N. Puspitasari, MD

Department of Cardiology and
Vascular Medicine
Faculty of Medicine University of
Airlangga
Dr. Soetomo General Hospital
Surabaya

Ardian Rizal, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Brawijaya
Dr. Saiful Anwar General Hospital
Malang

Badai Bhatara Tiksnadi, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Padjadjaran
University
Hasan Sadikin General Hospital
Bandung

Bambang Dwiputra, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Basuni Radi, MD, PhD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Benny Mulyanto Setiadi, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Sam Ratulangi
University
Prof. Dr. R. D Kandou Hospital
Manado

Beny Hartono, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Padjadjaran
University
Hasan Sadikin General Hospital
Bandung

Chaerul Achmad, MD, PhD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Padjadjaran
University
Hasan Sadikin General Hospital
Bandung

Citra Kiki Kreviani, MD

Department Cardiology
and Vascular Medicine
Faculty of Medicine, University of
Andalas
M. Djamil General Hospital
Padang

Daniel Tanubudi, MD

Eka Hospital BSD
Tangerang

Deddy Tedjasukmana, MD

Physical Medicine and Rehabilitation
Department Cipto Mangunkusumo
Hospital
Jakarta

Dewi Utari Djafar, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Sam Ratulangi
University
Prof. Dr. R. D Kandou Hospital
Manado

Dian Yaniarti Hasanah, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Dicky A. Hanafy, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita /
Heartology Cardiovascular Center
Jakarta

Dwita Rian Desandri, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Dyana Sarvasti, MD, PhD

Department of Internal Medicine
Faculty of Medicine Widya Mandala
Catholic University Surabaya
Husada Utama Hospital Surabaya
Indonesia

Endang Ratnaningsih, MD

Department of Cardiology
Tarakan Hospital
Jakarta

Erika Maharani, MD

Department of Cardiology and Vascular
Medicine
Faculty of Medicine Gadjah Mada
University
Sardjito Central General Hospital
Yogyakarta

Febtusia Puspitasari, MD

Department of Cardiology and Vascular
Medicine
Universitas Kristen Indonesia
Jakarta

Habibie Arifianto, MD

Department of Cardiology and Vascular
Medicine
Faculty of Medicine Sebelas Maret
University
Sebelas Maret University Hospital
Surakarta

Hauda El Rasyid, MD

Department Cardiology and
Vascular Medicine
Faculty of Medicine, University of
Andalas
M. Djamil General Hospital
Padang

Hawani Sasmaya, MD

Department of Cardiology and Vascular
Medicine
Faculty of Medicine Padjadjaran
University
Hasan Sadikin General Hospital
Bandung

Hilfan Ade Putra Lubis, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University
of North Sumatera
H. Adam Malik General Hospital
Medan

I Gde Rurus Suryawan, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University
of Airlangga
Dr. Soetomo General Hospital
Surabaya

I Made Junior Rina Artha, MD

Department of Cardiology and Vascular
Medicine
Faculty of Medicine University of
Udayana
Sanglah General Hospital
Bali

Ida Bagus Rangga Wibhuti, MD

Department of Cardiology and Vascular
Medicine
Faculty of Medicine University of
Udayana
Sanglah General Hospital
Bali

Ida Gunawan, MD, MS

Departement of Clinical Nutrition
University of Indonesia
Jakarta

Ima Ansari, MD

Department of Cardiology
and Vascular Medicine
Siloam Hospital
Yogyakarta

Indah Sukmawati, MD

Departement of Cardiology
and Vascular Medicine
Faculty of Medicine
University Pelita Harapan
Siloam Hospital Lippo Village
Banten

Indra Prasetya, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Brawijaya
Dr. Saiful Anwar General Hospital
Malang

Irnizarifka, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Sebelas Maret
University Sebelas Maret University
Hospital
Surakarta

Ismir Fahri, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Bengkulu
Dr. M. Yunus General Hospital
Bengkulu

Jetty RH. Sedyawan, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
Jakarta

Juang Zebua, MD

Department of Cardiology and
Vascular Medicine
Faculty of Medicine University of
North Sumatera
H. Adam Malik General Hospital
Medan

Jusup Endang, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Bengkulu
Dr. M. Yunus General Hospital
Bengkulu

Lely Puspita Candra Dewi, MD

Department Cardiology
and Vascular Medicine
Universitas Ciputra
Surabaya

Mefri Yanni, MD

Department Cardiology
and Vascular Medicine
Faculty of Medicine, University of
Andalas
M. Djamil General Hospital
Padang

Melawati Hasan, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Padjadjaran
University
Hasan Sadikin General Hospital
Bandung

Meilisa Rahmadani

Occupational Health and Safety
Unit
University of Indonesia Hospital
Jakarta

Miftah Pramudyo, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Padjadjaran
University
Hasan Sadikin General Hospital
Bandung

Mohammad Iqbal, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Padjadjaran
University
Hasan Sadikin General Hospital
Bandung

Muhammad Ferhat E.S., MD

Department of Cardiology and
Vascular Medicine
Faculty of Medicine University of
North Sumatera
H. Adam Malik General Hospital
Medan

Muhammad Yamin, MD, PhD

Department of Internal Medicine
University of Indonesia
Dr. Cipto Mangunkusumo National
Hospital
Jakarta

Muhammad Munawar, MD, PhD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
Bina Waluya Cardiac Center
Jakarta

Muhamad Rizki Fadlan, MD

Department of Cardiology and
Vascular Medicine
Faculty of Medicine University of
Brawijaya
Dr. Saiful Anwar General Hospital
Malang

Muzakkir Amir, MD

Department of Cardiology and
Vascular Medicine
Faculty of Medicine
Universitas Hasanuddin
Wahidin Sudirohusodo Makassar

Noorsasiwi, MD, PhD

Department of Cardiology
and Vascular Medicine
Dharmais National Cardiac Centre
Jakarta

Novi Kurnianingsih, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Brawijaya
Dr. Saiful Anwar General Hospital
Malang

Novita, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Syiah Kuala
Teaching Hospital
Dr. Zainoel Abidin General Hospital
Banda Aceh

Oktavia Lilyasari, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Paskalis Indra Suryajaya, MD

Department of Cardiology and
Vascular Medicine
Faculty of Medicine Universitas
Hasanuddin
Wahidin Sudirohusodo
Makassar

Paskariatne Probo Dewi Yamin, MD

Department of Cardiology
Gatot Subroto Central Army
General Hospital
Jakarta

Pipin Ardhianto, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Diponegoro
University
Dr. Kariadi General Hospital
Semarang

Prima Almazini, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Radityo Prakoso, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita /
Heartology Cardiovascular Center
Jakarta

Rarsari Soerarso, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Rerdin Julario, MD

Department of Cardiology and
Vascular Medicine Dr. Soetomo
General Hospital
Universitas Airlangga Medical School
Surabaya

Riana Handayani, MD

Department of Cardiology
and Vascular Medicine
Abdoel Moeloek Government Hospital
Lampung

Rini Pramesti, MD

Department of Cardiology
and Vascular Medicine
Fatmawati General Hospital
Jakarta

Rio Herdyanto, MD

Department of Cardiology
and Vascular Medicine
Dr. R. Sosodoro Djatikoesoemo General
Hospital
Bojonegoro

Rita Zahara, MD, PhD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Rizki, MD

Department of Cardiology
Karawang General Hospital
Karawang

Rosi Amrilla Fagi, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University
of Airlangga
Dr. Soetomo General Hospital
Surabaya

**Mohammad Saifur Rohman, MD,
PhD, Prof**

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Brawijaya
Dr. Saiful Anwar General Hospital
Malang

Santi Rahayu Dewayanti, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Sarah Humaira, MD, MRes

Faculty of Medicine
Universitas Indonesia
Jakarta

Saskia Dyah Handari, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Brawijaya
Dr. Saiful Anwar General Hospital
Malang

Sisca Natalia Siagian, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Sefri Noventi Sofia, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Diponegoro
University
Dr. Kariadi General Hospital
Semarang

Siti Elkana Nauli, MD

Department of Cardiology
and Vascular Medicine
Tangerang General Hospital
Tangerang

Sony Hilal Wicaksono, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
University of Indonesia Hospital
Jakarta

Suci Indriani, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Sukman T. Putra, MD, PhD, Prof

Department Pediatric Cardiology
Faculty of Medicine University of
Indonesia

Sumarni, MD

Department of Cardiology and
Vascular Medicine
Faculty of Medicine
Universitas Hasanuddin
Wahidin Sudirohusodo Makassar

Sunanto Ng, MD, PhD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine
University Pelita Harapan
Siloam Hospital Lippo Village
Banten

Sunu Budhi Raharjo, MD, PhD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita /
Heartology Cardiovascular Center
Jakarta

Susetyo Atmojo, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Syarif Hidayat Soeriasaputra, MD

Department of Cardiology
and Vascular Medicine
Dr. Drajat Prawiranegara Hospital
Serang

Taofan, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Tengku Winda Ardini, MD

Department of Cardiology and
Vascular Medicine
Faculty of Medicine University
of North Sumatera
H. Adam Malik General Hospital
Medan

Teuku Heriansyah, MD, PhD, Prof

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Syiah Kuala
Teaching Hospital
Dr. Zainoel Abidin General Hospital
Banda Aceh

Tri Astiawati, MD

Department Cardiology and
Vascular
Medicine dr. Iskak Hospital
Tulungagung

Triwedya Indra Dewi, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Padjadjaran
University
Hasan Sadikin General Hospital
Bandung

Victor Joseph, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine Sam Ratulangi
University
Prof. Dr. R. D Kandou Hospital
Manado

Vito Anggarino Damay, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine
University Pelita Harapan
Siloam Hospital Lippo Village
Banten

Yovi Kurniawati, MD

Department of Cardiology
and Vascular Medicine
Faculty of Medicine University of
Indonesia
National Cardiovascular Center
Harapan Kita
Jakarta

Yusra Pintaningrum, MD


Department of Cardiology
and Vascular Medicine
University of Mataram
Mataram

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CHAPTER 16

PREGNANCY AND CARDIOVASCULAR DISEASE

PRECLAMPSIA AND LONG-TERM CARDIOVASCULAR RISK

Sefri Noventi Sofia, MD

Department of Cardiology and Vascular Medicine, Diponegoro University
sefrinov@gmail.com

ABSTRACT

Preeclampsia is a hypertensive disorder of pregnancy that can cause detrimental outcomes. Current evidence demonstrates a higher risk for long-term cardiovascular disease in women with a history of preeclampsia. This increased risk might result from an underlying predisposition to cardiovascular disease, preeclampsia pathogenesis itself, or a combination of both. After pregnancy, women with preeclampsia show an increased risk of chronic hypertension, coronary heart disease, valvular heart disease, and heart failure. The onset and prevalence of cardiovascular risk factors depend on the severity of the preeclampsia and the coexistence of other pregnancy complications. There is no consensus regarding the management of these patients, but some approaches are proposed to minimize morbidity and mortality among these affected populations.

Keywords: *preeclampsia, cardiovascular, long-term risk, pregnancy*

INTRODUCTION

Preeclampsia (PE) is part of hypertension during pregnancy (HDP) disorders. The International Society for The Study of Hypertension in Pregnancy (ISSHP) issued an update that PE is defined as the novo appearance of hypertension after the 20th week of gestation along with evidence of maternal organ failure, which includes the following: new-onset proteinuria of >300 mg/day or other indications of renal insufficiency, a hematological complication such as thrombocytopenia and liver dysfunction, or neurological complications such as visual disturbance and/or evidence of uteroplacental dysfunction such as fetal growth restriction.¹

In Indonesia, the prevalence of preeclampsia is 3.4-8.5%. Based on Riset Kesehatan Dasar 2019, there were more than a thousand pregnancies accompanied by preeclampsia each year.² The prevalence increased in the last decade and is expected to continue to grow as an increase of HDP risk factors such as metabolic syndrome and advanced maternal age.

Although PE is a transient phenomenon, there are both acute and long-term significant consequences to mothers caused by this condition.³ The American Heart Association formally recognized a history of preeclampsia as an independent risk factor for cardiovascular disease (CVD). These women have a twofold to eightfold higher risk to develop cardiovascular disease later in life compared to women with normotensive pregnancies, depending on specific characteristics of the pregnancy.⁴ Preterm preeclampsia (< 37 weeks), severe preeclampsia, and recurrent preeclampsia have a higher risk to develop CVD. Furthermore, women with preeclampsia in combination with fetal growth restriction showed a higher risk for later CVD.^{4,5}

PATHOPHYSIOLOGY

Although the exact underlying pathophysiology of this long-term CVD risk remains unknown, the current literature suggests three pathways. First is a pregnancy-induced CVD risk, second is a prepregnancy predisposition towards an increased risk of CVD, or third is a combination of both pathways.

Preeclampsia is associated with an anomaly of the placentation and abnormal remodeling of the uteroplacental spiral arteries. The invasion of the trophoblast is defective, especially in early-onset preeclampsia, affecting the endovascular invasion pathway. This will create an abnormal uteroplacental flow which is later associated with placental oxidative and endoplasmic reticulum stress, probably due to ischemia-reperfusion injury, which provokes the release of pro-inflammatory cytokines and imposes excessive inflammatory stress on the maternal circulation. This systemic inflammation may result from a variety of circulating factors, such as pro-inflammatory cytokines, pro- and anti-angiogenic proteins, placental growth factors, and activating auto-antibodies against

the AT1-receptor. The target of these factors is the maternal vascular endothelium, leading to endothelial dysfunction and hypertension.⁶ Within days or weeks of delivery following a preeclamptic pregnancy, blood pressure usually returns to normal, but some of it can take up to 3 months. Despite their recovery to normal blood pressure, many women with preeclampsia have evidence of subclinical endothelial dysfunction and remain at increased risk to become CVD later in life.

Preeclampsia and CVD share several common metabolic abnormalities as risk factors, such as obesity, lipid abnormalities, and insulin resistance. Patients who are obese before pregnancy is at greater risk for preeclampsia. Pregnant women with diabetes have a double risk for hypertension and/or preeclampsia compared to non-diabetic controls. The pattern of increased small dense low-density lipoprotein and triglycerides which are known as atherogenic material has been described in coronary heart disease and in women with preeclampsia. Acute atherosclerosis in the placental bed, which is found in preeclampsia, is caused by oxidized LDL taken up by macrophages to form foam cells that closely resemble the atherosclerotic plaques. Leptin, a marker of increased risk for CVD, has been shown to be elevated significantly in preeclamptic mothers. Thus, elevated levels of leptin are suggestive of resistance to its metabolic effect and promote platelet aggregation, contributing to the hypercoagulable state in preeclampsia.⁷

LONG-TERM CARDIOVASCULAR CONSEQUENCES

Chronic Hypertension

Increasing evidence shows that women with a history of preeclampsia are at increased risk of chronic hypertension later in life. Bellamy, et al performed a systematic review and meta-analysis of a total of 13 studies involving 21,030 women examined the risk of hypertension subsequent to preeclamptic pregnancy. Over a mean follow-up of 14.1 years, the authors found that women with preeclampsia have a 3.7 relative risk to develop hypertension later in life. Several studies also reviewed the severity of hypertension during pregnancy in relation to the risk of developing chronic hypertension after pregnancy. Behrens et al revealed that women with severe preeclampsia had a higher risk to develop chronic hypertension one year after pregnancy (HR 6.45, 95% CI 5.35 to 7.78) than women with moderate preeclampsia.^{4,7} Bokslag et al, assess cardiovascular risk factors in women with a history of early-onset preeclampsia (< 34 weeks gestation) in the fifth decade of life. Apparently, women with a history of early-onset preeclampsia had significantly greater systolic and diastolic blood pressure in their fifth decade of life compared to previously normotensive pregnancy.⁸ The risk of chronic hypertension also depend on the number of pregnancies affected with hypertension, where recurrent preeclampsia had a higher risk to develop chronic

hypertension after pregnancy (RR 2.3; 95% CI 1.9 to 2.9) compare with uncomplicated pregnancy.^{4,7}

Coronary artery disease

After preeclampsia but before the clinical onset of coronary heart disease, there may be evidence of subclinical pathology recognized as cardiovascular risk factors such as obesity, endothelial dysfunction, sympathetic overactivity, increased peripheral vascular resistance, insulin resistance, and hyperlipidemia. This is followed by often-asymptomatic conditions that include hypertension and diabetes which appear more likely to develop after a preeclamptic pregnancy. Eventually, this will lead to premature coronary artery disease and a reduced life expectancy. Several systematic reviews and meta-analyses have shown that women with preeclampsia were more than twice as likely to develop future ischemic heart disease compared with women who had a normotensive pregnancy.⁹

In one meta-analysis, preterm preeclampsia (< 37 weeks) was associated with a calculated relative risk (RR) of death from future ischemic heart disease (IHD), RR 7.71 (95% CI 4.40-13.52) compared with women who had a normotensive pregnancy. There is a graded association between the severity of preeclampsia with future risk of ischemic heart disease. Compared with women who had a normotensive pregnancy, women who had mild-preeclampsia have a RR of future IHD of 2.00 (95% CI 1.83-2.19), for women who had moderate preeclampsia RR 2.99 (95% CI 2.51-3.58) and for those who had severe preeclampsia RR 5.36 (95% CI 3.96-7.27).⁵

Heart Failure and Arrhythmia

A retrospective study by Ray et. al. followed 75,342 women with preeclampsia for a median duration of 7.8 years. The study showed that women with preeclampsia had a 61% increase in the relative risk of heart failure or atrial arrhythmia, but no significant increase in ventricular arrhythmias. The effect persisted even after adjusting for coronary heart disease, hypertension, and metabolic syndrome, proving that a history of preeclampsia is an early marker for cardiovascular risk.¹⁰

Thayaparan et. al., performed a systematic review to analyze the existing evidence of echocardiographic cardiac assessment of women with a history of preeclampsia performed between 6 months to 18 years after pregnancy. Abnormal left ventricular (LV) geometry was demonstrated in most studies with concentric remodeling as the predominant finding, even at 4-10 year follow up at prevalence 67% in the preeclampsia cohort as compared with 33% of controls. The left ventricular mass index (LVMI) and the thickness of the septal and posterior wall were also increased, associated with heart failure stage B (HF-B) and with subsequent development of hypertension. Prevalence of HF-B varied from 23% at 4 years post-partum to 70% in women with preterm preeclampsia at 1-year follow-up. All of these studies revealed a significant difference in asymptomatic heart failure or HF-B as compared with controls.¹¹ Most studies reported normal LV systolic function in women with previous preeclamptic pregnancy at different time points of follow up. One study by Melchiorre found persistent LV mild systolic dysfunction in 20% of women with preterm preeclampsia at 1-year follow-up. Another study by Orabona found some early evidence of systolic dysfunction using tissue Doppler imaging (TDI) and speckle tracking echocardiography (STE). Diastolic dysfunction was the predominant findings. Melchiorre reported prevalence of diastolic dysfunction was 52% at one-year follow-up in women with preterm preeclampsia. Diastolic dysfunction was seen to recover in women with term preeclampsia. Bokslag reported a lower prevalence of diastolic dysfunction (19.1%) in women with preterm preeclampsia in their fifth decade of life.¹¹ Persistence of right ventricular (RV) systolic and diastolic dysfunction was reported in women with preterm preeclampsia, but apparently, the dysfunction mostly resolve in term preeclampsia women. A study using STE showed a reduction in RV strain in women with preterm preeclampsia as compared with controls.¹¹

Valvular heart disease

Honigberg discovered an increased risk of premature valvular disease in the form of aortic stenosis and mitral regurgitation. After adjustment for race and age at enrollment, significant associations were observed between prior preeclampsia and incident of aortic stenosis (HR 2.9; 95% CI 1.5-5.4) and mitral regurgitation (HR 5.0; 95% CI 1.5-17.1). Recent studies showed that sFlt-1, a circulating antiangiogenic protein implicated in the pathogenesis of preeclampsia, was found to have a strong association with calcific aortic stenosis in the general population. Mendelian randomization analysis found that a genetically associated increase of systolic blood pressure was associated with an incident of aortic stenosis, aortic regurgitation, and mitral regurgitation, further supporting the plausibility of the association between preeclampsia and valvular heart disease.¹²

CLINICAL APPROACH TO FOLLOW UP

In general, women with hypertension during pregnancy have relatively more cardiovascular risk factors even after 1 year postpartum. Women with preeclampsia, especially preterm preeclampsia, severe preeclampsia have the most adverse cardiovascular risk phenotype. Women with a history of preeclampsia have a significantly higher incidence of future cardiovascular disease compared to normotensive pregnancy. This underlines that it is important to initiate cardiovascular screening soon after delivery to optimize cardiovascular prevention. Nevertheless, uniform recommendations regarding cardiovascular follow-up after preeclampsia are lacking. These follow-up recommendations could be provided by various healthcare professionals, including general practitioners, cardiologists, internists, or obstetricians.¹³ Advise on how and when cardiovascular screening assessment should be carried out and by which healthcare provider is currently confusing since it differs between guidelines. At present only half of the most commonly used guidelines advise cardiovascular assessment after delivery. Initially, all women with preeclampsia should be informed about their increased risk of future cardiovascular disease even after delivery. Healthcare providers should encourage and support a healthy diet and lifestyle such as maintaining a normal BMI, smoking cessation, and regular exercise. The European Society of Cardiology/European Society of Hypertension, The American College of Obstetricians and Gynecologists, and American Stroke Association guidelines advise cardiovascular follow-up 6-12 months postpartum. The American Heart Association guideline recommends postpartum referral by the obstetrician to a primary care physician or cardiologist to monitor and control cardiovascular risk factors, and consider statin therapy in women with a 10-year ASCVD risk of 5%-7.5%.⁵ Thereafter, some guidelines recommend annual follow-up of blood pressure and metabolic factors by primary care physician, whereas others recommend repeating every 5 years. If hypertension persists or is uncontrolled, use echocardiography, check renal function and check for retinopathy.¹⁴ At age 50 years old, all women will qualify for regular cardiovascular risk assessment as recommended by all major international cardiovascular prevention guidelines (figure 1). Besides obtaining a uniform approach, it also remains a challenge to motivate women to attend a cardiovascular prevention program.

CONCLUSION

It has been established that preeclampsia infers a long-term risk of cardiovascular disease, causing serious maternal hazards morbidity, and mortality. Regardless of its clinical significance, preeclampsia as a risk factor for cardiovascular disease in women is under-appreciated clinically, insufficiently researched, and not given adequate attention in overall CVD risk prediction. Current guidelines are diverging and postpartum recommendations for cardiovascular assessment remain vague and deficient. The postpartum approach involves

close monitoring of this high-risk group (especially preterm and severe preeclampsia), education and support for a healthier

lifestyle, novel echocardiography technologies, and the development of specialized assessment methods.

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