

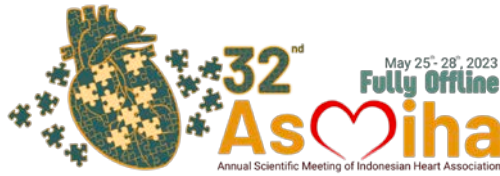


**Indonesian Journal of  
Cardiology**

Indonesian J Cardiol 2023;44:suppl\_A  
pISSN: 2830-3105 / eISSN: 2964-7304  
doi: 10.30701/ijc.1536



## **Abstract: Systematic Reviews and Meta-analysis**



## Left Atrial Strain as Predictor of Atrial Fibrillation Recurrence in Patients Undergoing Catheter Ablation: A Systematic Review and Meta-Analysis

R.A. Halim<sup>1</sup>, R. Mulawarman<sup>2</sup>, M.R. Felani<sup>1</sup>, M.S. Ramadhan<sup>2</sup>, M. Trifitriana<sup>2</sup>, H. Mulawarman<sup>2</sup>, A.E. Tondas<sup>3</sup>  
FKUI/RSJPD Harapan Kita<sup>1</sup>  
Sriwijaya University<sup>2</sup>  
Mohammad Hoesin General Hospital<sup>3</sup>

### Background and Aims:

Atrial fibrillation (AF) is a common cardiac arrhythmia that worsens patient quality of life, particularly as it contributes to increased risk of thromboembolic event and mortality. Catheter ablation (CA) is an effective rhythm restoring treatment in AF patient, but recurrence after CA is still a major problem, ranging as high as 25-30% of all cases. Recently, some studies suggested a relationship between left atrium (LA) strain, measured by two-dimensional speckle tracking echocardiography (2DSTE), and AF recurrence after CA. We aim to assess the latest evidence on the left atrial strain as a predictors of atrial fibrillation recurrence in patients after undergoing catheter ablation.

**Method:** We performed a comprehensive search on topics that assesses left atrial strain and atrial fibrillation recurrence from inception up until March 2023.

**Results:** There were a total of 991 patients from 8 studies. The pooled analysis showed that left atrial strain was lower in AF recurrence group (mean difference -6.36 [-7.73, -4.99],  $p = 0.0001$ ;  $I^2: 61\%$ ,  $p=0.01$ ). It also showed that the hazard ratio was (0.94 [0.88,1.00]  $p = 0.03$ ;  $I^2: 84\%$ ,  $p<0.0001$ ).

**Conclusion:** Left atrial strain is associated as predictors of atrial fibrillation recurrence in patients undergoing catheter ablation. These findings suggest that LA strain may have important implications for the selection of patients with AF undergoing catheter ablation. It implies the added value of LA strain measurement, and should be implemented as part of systemic evaluation of AF patients before CA. Further research is needed to explore the optimal cut-off values of LA strain for predicting AF recurrence and to validate the predictive value of LA strain in larger, multicenter studies.

**Keywords:** left atrial strain, predictors, atrial fibrillation recurrence, catheter ablation

**Clinical Outcomes of Coronary Intravascular Lithotripsy Versus Rotational Atherectomy in Severe Calcified Coronary Lesions: A Systematic Review and Meta-Analysis**

K.A.A.P. Pramana<sup>1</sup>, Y. Pintaningrum<sup>2</sup>

Cardiology and Vascular Department, Faculty of Medicine, Universitas Mataram, West Nusa Tenggara General Hospital, Mataram, Indonesia<sup>1</sup>

Interventional Cardiology Division, Cardiology and Vascular Department, Faculty of Medicine, Universitas Mataram, West Nusa Tenggara General Hospital, Mataram, Indonesia<sup>2</sup>

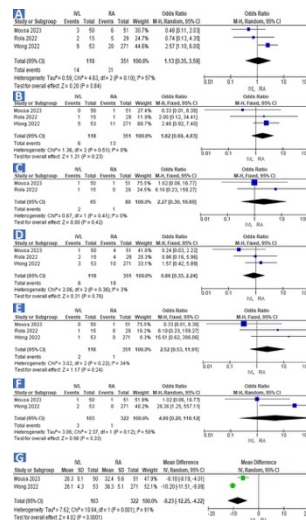
**Background:** Severe coronary artery calcification is linked with poor clinical outcomes in patients undergoing percutaneous coronary intervention (PCI). Adequate preparation plays an important role in achieving a good PCI outcomes. Rotational atherectomy (RA) and intravascular lithotripsy (IVL) are techniques used to optimize lesion preparation and facilitate stent implantation in this condition. However, their comparative clinical outcomes remain debatable. The aim of this study is to compare the clinical outcomes of coronary IVL versus RA in severe calcified coronary lesions.

**Methods:** Electronic journals searching were performed in PubMed, ScienceDirect, and Cochrane from January 2020 to March 2023 to identify studies assessing the clinical outcome of coronary intravascular lithotripsy and rotational atherectomy in calcified coronary lesions. Our outcome of interest were major adverse cardiovascular events (MACE), myocardial infarction (MI), target vascular revascularization (TVR), all cause mortality, stent thrombosis, stroke, and fluoroscopy time. Meta-analyses were performed on included studies. Odds ratio (OD), Mean Differences (MD) and 95% Confidence Interval (CI) were estimated using Review Manager v5.4.

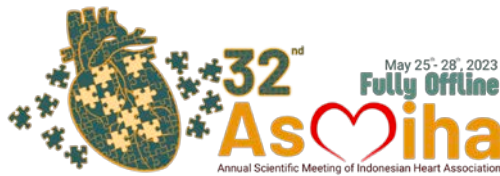
**Results:** A total of three studies were included in our analysis. After follow-up over a median of 4 months, there is no significant difference on MACE, MI, TVR, all cause mortality, stent thrombosis and stroke between IVL versus RA in severe calcified coronary lesions. IVL procedure significantly had shorter fluoroscopy time by 8.23 minutes ( $P < 0.0001$ ; MD -8.23; 95%CI -12.25 - -4.22) compared with RA procedure.

**Conclusion:** In general, this meta-analysis shows there is no significance difference on outcome in both IVL and RA for treatment of severe calcified coronary lesions. IVL has a shorter fluoroscopy time compared with RA.

**Keywords:** Intravascular lithotripsy, atherectomy, calcified lesion, coronary artery



Forest plots analysis of (A) MACE, (B) MI, (C) TVR, (D) all cause mortality, (E) stent thrombosis, (F) stroke, and (G) fluoroscopy time following IVL versus RA.



### Outcomes of Optical Coherence Tomography Compared with Intravascular Ultrasound to Guide Percutaneous Coronary Intervention: A Systematic Review And Meta-Analysis of Randomized Control Trials

K.A.A.P. Pramana<sup>1</sup>, Y. Pintaningrum<sup>2</sup>

Cardiology and Vascular Department, Faculty of Medicine, Universitas Mataram, West Nusa Tenggara General Hospital, Mataram, Indonesia<sup>1</sup>

Interventional Cardiology Division, Cardiology and Vascular Department, Faculty of Medicine, Universitas Mataram, West Nusa Tenggara General Hospital, Mataram, Indonesia<sup>2</sup>

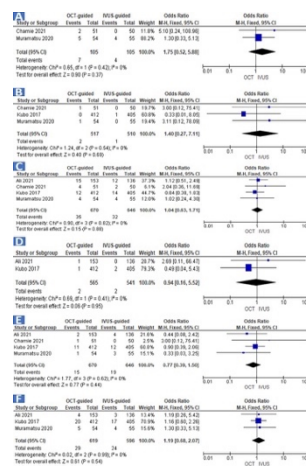
**Background and aim:** Angiography-guided percutaneous coronary intervention (PCI) has been the main stay in the treatment of culprit lesions in coronary artery disease. Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) are the alternative intravascular imaging modality and most commonly used to guide and optimize PCI in the recent. However, the comparative outcomes of IVUS-guided versus OCT-guided PCI remains debatable. The aim of this study is to compare the clinical outcomes between OCT and IVUS to guide PCI.

**Methods:** Electronic journals searching were performed in PubMed, ScienceDirect, and Cochrane from January 2015 to March 2023 to identify randomized control trial (RCT) studies that compare OCT-guided PCI to IVUS-guided PCI. The primary outcome were all cause mortality, cardiovascular mortality, major adverse cardiovascular events (MACE), stent thrombosis (ST), target lesion revascularization (TLR), and target vascular revascularization (TVR). Meta-analyses were performed on included studies and Odds ratio (OR) and 95% Confidence Interval (CI) were estimated using Review Manager v5.4.

**Results:** A total of four RCT enrolling 1316 participants were included in our analysis. There is no statistical significance was observed in the OCT versus IVUS comparison on all cause mortality [OR = 1.75, 95% CI (0.52, 5.88), p = 0.37], cardiovascular mortality [OR = 1.40, 95% CI (0.27, 7.11), p = 0.69], MACE [OR = 1.04, 95% CI (0.63, 1.71), p = 0.88], ST [OR = 0.94, 95% CI (0.16, 5.52), p = 0.95], TLR [OR = 0.77, 95% CI (0.39, 1.50), p = 0.44], and TVR [OR = 1.19, 95% CI (0.68, 2.07), p = 0.54].

**Conclusions:** In general, this meta-analysis shows there was no statistically significant difference in clinical outcomes observed in the comparison between OCT and IVUS-guided PCI.

**Keywords:** Optical coherence tomography, Percutaneous coronary intervention, Intravascular ultrasound.



Forest plot analysis comparing (A) all cause mortality, (B) cardiovascular mortality, (C) MACE, (D) Stent Thrombosis, (E) TLR, and (F) TVR following OCT-guided versus IVUS-guided PCI

## Determinant factors of Left Ventricular Hypertrophy Regression in Hypertensive Patients : A Systematic Review and Meta- Analysis

W. Huang<sup>1</sup>, A.R. Putri<sup>1</sup>

<sup>1</sup>Medical Doctor Profession Education, Faculty of Medicine, University of Padjadjaran, Bandung, Indonesia

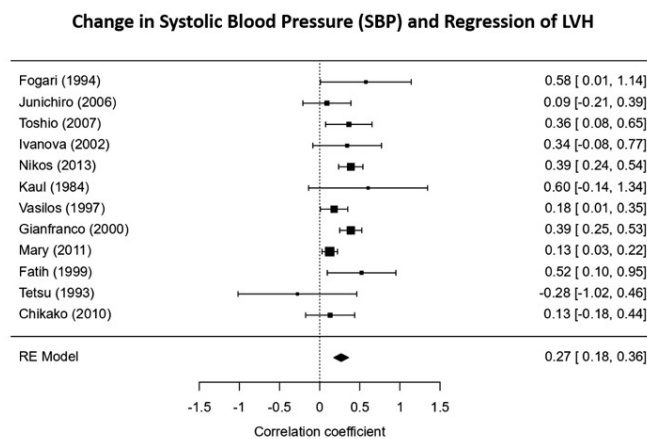
**Background:** Regression of left ventricular hypertrophy (LVH) caused by hypertension is associated with morbidity and mortality reduction and antihypertensive drugs use is crucial for treatment. Besides the choice of drugs selected, other factors to determine LVH regression are unknown. Hence, this review aims to determine factors of LVH regression in hypertensive patients.

**Methods:** A systematic review is conducted from PubMed database using PRISMA guideline until January 2023. Adults with essential hypertension treated with antihypertensive drugs are included and factors analyzed are change in systolic, diastolic blood pressure, and pulse pressure (SBP, DBP, PP), and baseline LVMI. Risk of biases are assessed accordingly and 95% confidence interval (CI) pooled correlation coefficient (PCOR) by meta-analysis with Fisher's Z transformation between associated factors and LVH regression is computed. Heterogeneity is overcome by sensitivity analysis and publication bias by funnel plots and Egger's test.

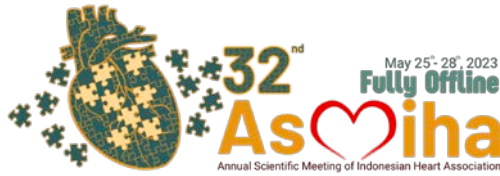
**Results:** 2807 articles are initially identified and 20 articles (18 trials, 5 observational) with no significant potential risk of biases comprising of 3715 patients are included in the analysis. Change in SBP during treatment resulted in PCOR 0.29 (95% CI: 0.20 – 0.38,  $p < 0.001$ ) with  $I^2 = 74.44\%$ . Change in DBP resulted in PCOR 0.32 (95% CI: 0.27 – 0.38,  $p < 0.001$ ), change in PP 0.34 (95% CI: 0.28 – 0.40,  $p < 0.001$ ), and baseline LVMI value 0.50 (95% CI: 0.45 – 0.55,  $p < 0.001$ ) with all 3 factors not having significant heterogeneity. Sensitivity analysis of change in SBP done by excluding observational studies resulted in PCOR of 0.27 (95% CI: 0.18 – 0.36,  $p < 0.001$ ) with  $I^2 = 41.03\%$ . Funnel plot is symmetrical and Egger's test is not significant in all associated factors.

**Conclusion:** Change of SBP, DBP, PP during treatment, and baseline LVMI value are positively correlated with regression of LVH in hypertensive patients.

**Keywords:** left ventricular hypertrophy, regression, hypertension



**Figure 1.** PCOR of change in SBP and regression of LVH after sensitivity analysis by excluding observational studies



## Comparison Between Biventricular Pacing Versus His Bundle Pacing in non-Ischemic Cardiomyopathy with Left Bundle Branch Block : A Systematic Review

R. Sutanto<sup>1</sup>, J.V. Lee<sup>1</sup>, A. Zebua<sup>1</sup>, F. Nathania<sup>1</sup>, K.Y. Rubismo<sup>1</sup>, N.M. Wijaya<sup>1</sup>, M.Z. Sabran<sup>1</sup>, C.F. Jhoputri<sup>1</sup>, J. Aurelia<sup>1</sup>, J.B. Lee<sup>2</sup>

Faculty of Medicine, University of Pelita Harapan<sup>1</sup>  
Faculty of Medicine, Atma Jaya Catholic University of Indonesia<sup>2</sup>

### Background

Cardiac Resynchronization Therapy (CRT) is indicated in heart failure patients with decreased Left Ventricular Ejection Fraction (LVEF) and Left Bundle Branch Block (LBBB) with LV dyssynchrony. His bundle pacing (HBP) is an alternative to biventricular pacing (BVP) for CRT. The study aims to compare the outcome of biventricular pacing versus his bundle pacing in non-ischemic cardiomyopathy patients with LBBB.

### Method

This review was systematically reviewed with Two independent researchers that had extracted data from several databases, such as PubMed Central (PMC), Science Direct, Europe PMC, and PUBMED. We used the following keywords “his bundle pacing”, “biventricular pacing”, “heart failure” and “left bundle branch block”. The extracted studies were then analyzed and extracted accordingly to our inclusion criteria such as studies from the last 5 years, cohort studies, and non-ischemic cardiomyopathy patients with left bundle branch block. We then excluded systematic reviews, meta-analyses, case series, case reports, studies on pregnant women, children. All eligible studies were assessed using New-Castle Ottawa Scale (NOS).

### Result

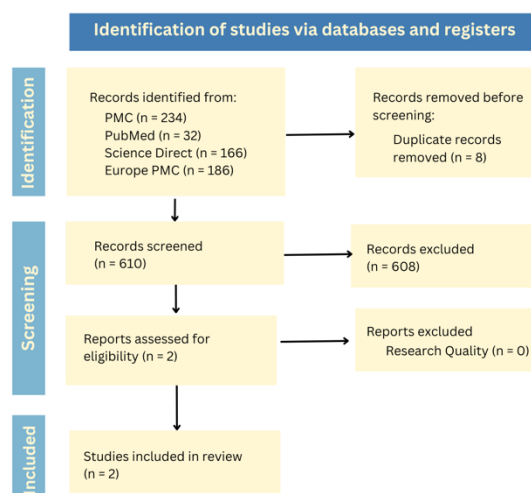
We found 2 cohort studies with a total of 240 subjects comparing biventricular and his bundle pacing in non-ischemic cardiomyopathy patients. Both studies showed His bundle pacing significantly increased LVEF compared to BVP. In one of the studies, it is shown that there is a significant improvement in symptoms by NYHA class. All studies have proven good quality based on NOS.

### Conclusion

In conclusion, his bundle pacing showed a greater improvement in outcome as an alternative CRT method if compared to biventricular pacing in non-ischemic cardiomyopathy patients with LBBB. However, further studies are required to confirm these findings.

**Keywords** his bundle pacing; biventricular pacing; heart failure; left bundle branch block

**Keywords:** his bundle pacing, biventricular pacing, heart failure, left bundle branch block





## The association of high temperature on the cardiovascular mortality in Asia : Systematic Review

R. Sutanto<sup>1</sup>, M.Z. Sabran<sup>1</sup>, M. Sutanto<sup>1</sup>, W.S. Atmaja<sup>1</sup>, J.V. Lee<sup>1</sup>  
Faculty of Medicine, University of Pelita Harapan<sup>1</sup>

### Background

Climate change has made heatwaves a more frequently occurring incident worldwide. Accordingly, rise in temperature has increasingly becoming a concern for its effects and consequences towards the health of the human's life. However the association of increasingly high temperature combined with cardiovascular as the leading cause of death globally is still not well known. This study aims to evaluate the association between exposure of high temperature and cardiovascular mortality in Asia.

### Method

This study was conducted on 9- 15 March 2023. Five researchers systematically extracted data of several studies from PUBMED by using MesH terminology of keywords temperature and cardiovascular mortality. The data derived were evaluated and selected to our inclusion criteria such as studies that were published in the last 5 years, cohort studies and case-control studies. We excluded systematic reviews and meta-analysis, case reports, case studies and studies that were conducted outside Asia. Research quality was then assessed using Newcastle-Ottawa (NOS).

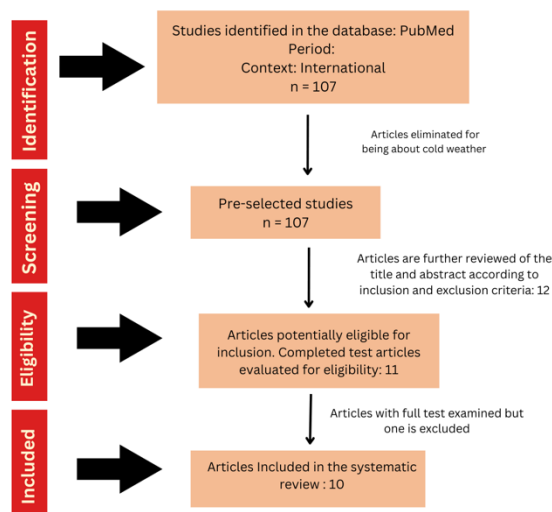
### Result

After screening 107 studies, we extracted data from 10 retrospective cohort studies. The studies included 3.178.906 subjects in total from various countries in Asia. All of the studies showed a positive association between High temperature and cardiovascular mortality. Where in countries with high temperature measured, there is a higher risk of cardiovascular mortality occurrence compared to days without high temperature measured. 10 studies have proven good quality based on NOS.

### Conclusion

In conclusion, our study finds that an increase in daily temperature could also increase risk of cardiovascular mortality. This showed exposure to high temperature is associated with increase in cardiovascular mortality. Therefore, we hope that this could raise awareness towards the climate change that is actively contributing to the raising temperatures globally. However, further study is still needed to confirm these findings.

**Keywords:** High temperature, Cardiovascular mortality





## The age group that is most susceptible to cardiovascular mortality in climate change in Asia : Systematic Review

R. Sutanto<sup>1</sup>, M.Z. Sabran<sup>1</sup>, M. Sutanto<sup>1</sup>, W.S. Atmaja<sup>1</sup>, J.V. Lee<sup>1</sup>  
Faculty of Medicine, University of Pelita Harapan<sup>1</sup>

### Background

Climate change has made heatwaves a more frequently occurring incident worldwide. Accordingly, rise in temperature has increasingly becoming a concern for its effects and consequences towards the health of the human's life. However, the association of increasingly high temperature combined with cardiovascular as the leading cause of death globally is still not well known. This study aims to evaluate the age group that is most susceptible to cardiovascular mortality during high temperatures in Asia.

### Method

This study was conducted on 9-15 March 2023. Five researchers systematically extracted data from several studies from PUBMED by using MesH terminology of keywords temperature and cardiovascular mortality. The data derived were then evaluated and selected in accordance to our inclusion criteria such as studies that were published in the last 5 years, cohort studies and case-control studies. We excluded systematic reviews and meta-analysis, case reports, and studies that were conducted outside Asia. Research quality was then assessed using Newcastle-Ottawa (NOS).

### Result

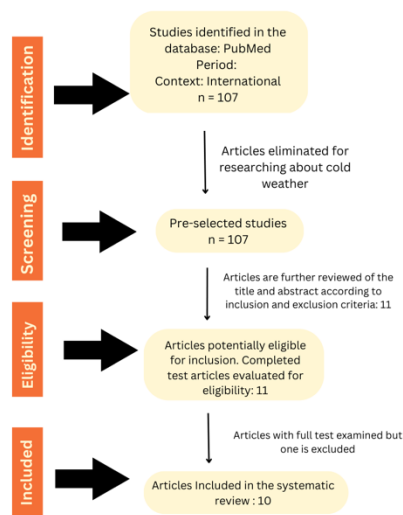
From 10 retrospective cohort studies with 3.178.906 subjects in total from various countries in Asia, Some studies showed results of elderly subjects with age above 65 years old are more susceptible to cardiovascular mortality in high temperature surroundings compared to the age group younger than 65.. 10 studies have proven good quality based on NOS

### Conclusion

In conclusion, elderly, especially those who belong in the age group above 65 years old, are more susceptible to cardiovascular mortality in a high temperature environment. This could raise awareness towards elderly groups with cardiovascular related health problems in this time where climate change is constantly contributing to rise in temperature. However, further study is needed to confirm these findings.

**Keywords** “High Temperature” AND “Cardiovascular mortality”

**Keywords:** high temperature, cardiovascular mortality



## Overall Outcomes Between Ticagrelor and Aspirin Versus Aspirin Alone in Patient with Acute Ischemic Stroke : Systematic Review

M.Z. Sabran<sup>1</sup>, A. Zebua<sup>1</sup>, J.A. Harjanto<sup>1</sup>, F. Nathania<sup>1</sup>  
Universitas Pelita Harapan<sup>1</sup>

### Background

Stroke is a condition of damage to brain cells due to decreased blood supply to the brain. Stroke is the second most common cause of death worldwide. Sixty-eight percent of them are acute ischemic stroke. Currently, aspirin is the standard treatment for patients with acute ischemic stroke. However, the combination treatment of ticagrelor and aspirin still remains unclear. This systematic review aims to compare the best results between dual antiplatelet therapy with aspirin alone.

### Method

Extracted studies were retrieved from the Pubmed database using MeSH terminology such as "ticagrelor" AND "aspirin" AND "acute" AND "ischemic" AND "stroke". The extracted studies were taken from the last 5 years and were selected using several inclusion criteria such as randomized-controlled trials and clinical trials. Exclusion criteria in this study were patient under 18 years old, patient with comorbids, non-randomized controlled trials, and animal studies. The Newcastle-Ottawa Scale (NOS) was used in assessing the included study.

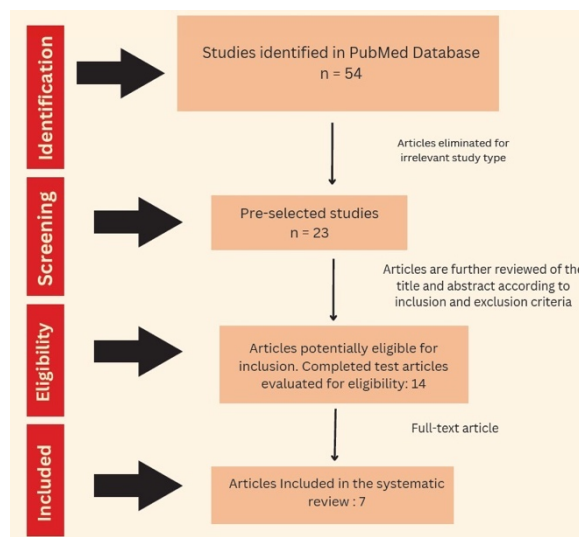
### Result

Seven studies were included out of 23 eligible studies which contained 44643 patients with acute ischemic stroke above 18 years old. From the seven studies included, six of them were randomized-controlled trials and the other one was a clinical trial. All of the studies included have decent quality and shows that combination treatment between ticagrelor and aspirin has a better overall outcome than aspirin alone in patient with acute ischemic stroke, such as safety, efficacy, toxicity, hemorrhagic condition and ischemic event.

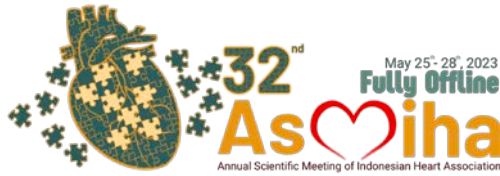
### Conclusion

In conclusion, antiplatelet dual therapy treatment using ticagrelor and aspirin show a superior outcomes and benefits than using aspirin alone in patients with acute ischemic stroke.

**Keywords:** ticagrelor, aspirin, acute ischemic stroke



PRISMA Chart



## Effectiveness Of Sacubitril-Valsartan in The Prevention of Atrial Fibrillation Incidence in Patients With Heart Failure : A Systematic Review

F.S.M. Pratistha<sup>1</sup>, I.W.S. Ardiana<sup>1</sup>

1.Faculty Of Medicine, Udayana University, Denpasar, Bali, Indonesia

**Background and aims:** Heart failure is a strong risk factor for atrial fibrillation. Sacubitril-valsartan is currently recommended for the treatment of heart failure. The purpose of this study was to systematically review the effectiveness of using sacubitril-valsartan in heart failure patient with kidney failure as comorbid disease to prevent atrial fibrillation related to published articles.

**Methods:** This study is a systematic review study. The research was conducted using the PRISMA method. Article searches were carried out by online publications through PubMed, Google Scholar, and Science Direct that met the inclusion and exclusion criteria. The population is an article about the use of sacubitril-valsartan in patients with kidney failure to prevent atrial fibrillation. A search was performed using the keywords "sacubitril", "valsartan", "LCZ696", "heart failure", and "atrial fibrillation". The methodological assesment was carried out using the Newcastle Ottawa Scale. There were no restrictions regarding the publication date or publication status. The results presented were the prevalence of atrial fibrillation after treatment.

**Results:** These results were obtained from 9 articles published from 2005 to 2023 with the result that the use of sacubitril-valsartan can prevent the occurrence of atrial fibrillation in patients with kidney failure with an effectiveness of 52.10-100% during a follow-up of 3 to 35 months. The effectiveness of sacubitril-valsartan in reducing the occurrence of atrial fibrillation is higher than valsartan. It is possible to prevent paroxysmal atrial fibrillation more effectively using valsartan than sacubitril-valsartan, but further supporting evidence is needed.

**Conclusion:** The combination of sacubitril and valsartan provides a synergistic effect that can effectively prevent atrial fibrillation in heart failure patients.

**Keywords:** Atrial Fibrillation, Heart Failure, Sacubitril-Valsartan, LCZ696, Systematic Review

## The Value of R Wave Amplitude in Lead V1 as Outcome Predictor in Pulmonary Arterial Hypertension: A Systematic Review

M.Z. Sabran<sup>1</sup>, A. Zebua<sup>1</sup>, F. Nathania<sup>1</sup>, J.V. Lee<sup>1</sup>, N.M. Wijaya<sup>1</sup>, K.Y. Rubismo<sup>1</sup>, C.F. Jhoputri<sup>1</sup>, J.A. Harjanto<sup>1</sup>, J.B. Lee<sup>2</sup>

Universitas Pelita Harapan<sup>1</sup>  
Atma Jaya Catholic University<sup>2</sup>

### Background

Prognosis stratification of Pulmonary Artery Hypertension (PAH) requires extensive assessment and investigation. The result of the assessment will categorized patients starting from low to high risk and subsequently will guide the management strategy. The aim of this study is to find out whether R Wave Amplitude in lead V1 could predict the prognosis of PAH patients.

### Method

This review was systematically reviewed. Two independent researchers extracted data from several databases, such as PubMed Central (PMC), Science Direct, Europe PMC, and PUBMED by using the following keywords “r wave amplitude”, “pulmonary arterial hypertension”, and “prognosis”. The extracted studies were then analyzed and extracted according to our inclusion criteria such as cohort studies, case-control studies within the last 10 years, and patients with PAH. We excluded systematic reviews, meta-analyses, case series, case reports, studies on pregnant women, children. All eligible studies were assessed using New-Castle Ottawa Scale (NOS).

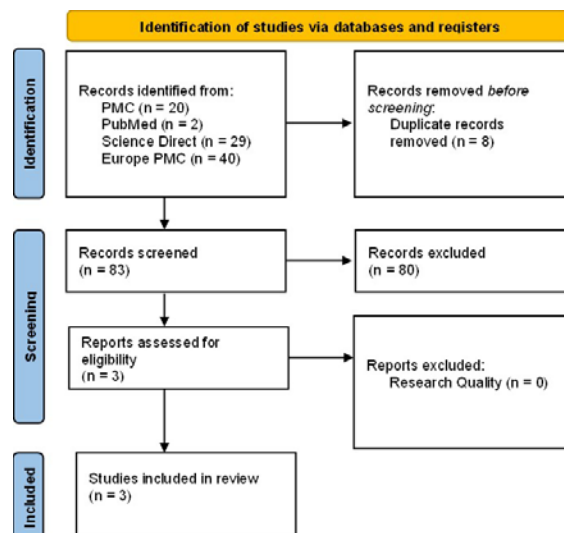
### Result

From 3 eligible cohort studies (415 subjects), all of them showed the R wave in V1 could determine the survival in patients with PAH. The lower the amplitude of the R wave results in better survival. Otherwise, one of the studies showed the increase of R wave amplitude became a significant mortality predictor. We used NOS to evaluate the quality of the studies and all studies showed to be in good quality.

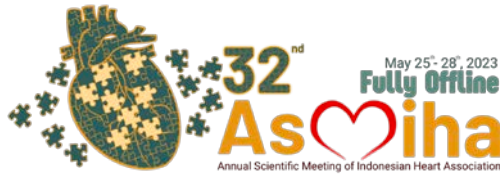
### Conclusion

In conclusion, the R wave amplitude in lead V1 is able to predict the prognosis of PAH patients. In this case, the prediction of population survival. However further studies were required to confirm these findings.

### Keywords:



PRISMA Chart for This Study



## Comparing $\geq 12$ -Months Versus Shorter Dual Antiplatelet Therapy in Patients After Percutaneous Coronary Intervention, Who's Better? : A Systematic Review

J.V. Lee<sup>1</sup>, A. Sihombing<sup>1</sup>, D.R.T. Subroto<sup>1</sup>, M. Sutanto<sup>1</sup>, R. Sutanto<sup>1</sup>, J.B. Lee<sup>2</sup>  
Faculty of Medicine, University of Pelita Harapan<sup>1</sup>  
Faculty of Medicine, Atma Jaya Catholic University of Indonesia<sup>2</sup>

### Background

Dual antiplatelet therapy (DAPT) is recommended to prevent thrombotic events after percutaneous coronary intervention (PCI). However, giving DAPT also increases the risk of bleeding. The purpose of this study was to find out the outcome of  $< 12$  months compared with  $\geq 12$  months DAPT in patients after PCI.

### Method

This review was conducted on 1-8 October 2022. Two independent researchers systematically extracted data from several databases, such as PubMed Central (PMC), Science Direct, and PUBMED by using MeSH terminology of keywords dual antiplatelet therapy, percutaneous coronary intervention, duration, and outcome. The extracted studies were then analyzed and selected according to our inclusion criteria such as studies in the last 5 years, cohort studies, case-control studies, and coronary artery disease patients. We excluded systematic reviews, meta-analyses, case series, case reports, studies on pregnant women, children, animals, coagulopathy, and COVID-19 patients. Research quality was assessed using Newcastle-Ottawa (NOS).

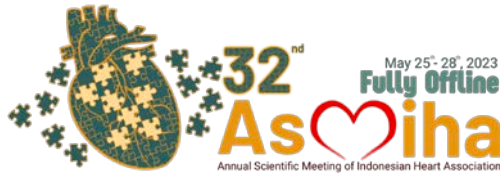
### Result

From 7 cohort studies (20.484 subjects from various countries), all of them showed  $\geq 12$  months DAPT had significant risk reduction of ischemic events and adverse cardiovascular events. Six of them showed there is no significant increase of bleeding risk; All studies have proven good quality based on NOS.

### Conclusion

In Conclusion,  $\geq 12$  months DAPT were giving more clinical benefit than  $< 12$  month DAPT in patients after PCI. However, further study is needed to confirm these findings.

**Keywords:** dual antiplatelet therapy, percutaneous coronary intervention, duration, outcome



## Electrocardiographic Features Correlated with Mean Pulmonary Arterial Pressure in Pulmonary Arterial Hypertension, How Many?: A Systematic Review

J.V. Lee<sup>1</sup>, A. Zebua<sup>1</sup>, F. Nathania<sup>1</sup>, K.Y. Rubismo<sup>1</sup>, N.M. Wijaya<sup>1</sup>, M.Z. Sabran<sup>1</sup>, C.F. Jhoputri<sup>1</sup>, J.A. Harjanto<sup>1</sup>, J.B. Lee<sup>2</sup>

Faculty of Medicine, University of Pelita Harapan<sup>1</sup>  
Faculty of Medicine, Atma Jaya Catholic University of Indonesia<sup>2</sup>

### Background

Pulmonary Hypertension (PH) were diagnosed if the mean Pulmonary Arterial Pressure (mPAP)  $\geq 25$ mmHg. However, study correlates mPAP with the electrocardiographic features in pulmonary arterial hypertension (PAH) still limited. The aim of this study is to find out what electrocardiographic features correlated with mPAP in the PAH population.

### Method

Two independent researchers systematically extracted data from several databases, such as PubMed Central (PMC), Science Direct, Europe PMC, and PUBMED by using the following keywords “r wave amplitude”, “pulmonary arterial hypertension”, and “prognosis”. The extracted studies were then analyzed and extracted according to our inclusion criteria such as cohort studies, case-control studies within the last 10 years, and patients with PAH. We excluded systematic reviews, meta-analyses, case series, case reports, studies on pregnant women, children. All eligible studies were assessed using New-Castle Ottawa Scale (NOS).

### Result

From 3 eligible cohort studies (273 subjects), we found several electrocardiographic features correlated with mPAP. Michalski et al showed the R wave in lead aVR ( $r = 0.446$ ,  $p = 0.033$ ) and RV Sokolow Lyon Index ( $r = 0.62$ ,  $p = 0.0016$ ) correlated with mPAP. Study by Cheng et al showed P wave amplitude in lead II ( $r = 0.349$ ,  $p \leq 0.001$ ), R wave amplitude in lead V1 ( $r = 0.359$ ,  $p \leq 0.001$ ), S wave amplitude in lead V6 ( $r = 0.259$ ,  $p = 0.030$ ) correlated with mPAP. Igata et al showed RV1+SV5/6 amplitude correlated with mPAP ( $R^2 = 0.282$ ). We used NOS to evaluate the quality of the studies and all studies showed to be in good quality.

### Conclusion

In conclusion, there were many electrocardiographic features found correlated with mPAP in PAH. The majority of them were the features of right ventricular hypertrophy and reflecting right ventricular overload hemodynamics. However further studies were required to confirm these findings.

**Keywords:** r wave amplitude, pulmonary arterial hypertension, prognosis

## Early Administration of Sacubitril/Valsartan versus Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blocker After Acute Myocardial Infarction: An Updated Meta-Analysis of Randomized Clinical Trials

M.E. Ananta<sup>1</sup>, I. Ivan<sup>2</sup>, A.D. Wijaya<sup>1</sup>, C.F. Albab<sup>3</sup>, S.S. Danny<sup>4</sup>

Faculty of Medicine, Alumnus of Universitas Indonesia, Jakarta, Indonesia<sup>1</sup>

Faculty of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia<sup>2</sup>

Faculty of Medicine, Alumnus of Universitas Airlangga, Surabaya, Indonesia<sup>3</sup>

Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Indonesia, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia<sup>4</sup>

**Background and Aims:** A recently published large RCT (PARADISE-MI) failed to show any individual cardiovascular outcome benefit in Acute Myocardial Infarction (AMI) patients with reduced ejection fraction who received sacubitril/valsartan instead of ramipril. We aimed to compare the impact of sacubitril/valsartan and ACEI/ARB early administration on cardiovascular outcomes of AMI patients irrespective of LVEF level.

**Methods:** Systematic search through Pubmed, Embase, and Cochrane Library was conducted in 17<sup>th</sup> March 2023 using keywords “AMI” AND “ARNI” AND (“ACEI” OR “ARB”) AND “prognosis” and their variations. We included RCTs recruiting hospitalized AMI patients, who were given ARNI starting from index hospital stay. The comparison is any ACEI/ARB regimen. The primary outcome was Major Adverse Cardiovascular Events (MACE). Pairwise meta-analysis was conducted to pool Risk Ratios (RRs) with corresponding 95%CI. Risk of bias (RoB) assessment was conducted using RoB-2 tool.

**Results:** Nine RCTs consisting of 3375 treatments and 3325 controls were included. Meta-analyses found ARNI was significantly associated with lower incidence of Hospitalizations due to Heart failure/HHF (RR 0.77; 0.65–0.91; I<sup>2</sup>=37%) and MACEs (RR 0.82; 0.73–0.92; I<sup>2</sup>=44%). In subgroup analyses, sacubitril/valsartan decrease MACEs significantly better in studies not limiting LVEF (RR 0.59; 0.47–0.75; I<sup>2</sup>=0%), conducted in STEMI patients (RR 0.60; 0.48–0.76; I<sup>2</sup>=0%), and follow-up of 6 months (RR 0.59; 0.47–0.75; I<sup>2</sup>=0%). However, symptomatic hypotension was more frequent with ARNI (RR 1.30; 1.19–1.42; I<sup>2</sup>=0%). Meta-regression showed studies with higher proportion of DM (p = 0.0089) or higher proportion of HT (p = 0.006), and longer follow-up duration (p = 0.0021) derived less benefits from ARNI in MACE and HHF reduction.

**Conclusion:** Sacubitril/valsartan should be prioritized over ACEI/ARB in AMI patients as it decreases incident MACE and HHF. Also, ARNI maybe considered to be used in AMI patients without LVSD.

**Keywords:** AMI, ARNI, ACEI, ARB, MACE

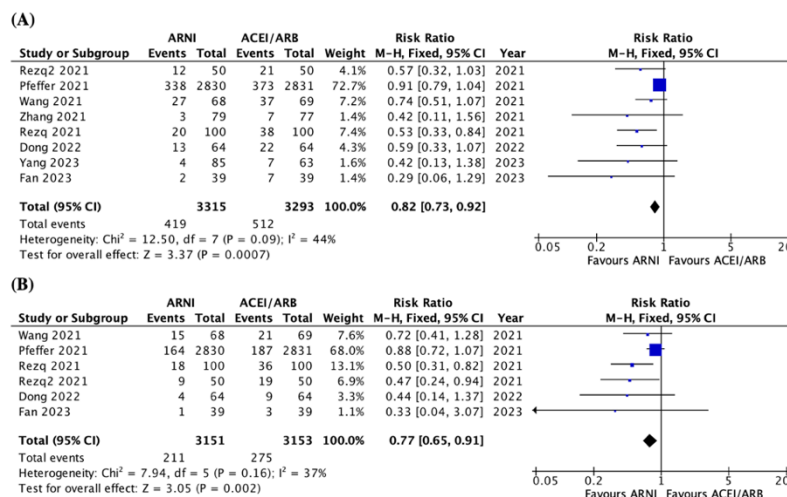
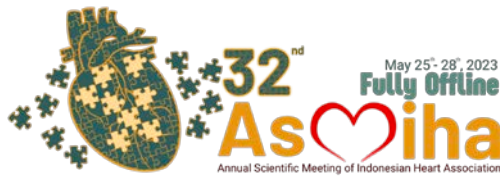


Figure 1. Forest Plot of (A) Meta-analysis of of ARNI vs ACEI/ARB in incidence of MACEs and (B) Meta-analysis of ARNI vs ACEI/ARB and incidence of HHF.



## Predictive Value of PRECISE-DAPT Score on Post-Myocardial Infarction Mortality: A Systematic Review

A. Zebua<sup>1</sup>, J.V. Lee<sup>1</sup>, F. Nathania<sup>1</sup>, K.Y. Rubismo<sup>1</sup>, N.M. Wijaya<sup>1</sup>, M.Z. Sabran<sup>1</sup>, C.F. Jhoputri<sup>2</sup>, J.A. Harjanto<sup>1</sup>, J.B. Lee<sup>2</sup>

Faculty of Medicine, University of Pelita Harapan<sup>1</sup>  
Faculty of Medicine, Atma Jaya Catholic University<sup>2</sup>

### Background

PRECISE-DAPT score were tools to guide the decision of Dual Antiplatelet Therapy (DAPT) duration in balancing between bleeding risk and ischemic prevention. However, there were still limited studies examining the predictive value of PRECISE-DAPT score in post-MI patients. This study wants to know if PRECISE-DAPT score could predict mortality in post-MI patients.

### Method

This review was systematically reviewed. Two independent researchers extracted data from several databases, such as PubMed Central (PMC), Science Direct, Europe PMC, and PUBMED by using the following keywords “precise dapt score” and “prognosis”. The extracted studies were then analyzed and extracted according to our inclusion criteria such as cohort studies, case-control studies within the last 5 years, and post-MI patients. We excluded systematic reviews, meta-analyses, case series, case reports, studies on pregnant women, children. All eligible studies were assessed using New-Castle Ottawa Scale (NOS).

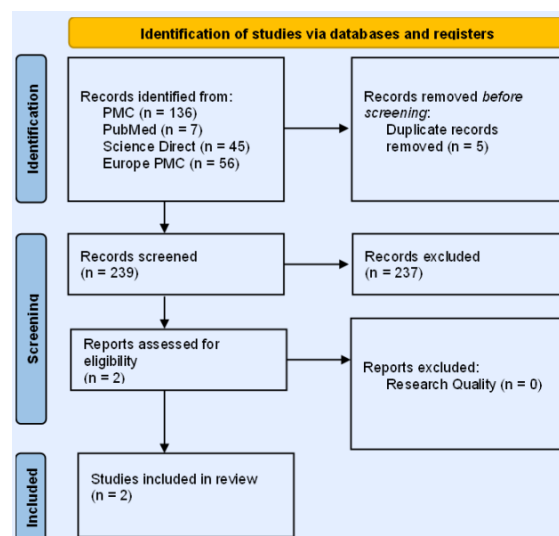
### Result

We found 2 cohort studies (895 patients) that showed PRECISE-DAPT scores were an independent predictor in predicting all-cause mortality of post-MI patients. The analysis in these two studies showed the higher score of PRECISE-DAPT was associated with higher mortality ( $p=0.02$ ;  $p<0.001$ ). We used NOS to evaluate the quality of the studies and all studies showed to be in good quality.

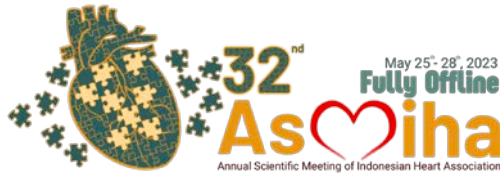
### Conclusion

Besides their function as bleeding risk predictor, PRECISE-DAPT score had a value on predicting mortality in post-MI patients. However further studies were required to confirm these findings.

**Keywords:** precise dapt score; prognosis



## Effects of Empagliflozin SGLT2i in Patient with Heart Failure and Reduced Ejection Fraction: A Systematic Review



C.A. Sutedja<sup>1</sup>, C.E.O.L. Hutauruk<sup>1</sup>, E. Budiarti<sup>1</sup>, Christian<sup>1</sup>, M.Z. Sabran<sup>1</sup>  
Universitas Pelita Harapan<sup>1</sup>

### Background and Aims

Heart failure have a relatively high rate of hospitalization along with increased mortality and morbidity. Previously, SGLT2i is an agent for managing adults patients with type 2 diabetes mellitus (DM) but nowadays SGLT2i often used as an agent for managing heart failure. Empagliflozin is the example of SGLT2i. However the effect of empagliflozin in patients with heart failure and reduced ejection fraction is remainly unclear. This study aims to know the effects of empagliflozin to the patients with heart failure and reduced ejection fraction.

### Methods

This study is extracted from several databases such as PubMed, PMC, Science Direct, and Euro PMC using keywords MeSH such as “reduced ejection fraction” AND “empagliflozin” AND “heart failure” AND “SGLT2i.” This study uses several inclusion criterias such as randomized controlled trial, clinical trial, cohort studies, and within 10 years publications. Systematic reviews, animal studies, pediatric patients, case reports, case series, meta analysis, and unfull papers are excluded for this study. All eligible studies were assessed using the Newcastle-Ottawa Scale.

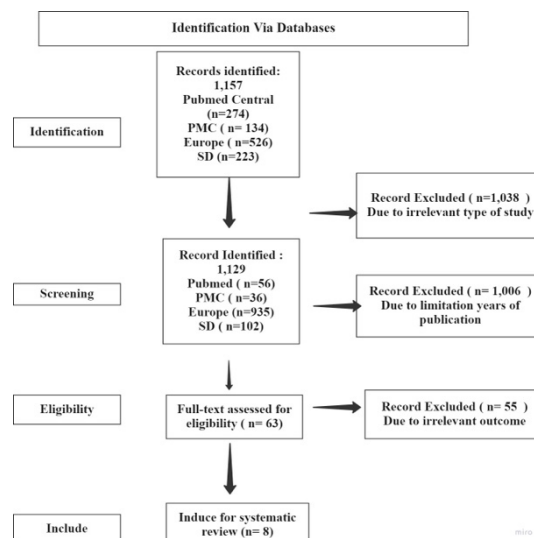
### Results

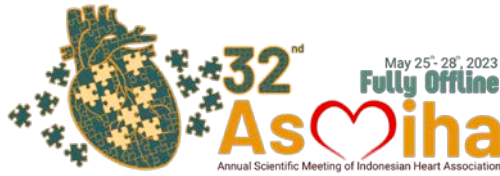
Eight studies were extracted through several inclusion criteria mentioned above from sixty-three eligible ones. These studies included six randomized controlled trial and two clinical trials consisting of 4294 patients with heart failure and reduced ejection fraction. All of these studies have decent quality. Six studies show that empagliflozin is effective to reduce serious heart failure outcomes, hospitalization, and cardiovascular death in patient with HFrEF. Therefore, 2 studies show that use of empagliflozin doesn't have a significant differences with non-empagliflozin managements for patients with heart failure and reduced ejection fraction.

### Conclusion

In conclusion, empagliflozin is effective as a treatment option for patients with heart failure and reduced ejection fraction. However, this study need more further studies to clarify the results.

### Keywords:





## Impact of preeclampsia on ventricular repolarization indices: A systematic review and meta-analysis

A. Adhyatma<sup>1</sup>, N.M. Nastiti<sup>1</sup>

Faculty of Medicine, Public Health, and Nursing Universitas Gadjah Mada<sup>1</sup>

### Backgrounds and aims

Preeclampsia (PE) remains a major cause of maternal death worldwide, complicating 10-15% of all pregnancies. Recent studies suggested that PE might be linked to an increased risk of developing future cardiovascular diseases, including ventricular arrhythmias. We aimed to investigate the impact of PE on ventricular repolarization indices on the electrocardiogram.

### Methods

PubMed and Google Scholar databases were searched for eligible studies up to February 2023. Observational studies investigating the association of preeclampsia with ventricular repolarization indices such as QT, QTc, Tp-e intervals, Tp-e/QT, and Tp-e/QTc ratios were included. Mean difference estimates were pooled by random-effect models and 95% confidence interval (CI).

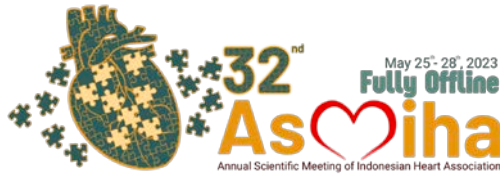
### Results

Eight studies, representing a total of 635 participants, were included. Compared with healthy pregnant women as the control group, preeclampsia was associated with significant prolongation of QT interval (mean difference = 25.08 ms, 95% CI = 15.82-34.33,  $I^2 = 73%$ ,  $p < 0.00001$ ), QTc interval (mean difference = 17.56 ms, 95% CI = 10.89-24.23,  $I^2 = 67%$ ,  $p < 0.00001$ ), and Tp-e interval (mean difference = 20.83 ms, 95% CI = 13.59-28.07,  $I^2 = 83%$ ,  $p < 0.00001$ ). Further analysis showed that preeclampsia was associated with a higher Tp-e/QTc ratio (mean difference = 0.03, 95% CI = 0.01-0.06,  $I^2 = 96%$ ,  $p = 0.002$ ). No difference in Tp-e/QT ratio was found between preeclampsia and the control group (mean difference = 0.04, 95% CI = -0.01-0.08,  $I^2 = 98%$ ,  $p = 0.15$ ).

### Conclusions

Preeclampsia has a significant unfavorable impact on ventricular repolarization indices compared to healthy pregnant women. This alteration suggested that preeclampsia might be associated with an increased risk of developing undesirable ventricular arrhythmias. However, further studies with longer follow-up and larger participants are warranted to elaborate more on this finding.

**Keywords:** preeclampsia, ventricular repolarization indices, systematic review, meta-analysis



## One Year Change in Ejection Fraction and Outcomes in Patients with Heart Failure Mid-Range Ejection Fraction (HFmrEF): A Systematic Review

K.K. Aziz<sup>1</sup>

Puskesmas Kota Dalam Pesawaran, Lampung<sup>1</sup>

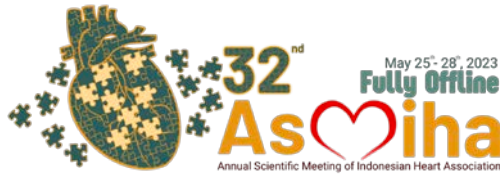
**Background** Mid-range ejection fraction is a new entity of heart failure (HF) with undetermined prognosis until now. The prevalence of patients with Heart Failure with Mid-Range Ejection Fraction (HFmrEF) remains unchanged regardless of healthcare strategies. HFmrEF has mixed characteristics and treatment of Heart Failure with Preserved Ejection Fraction (HFpEF) and Heart Failure with Reduced Ejection Fraction (HFrEF). In our systematic review we assessed the outcomes ejection fraction of HFmrEF in one year evaluation given treatment HFrEF.

**Methods** We conducted our search in March 2022 until March 2023 in the following databases for relevant articles: PubMed, Google Scholar and Web of Science. Four study include observational and cohort studies evaluating total population of 6.143 HFmrEF patient given treatment HFrEF whose met inclusion criteria (patients diagnosed with chronic heart failure aged  $\geq 40$  years in stable condition; women and men given heart failure therapy RAS inhibitors, B-blockers, MRA and SGLT2 inhibitors; and no comorbid diseases such as DM, AKI/CKD and stroke).

**Results** 6.143 of HFmrEF patients from 4 studies after one year follow up, showed that 38% (n=2.326) had persistent HFmrEF (EF 40-49%), 34% (n=2.101) of patients had an EF improved to HFpEF (EF  $\geq 50\%$ ) and 28% (n=1.715) of the patients worsening to HFrEF (EF  $\leq 40\%$ ). Amongst patients with HFmrEF given treatment HFrEF showed more increase ejection fraction than decreased ejection fraction, although most of HFmrEF remained persistent in HFmrEF condition.

**Conclusions** Categorizing HFmrEF patients based on LVEF provides meaningful clinical information, may assist clinicians with management decisions and this change was associated with survival. The treatment of HFmrEF was recommended to be similar to the treatment of HFpEF in the 2016 guidelines of European Society of Cardiology (ESC) but was changed, in this study treatment of HFmrEF was similar to that of HFrEF in according to 2021 ESC guidelines.

**Keywords:** HFmrEF, HFpEF, HFrEF



## **Biventricular Pacing Versus Left Bundle Branch Pacing in Heart Failure with Left Bundle Branch Block, Who's Better?: A Systematic Review**

K.Y. Rubismo<sup>1</sup>, A. Zebua<sup>1</sup>, F. Nathania<sup>1</sup>, J.V. Lee<sup>1</sup>, N.M. Wijaya<sup>1</sup>, M.Z. Sabran<sup>1</sup>, C.F. Jhoputri<sup>1</sup>, J.A. Harjanto<sup>1</sup>, J.B. Lee<sup>2</sup>

Universitas Pelita Harapan<sup>1</sup>  
Universitas Katolik Indonesia Atma Jaya<sup>2</sup>

### **Background**

Cardiac Resynchronization Therapy (CRT) is indicated in heart failure patients with decreased Left Ventricular Ejection Fraction (LVEF) and Left Bundle Branch Block (LBBB) with LV dyssynchrony. Left bundle branch pacing gives new modality in treating heart failure patients with LBBB. This study aims to compare the outcome between biventricular pacing versus left bundle branch pacing in patients with heart failure and left bundle branch block.

### **Method**

This review was systematically reviewed. Two independent researchers extracted data from several databases, such as PubMed Central (PMC), Science Direct, Europe PMC, and PUBMED by using the following keywords "biventricular pacing", "left bundle branch pacing", "cardiac resynchronization therapy", and "heart failure". The extracted studies were then analyzed and extracted according to our inclusion criteria such as cohort studies, case-control studies within the last 5 years, and heart failure patients with left bundle branch block. We excluded systematic reviews, meta-analyses, case series, case reports, studies on pregnant women, children. All eligible studies were assessed using New-Castle Ottawa Scale (NOS).

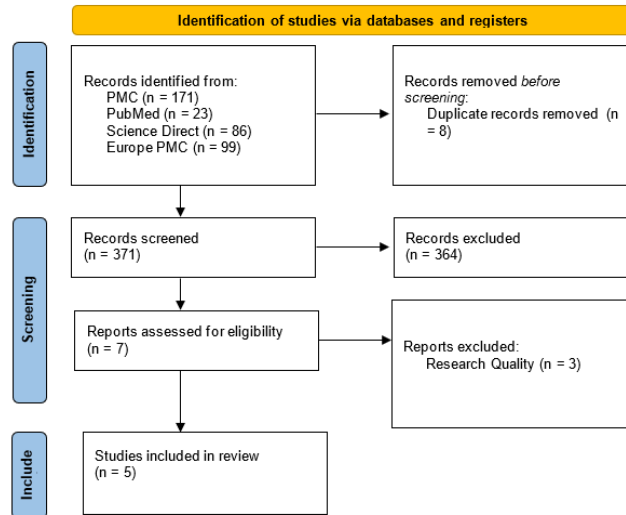
### **Result**

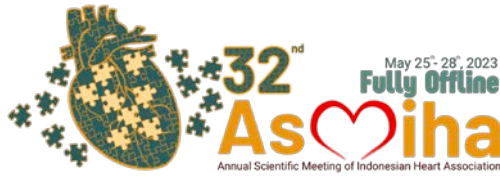
We found 5 cohort studies (261 subjects). All of them showed left bundle branch pacing resulted in significantly greater reduction of QRS duration than biventricular pacing. Results from 3 studies showed there was a better LVEF improvement in patients treated with left bundle branch pacing than biventricular pacing. We used NOS to evaluate the quality of the studies and all studies showed to be in good quality.

### **Conclusion**

In this study, we found that left bundle branch pacing had a greater performance than biventricular pacing on improvement of heart failure patients with LBBB. However further studies were required to confirm these findings.

**Keywords:**





## Comparison of the Effectiveness of ACE inhibitors with Calcium Channel Blockers (CCB) on the Progression of Diabetic Nephropathy in Hypertension and Type 2 Diabetes Mellitus Patients

I.A. Putri<sup>1</sup>, I. Fitriani<sup>1</sup>, A.C. Azzahra<sup>1</sup>  
Fakultas Kedokteran Universitas Indonesia<sup>1</sup>

**Background and aims:** Nephropathy is one of the complications of hypertension and diabetes mellitus which is the most common cause of terminal kidney disease and occurs in 40% of all patients with type 1 diabetes mellitus and type II DM. The level of proteinuria / albuminuria in patients is closely related to the progression of nephropathy and cardiovascular events. Both ACE-inhibitors and Calcium Channel Blockers (CCB) can reduce blood pressure and proteinuria/albuminuria in diabetic nephropathy patients.

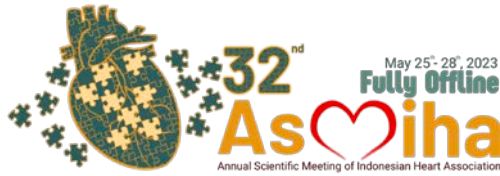
This case report aims to determine the effectiveness between the use of ACE-I and CCB combination therapy with single ACE-I therapy on the progression of nephropathy in hypertension and type II DM patients.

**Methods:** Literature search was carried out in 4 internet databases of medical scientific journals including PubMed, Cochrane, Clinical Key, and Scopus using keywords type II diabetes mellitus, ACE inhibitors, Calcium Channel Blockers, diabetic nephropathy, and diabetic kidney disease. Then filtering articles was carried out based on intervention reviews, inclusion criteria and exclusion criteria. There were 2 articles to be taken on the critical review using intervention methods in accordance with the Oxford Center for Evidence Based Medicine 2011.

**Results:** There was a significant difference in the rate of albuminuria ( $p < 0.05$ ) before and after treatment with combination therapy of ACEI and CCB. This difference is indicated by a greater decrease in the rate of albuminuria in ACEI-CCB combination therapy compared to ACEI single therapy.

**Conclusion:** ACEI and CCB combination therapy can significantly reduce the rate of albuminuria at the end of treatment which can play a role in preventing the progression of diabetic nephropathy.

**Keywords:** Type II Diabetes Mellitus, Hypertension, ACE inhibitor (ACE-I), Calcium Channel Blocker (CCB), Diabetic Nephropathy



## **Comparison Between Biventricular Pacing Versus His Bundle Pacing in Heart Failure with Left Bundle Branch Block: A Systematic Review**

J.B. Lee<sup>1</sup>, A. Zebua<sup>2</sup>, F. Nathania<sup>2</sup>, K.Y. Rubismo<sup>2</sup>, N.M. Wijaya<sup>2</sup>, M.Z. Sabran<sup>2</sup>, C.F. Jhoputri<sup>2</sup>, J.A. Harjanto<sup>2</sup>, J.V. Lee<sup>2</sup>

Faculty of Medicine, Atma Jaya Catholic University of Indonesia<sup>1</sup>  
Faculty of Medicine, University of Pelita Harapan<sup>2</sup>

### **Background**

Cardiac Resynchronization Therapy (CRT) is indicated in heart failure patients with decreased Left Ventricular Ejection Fraction (LVEF) and Left Bundle Branch Block (LBBB) with LV dyssynchrony. There is his bundle pacing (HBP) as an alternative to biventricular pacing (BVP) for CRT. The aim of this study is to compare the outcome of biventricular pacing versus his bundle pacing in heart failure patients with LBBB.

### **Method**

This review was systematically reviewed. Two independent researchers extracted data from several databases, such as PubMed Central (PMC), Science Direct, Europe PMC, and PUBMED by using the following keywords "his bundle pacing", "biventricular pacing", "heart failure" and "left bundle branch block". The extracted studies were then analyzed and extracted according to our inclusion criteria such as cohort studies, case-control studies within the last 5 years, and heart failure patients with left bundle branch block. We excluded systematic reviews, meta-analyses, case series, case reports, studies on pregnant women, children. All eligible studies were assessed using New-Castle Ottawa Scale (NOS).

### **Result**

We finally found 4 cohort studies (132 subjects) comparing biventricular and his bundle pacing. Two studies showed his bundle pacing resulted in more effective ventricular resynchronization with shortened left ventricle activating time than biventricular pacing. Other two studies showed patients treated with his bundle pacing had greater improvement in LVEF & LV end systolic volume than those treated with biventricular pacing. We used NOS to evaluate the quality of the studies and all studies showed to be in good quality.

### **Conclusion**

In conclusion, his bundle pacing as a newer CRT method showed a greater improvement than biventricular pacing in heart failure patients with LBBB. However further studies were required to confirm these findings.

**Keywords:** his bundle pacing, biventricular pacing, heart failure, left bundle branch block

**The Impact of Obstructive Sleep Apnoea on Thromboembolic Events in Atrial Fibrillation Patients**

A.H. Alamsyah<sup>1</sup>, K.A.A.I. Arini<sup>1</sup>, S.C. Surya<sup>1</sup>, I.M.P. Swiantara<sup>2</sup>

Faculty of Medicine, Udayana University, Prof. I.G.N.G. Ngoerah General Hospital, Bali, Indonesia<sup>1</sup>

Department of Cardiology and Vascular Medicine, Faculty of Medicine, Udayana University, Prof. I.G.N.G. Ngoerah General Hospital, Bali, Indonesia<sup>2</sup>

**Background & Aims:** Obstructive sleep apnoea (OSA) is a known risk factor for atrial fibrillation (AF). Currently, the goals of OSA management are focusing on preventing the occurrence of AF in high-risk patients and preventing the progression of AF in AF-presenting patients. However, several studies have proposed the association of OSA with stroke/thromboembolic event (TEE) in general populations. Although, those studies were still few, with different results and unspecific populations. Our study aim is to understand the impact of OSA on stroke/TEE in, already pre-existing, AF patients.

**Methods:** Several databases were searched on cohort studies of OSA versus No OSA in AF Patients. All English articles were included until February 2023. The primary outcome is stroke/TEE. The secondary outcomes are the mean CHA2DS2VASc score and the number of events from each point of the CHA2DS2VASc score. Analysis was done using the Review Manager ver. 5.4.

**Results:** Ten studies were included with a total of 466,404 AF patients. The mean age is 62.5 years old and 66.2% were male. OSA is present in 97,403 (20.1%) and stroke/TEE occurs in 25,838 (5.3%) with a mean follow-up period of 21.2 months. On our primary outcome, the OSA group has a significantly higher stroke/TEE compared to the No OSA group (OR: 1.51; 95%CI: 1.42-1.60; p<0.01). Interestingly, the mean CHA2DS2VASc score isn't significantly different between the two groups (MD: 1.07; 95%CI: (-0.31)-(2.45); p=0.13) suggesting that the increased stroke/TEE is not directly associated with the CHA2DS2VASc score.

**Conclusion:** Our result showed that OSA, known as a risk factor of AF, was also associated with an increased risk of thromboembolic events in those populations. These findings give a reasonable approach to physicians to diagnose and treat OSA properly, with the primary goal being to prevent stroke/TEE. Clinical trial studies with a well-controlled sample were required to validate our findings.

**Keywords:** Obstructive Sleep Apnoea, Stroke, Thromboembolic Event, Atrial Fibrillation

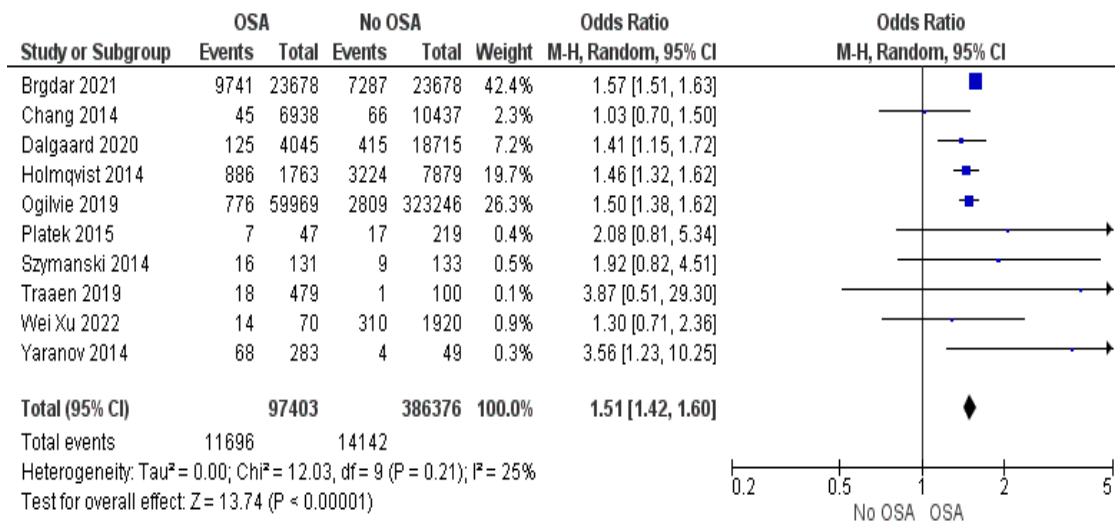


Figure 1. Forest plot of OSA versus No OSA on Stroke/Thromboembolic Event in Atrial Fibrillation Patients.



## **Menopausal Hormone Replacement Therapy for Treating Cardiovascular Disease: Is it effective?**

A. Sakh<sup>1</sup>, R.C. Harliman<sup>1</sup>, N.M. Wijaya<sup>1</sup>, N. Aurelia<sup>1</sup>, M.Z. Sabran<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Pelita Harapan University, Tangerang, Banten, Indonesia

### **Background**

Hormone Replacement Therapy (HRT) is commonly used to treat women showing menopausal symptoms during their menopausal phase. The increase of age reaching 50 years old in women causes a rapid transition of the menopausal phase which can be an intuitive health concern especially towards cardiovascular diseases (CVD). This study aims to highlight the effectiveness of HRT and its detailed contribution for treating CVD.

### **Method**

This systematic review used a literature search from PubMed, ScienceDirect, PMC, Euro PMC database. (("Hormone replacement therapy"[Mesh]) AND "Cardiovascular disease"[Mesh]) AND "Menopause"[Mesh] were used as keywords to search the literature. The inclusion criteria implemented for the literature search was the study had to use a design of either randomized clinical trial, population study, cross-sectional study, and/or cohort in the last five years. The Newcastle-Ottawa Scale was used to assess the quality of the included studies.

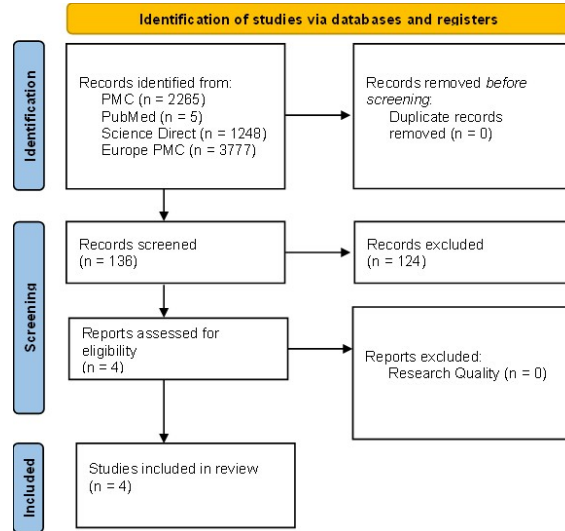
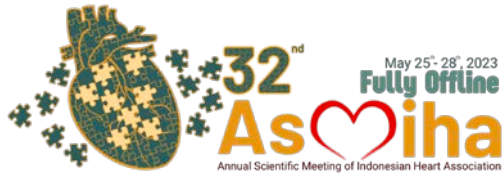
### **Result**

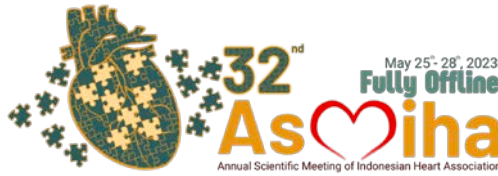
A big number of randomized clinical trial data intersecting with results from cross-sectional studies were selected for this study, which are relatively on the higher side of quality of the Newcastle- Ottawa Scale, and indicate a variety of clinical outcomes. The prospective randomized Women's Health Initiative (WHI) and the Early Versus Late Intervention Trial (ELITE) showed that starting HRT within 5 to 10 years of menopause fundamentally affects succession of estrogen's cardioprotection in postmenopausal women without adverse effects. From 1604 post-menopausal women, 513 (32%) underwent MHT  $\geq 3$  years. In the MHT cohort, median age at menopause was 50 (IQR: 45–52) and median duration of MHT was 8 years. In the non-MHT cohort, median age at menopause was 51 (IQR: 48–53).

### **Conclusion**

Although some data show some effectiveness of HRT on treating other clinical abnormalities, yet in the case of CVD, it requires more approaches and evidence.

**Keywords:** Hormone replacement therapy, Cardiovascular disease, Menopause





## Current Real-World Data of Clinical and Pregnancy-Related Factor Associated with Development and Improvement of Peripartum Cardiomyopathy and Therapeutic Outcomes of Bromocriptine: Systematic Review and Meta-Analysis

G.N.P. Jagannatha<sup>1</sup>, L.O.S. Suastika<sup>2</sup>, I.G.B.M.A. Pradnyaandara<sup>1</sup>, F. Deantri<sup>1</sup>, I.B.S. Wibawa<sup>1</sup>, I.W.A.S. Pradnyana<sup>1</sup>

Faculty of Medicine Udayana University, Prof. Dr. I.G.N.G Ngoerah General Hospital<sup>1</sup>  
Department of Cardiology and Vascular Medicine, Faculty of Medicine of Udayana University, Udayana University Hospital, Denpasar, Bali, Indonesia.<sup>2</sup>

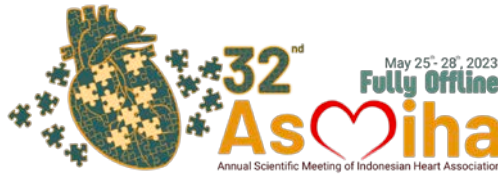
**Background:** Peripartum Cardiomyopathy (PPCM) is a heart failure (HF) phenotype associated with pregnancy with a wide knowledge gap. This meta-analysis aims to holistically evaluate factors associated to the development, improvement of PPCM, and the outcome of bromocriptine therapy.

**Methods:** A systematic search of studies examining factors associated to PPCM recovery and outcomes of bromocriptine therapy were performed in multiple databases. In general definition PPCM recovery is improvement of LVEF to >50%. We compared each risk factor between recovered PPCM and non-recovered PPCM patients and compared the outcomes of bromocriptine therapy to standard HF treatment as the endpoint. Synthesis of baseline risk factor data was also performed and served as proportion in overall population. Outcomes were analysed using Review Manager 5.4 and R Studio.

**Results:** Data from 25 studies with 1,651 of PPCM patients were included in this meta-analysis. Caesarean section and anemia during pregnancy were the most common risk factors of PPCM patients (Proportion=53%, 95CI=41%-66%, and Proportion=51%, 95CI=38%-65%, respectively). Other common risk factors were age at pregnancy >30 years (45%), primipara (44%), and African/black race (41%). The non-recovered PPCM population was significantly younger (MD=-1.04 years old, 95CI=-1.82-(-0.27), P=0.008) and black/African (OR=1.82, 95%CI=1.43-2.31, P<0.001). The absence of hypertension during pregnancy (OR=0.73, 95CI=0.60-0.88, P=0.001) and multipara (OR=0.81, 95CI=0.66-0.99, P=0.04) had a significantly lower recovery rate. Non-recovered PPCM patients also had higher baseline serum creatinine levels, lower LVEF, larger LVEDD, larger LVESD, and lower FS (all P-values <0.05). Bromocriptine therapy was significantly reduce major adverse cardiac events, and mortality (OR=0.38, 95CI=0.22-0.65, P<0.001; OR=0.32 95CI=0.15-0.65, P=0.002, respectively).

**Conclusion:** Populations with younger age at pregnancy, black race, absence of hypertension, and multipara may have poorer recovery prognosis. Bromocriptinetherapy has been shown to provide superior benefits in reducing the number of adverse events in PPCM patients.

**Keywords:** Peripartum cardiomyopathy, Pregnancy, Heart failure, Recovery, Bromocriptin, Risk Factor



## Potential Addition of Thiazide to Improve The Body Weight Reduction in Patient with Acute Heart Failure: A Systematic Review

M. Mohamad<sup>1</sup>, A.P. Febrianto<sup>2</sup>, H. Arifianto<sup>2</sup>

Faculty of medicine, Sebelas Maret University, Surakarta, Indonesia<sup>1</sup>

Departement Cardiology and Vascular Medicine, UNS Hospital, Surakarta, Indonesia<sup>2</sup>

**Background and Aims:** Acute heart failure (AHF) is a clinical syndrome characterized by signs and symptoms of fluid overload as consequence with high mortality and hospital readmission rate. The adding of thiazide to usual treatment may produce diuretic synergy via sequential blockade. This combination therapy suggested the increase urine excretion, induce weight loss and resolve congestion problem We analyzed the effect of additional thiazide to loop-diuretic therapy and evaluate the improvement of the combination.

**Method:** A literature search was conducted using PubMed and capturing the data from the past 10 years. Terms used included MeSH headings for thiazide and loop and acute heart failure. A systematic review of published study was performed. Randomized Controlled Trial Article including acute heart failure patients being treated with loop-diuretics and thiazide were included. We analyzed the effect of additional thiazide therapy to loop-diuretic therapy in patient with acute heart failure

**Result:** A total of 3 randomized controlled trials (RCTs) consisted of 317 patients as study participants were obtained from PubMed database. Eligible studies show that thiazide additional therapy, statically significant, help loop-diuretic reduce the body-weight, especially with loop-diuretic (furosemide) in dose 40-240mg/day (P<0.05). The congestion symptoms also reduced in patient who received thiazide additional therapy in this 3 studies. But, the increased of serum creatinine also happen in patient that got thiazide additional therapy.

**Conclusion:** This systematic review showed that thiazide additional therapy reduces the body weight and congestion symptoms in AHF patient that received loop-diuretic daily therapy, despite it is also increasing serum creatinine level.

**Keywords:** thiazide diuretic, loop-diuretic, acute heart failure, systematic review

Study	Location	Design	N	Inclusion Criteria	Body weight Reduction	Dyspnea Score Reduction	Serum Creatinine
Trullas, J.C et al, 2022	Spain	Prospective, double-blind, placebo-controlled trial	230	History of CHF, received furosemide oral 80-240mg/day, admission for ADHF	Change in weight at 72h HCTZ: -2.3 (-3.9 to -1.2) Placebo: -1.5 (-3.2 to 0.0) p=0.002	AUC for dyspnoea at 72h HCTZ: 960 (360-1620) Placebo: 720 (240-1455) p=0.497	Increase in creatinine >26.5 µmol/l HCTZ n=53 (46.5%) Placebo n=20 (17.2%) p=<0.001
Piardi, D et al, 2021	Brazil	Randomized, single-center, parallel, double-blind	47	ADHF, EF<45%, creatinine clearance >30ml/min, sign of congestion	Diuretic response HCTZ: -0.74 ± 0.47 kg/40mg Placebo: -0.33 ± 0.80 kg/40mg p=0.032	Congestion score HCTZ: -5.4 ± 4.6 Placebo: -4.8 ± 4.6 p=0.68	Change in creatinine (mg/dL) HCTZ: 0.50±0.37 Placebo: 0.27±0.40 p=0.05 Increased creatinine >0.3mg/dL HCTZ=58%, placebo=41%; p=0.38
Cox, Z et al, 2020	USA	Prospective, Randomized, double-blinded	60	Hypervolemic AHF, diuretic resistance	Weight loss (kg) in 48h metolazone 4.6±2.7 chlorothiazide 5.8±2.7 tolvaptan 4.1±3.3 p value: chlorothiazide vs metolazone: 0.292 tolvaptan vs metolazone: 0.456	Congestion score metolazone: 4.0 (2.5-7.0) chlorothiazide: 3.0 (2.0-4.6) tolvaptan: 3.0 (2.0-5.0) P value chlorothiazide vs metolazone: 0.317 tolvaptan vs metolazone: 0.351	Change in serum creatinine from baseline (mEq/l) metolazone 0.3 ± 0.3 chlorothiazide 0.5 ± 0.5 tolvaptan 0.03 ± 0.3 P value chlorothiazide vs metolazone: 0.103, tolvaptan vs metolazone: 0.006

Table 1. Thiazide Additional Therapy Trial Characteristic

## The association between shift work and C-reactive protein level: a systematic review and meta-analysis

A. Adhyatma<sup>1</sup>, M.R. Hadwiono<sup>1</sup>

Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Indonesia<sup>1</sup>

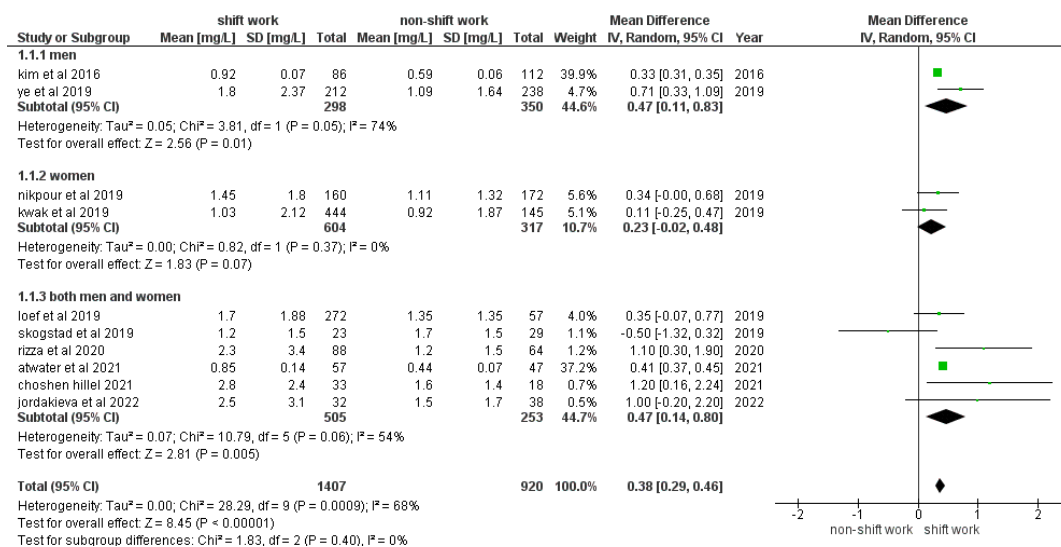
**Backgrounds and aims:** In modern society, shift work has become more prevalent due to its economic and social demands. Recent studies suggested that shift work might be associated with increased C-reactive protein (CRP) level, however, such results remain inconsistent. Therefore, we aimed to evaluate the association between shift work and CRP level.

**Methods:** PubMed and Google Scholar databases were searched from inception to April 2022. Epidemiological studies evaluating the difference in CRP level between shift and non-shift work were included. The mean differences in CRP level were combined in a random-effects model, expressed as pooled mean differences and a 95% confidence interval (CI).

**Results:** We included 10 studies, comprising 1407 shift workers and 920 non-shift workers. Compared to non-shift workers as a control group, the overall mean CRP level was significantly higher in shift workers compared to non-shift workers (mean difference of 0.38 mg/L, 95% CI 0.29–0.46,  $p < 0.00001$ ,  $I^2 = 68\%$ ). Similarly, significant higher CRP levels were also observed in sub-group analysis among men workers (mean difference of 0.47 mg/L, 95% CI 0.11–0.83,  $p = 0.01$ ,  $I^2 = 74\%$ ), both men and women workers (mean difference of 0.47 mg/L, 95% CI 0.14–0.80,  $p = 0.005$ ,  $I^2 = 54\%$ ). However, sub-group analysis in women workers did not show any significant mean CRP level difference (mean difference of 0.23 mg/L, 95% CI -0.02–0.48,  $p = 0.07$ ,  $I^2 = 0\%$ ).

**Conclusions:** This study suggests that shift work is associated with a higher CRP level compared to non-shift work. Our finding may suggest that shift work could be an important risk factor for cardiovascular diseases. However, further studies with a long follow-up period and a larger number of participants are needed to confirm such an association.

**Keywords:** shift work, C-reactive protein, CRP, systematic review, meta-analysis



Forest plot, shift work and C-reactive protein level

## Overall Outcomes of Treprostinil vs Placebo as a Treatment Option in Patient with Pulmonary Hypertension Due to ILD : a Systematic Review

E.W. Mokalul<sup>1</sup>, M.Z. Sabran<sup>1</sup>, V. Jonathan<sup>1</sup>, K.Y. Rubismo<sup>1</sup>, A. Zebua<sup>1</sup>  
Universitas Pelita Harapan<sup>1</sup>

### Background

Pulmonary hypertension (PH) is a condition when the pressure in the lung blood vessels becomes too elevated. Pulmonary hypertension can occur due to many conditions. One of the causes of pulmonary hypertension is due to chronic lung disease which is classified as WHO Group 3 PH. Chronic lung disease may vary however, the most common etiology is interstitial lung disease and as of currently, there is still no approved therapy used in this condition. However, this study aims to evaluate the overall outcomes of treprostinil as a monotherapy treatment in patients with PH-ILD.

### Method

Studies were systematically extracted from PubMed database using MeSH terminology, such as “treprostinil” AND “pulmonary hypertension” AND “interstitial lung disease”. There were several inclusion criteria in this systematic review, such as RCTs, clinical trials, and cohort studies that were published in the last 10 years. This study excluded meta-analysis, systematic reviews, animal studies, pediatric patients, and case reports or series. Newcastle-Ottawa Scale is used to assess the quality of included study.

### Result

Through inclusion criterias mentioned above, six studies were extracted from 31 eligible ones. This study included 3 RCTs, 2 clinical trials, and 1 cohort study which consisted of 440 patients. All of the studies included were of decent quality after being assessed with NOS. Studies included shows that use of treprostinil improved exercise capacity, decreased NT-proBNP levels, and lower incidence of clinical worsening events. From this result, we interpret that use of Treprostinil can be a treatment option in patients with PH-ILD associated.

### Conclusion

Use of Treprostinil in patients with pulmonary hypertension due to interstitial lung disease may improve overall outcomes with low incidence of worsening events. However, further studies are needed to support these findings.

**Keywords:** Treprostinil, Pulmonary hypertension, Interstitial lung disease

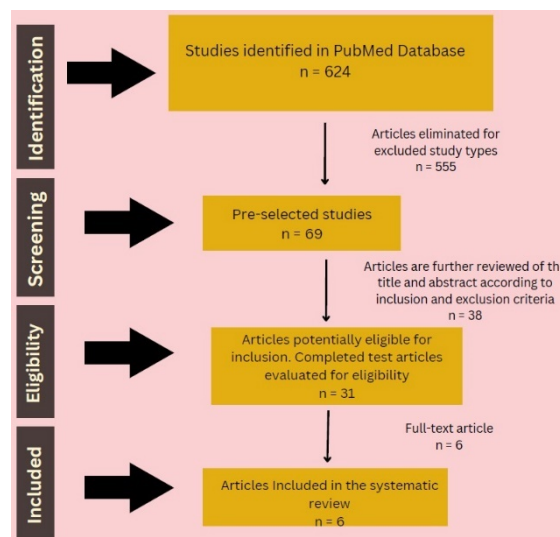
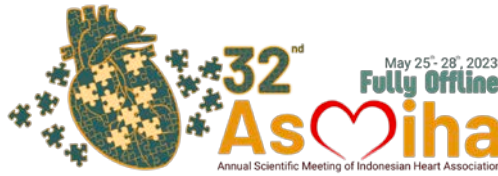


Figure 1. PRISMA Chart



### The Association Between Alcohol Consumption and Incident of Heart Failure: a Systematic Review and Meta-Analysis

I.M.F. Wikananda<sup>1</sup>, I.B.B.D. Kusuma<sup>1</sup>, G.D.D. Wikananda<sup>1</sup>, K.D. Chandita<sup>2</sup>, P.P Jaya<sup>3</sup>, I.G.R. Widiana<sup>4</sup>  
Faculty of Medicine Udayana University<sup>1</sup>  
Faculty of Medicine Airlangga University<sup>2</sup>  
Department of Cardiology Wangaya Regional Hospital Denpasar<sup>3</sup>  
Department of Internal Medicine IGNG Ngerah Hospital Denpasar/ Udayana University<sup>4</sup>

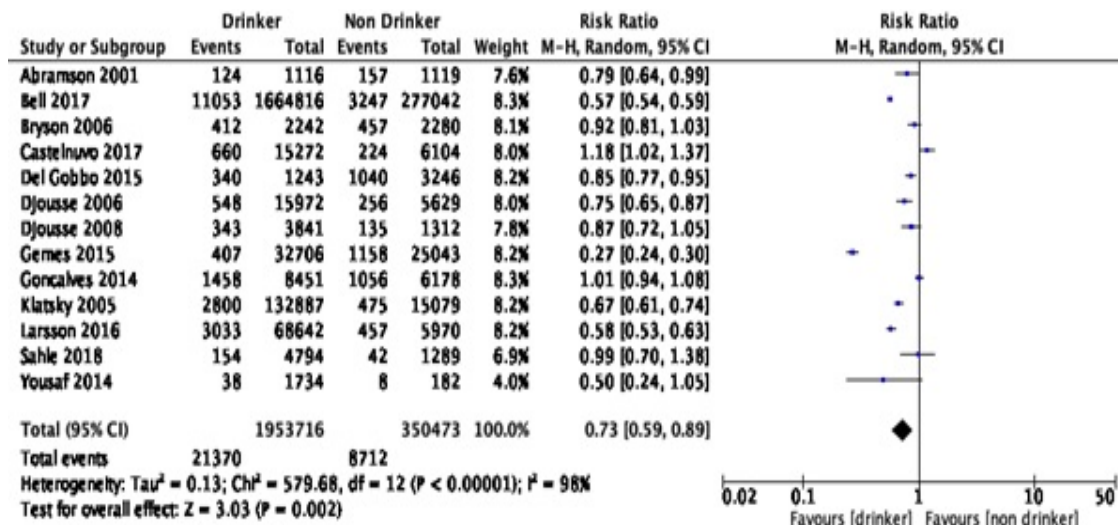
**Background and aims:**Alcohol consumption has been extensively studied as a modifiable risk factor for cardiovascular diseases; that is a common risk factor for heart failure, could have different associations depending on the amount. Light to moderate alcohol consumption is associated with lower risk of cardiovascular disease than those who consume no alcohol and or have very high consumption. In this study, we aimed to assess the association between moderate alcohol intakes with the incident of heart failure.

**Methods:** We searched the online databases PubMed, ScienceDirect, and Cochrane Library for relevant studies evaluating the effect of alcohol consumption on the risk of heart failure compared to never drinkers. Using a random effects model, weighted relative risk (WRR) with 95% confidence interval (CI) were used to measure the effect of alcohol consumption on the risk of heart failure.

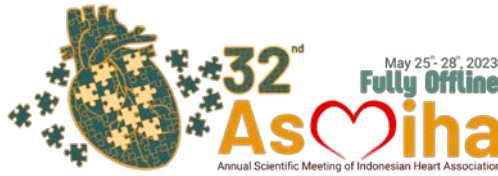
**Result:** To assess the relationship between moderate alcohol consumption and incidence of heart failure, we analysed 13 Cohorts. Overall alcohol consumption significantly reduce the risk of heart failure compared to non-drinkers. (WRR 0.73, I<sup>2</sup>=98%; 95% CI [0.59;0.89] p<0.001. Dose response analysis shows former drinkers have significantly higher risk for heart failure (WRR 1.56, I<sup>2</sup>=98%; 95% CI [1.06;2.31] p<0.001). Light and moderate drinkers have significantly lower risk of heart failure (WRR 0.68, I<sup>2</sup>=97%; 95% CI [0.54;0.84] p<0.001) and (WRR 0.64, I<sup>2</sup>=95%; 95% CI [0.52;0.78] p<0.001). Heavy drinkers have no significant difference risk of heart failure (WRR 0.76, I<sup>2</sup>=98%; 95% CI [0.49;1.16] p=0.2)

**Conclusion:** We found that overall alcohol consumption, light alcohol consumption and moderate alcohol consumption significantly reduces the risk of heart failure compared to never drinkers. Former drinkers significantly have higher risk of heart failure compared to never drinkers. Heavy drinkers have no significant difference in risk of heart failure compared to never drinkers.

**Keywords:** Heart Failure, Congestive Heart Failure, Alcohol, Drinking, Alcohol Consumption



The risk of heart failure on all alcohol consumption compared to non-drinkers.



**Could Revascularization be Superior over Medical Therapy for Renal Artery Stenosis?: A Systematic Review and Meta-Analysis**

T. Tarigan<sup>1</sup>, K.C. Prasiddha<sup>2</sup>, A.A. Rezquila<sup>3</sup>, R. Triatmaja<sup>4</sup>, D.S. Maulida<sup>5</sup>  
 Happy Land Medical Center, Yogyakarta, Indonesia<sup>1</sup>  
 Yogyakarta Regional General Hospital, Yogyakarta, Indonesia<sup>2</sup>  
 Mitra Paramedika Hospital, Yogyakarta, Indonesia<sup>3</sup>  
 Muhammadiyah Yogyakarta University<sup>4</sup>  
 Faculty of Medicine, Nursing and Public Health, Gadjah Mada University<sup>5</sup>

**Background**

Atherosclerotic renal artery stenosis (ARAS) is the most prevalent cause of secondary hypertension and it's linked to several complications, including renal failure, coronary artery disease, cardiac instability, and stroke. In the administration of ARAS, medical therapy is the central component, and numerous clinical studies have compared it to revascularization as an alternative treatment. The purpose of this research was to evaluate the effectiveness of revascularization versus medical therapy in patients with atherosclerotic renal artery stenosis.

**Methods**

We extracted randomized controlled trials and observational studies from 4 databases, including PubMed, Proquest, Cochrane Library, and Google Scholar that were published from 1998 to 2017. Studies that compared the outcome of revascularization and medical therapy in patients with ARAS were included. The primary outcome parameters were mortality, nonfatal myocardial infarction (MI), congestive heart failure (CHF), deterioration in renal function, and stroke. The pooled-risk ratio (RR) for each outcome was analyzed.

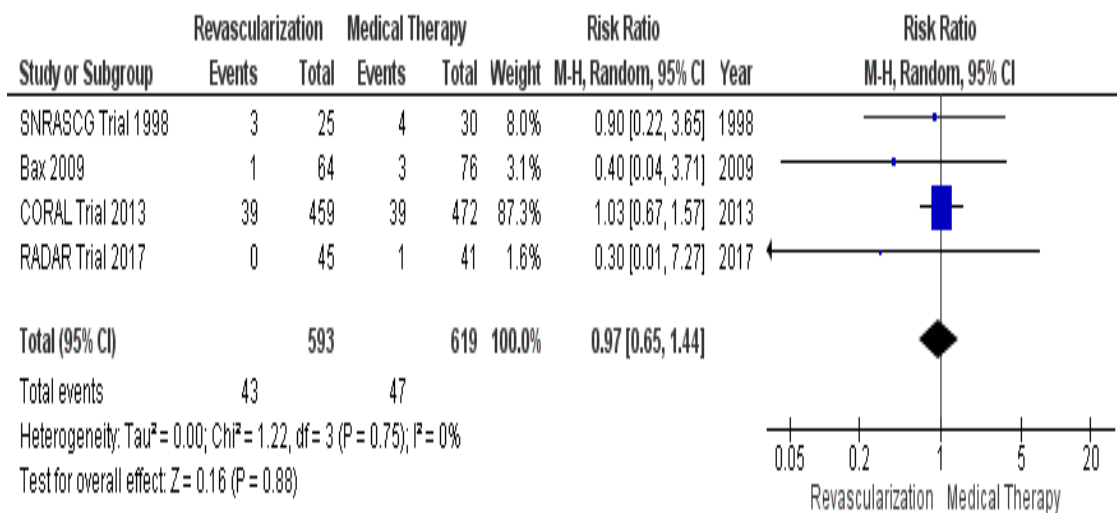
**Results**

The study includes 10 randomized controlled trials and observational studies with 1661 ARAS patients. Revascularization was not superior to medical treatment in terms of mortality (RR: 0.86; 95% CI: 0.65 to 1.15; P= 0.31), non-fatal MI (RR: 1.07; 95% CI: 0.72 to 1.60; P= 0.72), CHF (RR: 0.97; 95% CI: 0.65 to 1.44; P= 0.88), renal event (RR: 0.99; 95% CI: 0.79 to 1.24; P= 0.93), and stroke (RR: 0.75; 95% CI: 0.44 to 1.28; P= 0.30). In subgroup analysis, neither stenting nor angioplasty itself was superior to medical treatment in any terms.

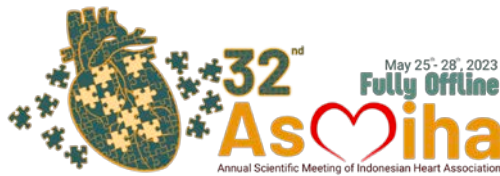
**Conclusions**

In conclusion, revascularization does not enhance outcomes in patients with ARAS when compared to medical therapy. Future studies should investigate to identify other patient subgroups that may benefit from such an intervention.

**Keywords:** Atherosclerotic renal artery stenosis, revascularization, medical therapy, comparison



**Quality of Life Patient with Heart Failure Preserved Ejection Fraction (HFpEF) in Vericiguat Therapy via Kansas City Cardiomyopathy Questionnaire (KCCQ): Meta-analysis**



Y. Pintaningrum<sup>1</sup>, P. Mahadewi<sup>1</sup>  
Mataram University<sup>1</sup>

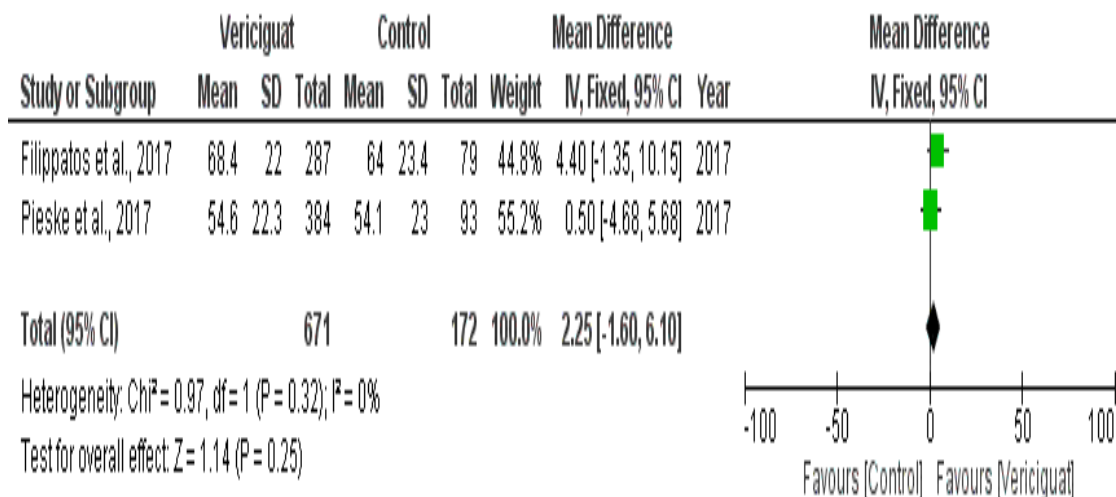
**Background and aims:** HFpEF is a subtype of heart failure with left heart pump function  $\geq 50\%$ [2]. The incidence of HFpEF over time tends to increase compared to the incidence of HFrEF[2]. One of many pathophysiology of HFpEF is the suppression of cGMP production which causes myocardial and vascular dysfunction[1,3]. Vericiguat is one of the Soluble Guanylate Cyclase (sGC) stimulating drugs that can increase cGMP activation[3,4]. Based on this, the authors are interested in researching the effectiveness of vericiguat therapy on the quality of life and health status HFpEF patients with Kansas City Cardiomyopathy Questionnaire (KCCQ)[3,5].

**Methods:** This study used a systematic search using PRISMA principle in several online databases (Pubmed, Cochrane library and Google scholar). The selected study was an RCT or clinical trial with a population of HFpEF patients who were given vericiguat therapy interventions, and a comparison was made of the quality of life and health status of patient in placebo group via KCCQs. Selected study will be assessed and analyzed using Review Manager software version 5.4 with 95% CI.

**Result:** The two studies selected in this meta-analysis had a total sample size of 671 in the intervention group and 172 in the placebo group. Heterogeneity test obtained [ $p > 0,05$ ;  $I^2 0\%$ ], indicating that the heterogeneity of the research data is very low and the study is recommended to use the fixed effect method. The result of the analysis test related to KCCQs scores of the intervention and placebo groups [RR 2.25 (95% CI -1.60-6.10),  $p 0.25$ ] found no significant difference between 2 groups.

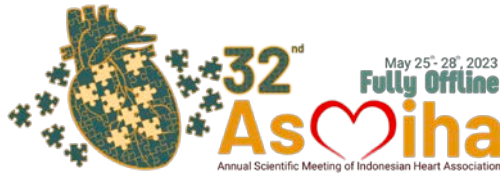
**Conclusion:** The results showed that vericiguat therapy had no effect or significant improvement on the quality of life and health status of patient with HFpEF based on KCCQs scoring.

**Keywords:** Vericiguat, HFpEF, KCCQ, Preserved Ejection Fraction



### Echocardiographic Pressure Half Time (PHT) for Evaluation of Pulmonary Regurgitation in Patients with Repaired Tetralogy of Fallot (rTOF) : A Systematic Review and Meta-Analysis

N.P.B.S. Utami<sup>1</sup>, F. Harmen<sup>2</sup>, M.E. Ananta<sup>3</sup>, N. Karima<sup>4</sup>, R. Ariani<sup>5</sup>  
Kardinah Regional General Hospital, Tegal, Central Java, Indonesia<sup>1</sup>



Perdagangan Regional General Hospital, Simalungun, North Sumatra, Indonesia<sup>2</sup>  
Faculty of Medicine, Alumnus of Universitas Indonesia, Jakarta, Indonesia<sup>3</sup>

Permata Depok Hospital, Depok, West Java, Indonesia<sup>4</sup>

Division of Non-Invasive Diagnostic and Cardiovascular Imaging, Department of Cardiology and Vascular  
Medicine, Faculty of Medicine Universitas Indonesia/National Cardiovascular Center Harapan Kita<sup>5</sup>

**Background:** Repaired Tetralogy of Fallot (rToF) patients have a lifetime risk of developing pulmonary regurgitation (PR), which insidiously deteriorates RV function if left untreated, necessitating its early diagnosis. We aimed to evaluate the diagnostic performance of echocardiographic pressure half time (PHT) in assessing PR.

**Method:** A systematic search of literature was performed through PubMed, EMBASE, Cochrane Library, Scopus, ScienceDirect, and Proquest for articles published from inception until November 17<sup>th</sup> 2022. We included studies evaluating the performance of echocardiographic PHT in diagnosing hemodynamically significant and/or severe PR. The comparator was PR Fraction (PRF) assessed by Cardiac Magnetic Resonance (CMR), which is the gold standard. Risk of bias assessment was conducted using QUADAS-2 tool. All meta-analyses were performed using Review Manager version 5.4 and STATA.

**Result:** From 1609 studies, we included 12 studies with a total of 742 patients in this systematic review. Four studies evaluating hemodynamically significant PR (hsPR) and two studies evaluating severe PR were included in the meta-analysis. The diagnostic odds ratio (DOR) of PHT was 34.928 (95% CI 13.525-90.199) for evaluating hsPR and 8.08 (95% CI 2.22-29.38) for evaluating severe PR. The area under the ROC curve of PHT in evaluating hsPR (PRF $\geq$  20%) and severe PR (PRF $\geq$  40%) was 0.94 (95% CI 0.91-0.96) and 0.769 respectively. The pooled sensitivity and specificity of PHT for hsPR were 0.80 (95% CI 0.47-0.95) and 0.91 (95% CI 0.65-0.98) respectively. The pooled sensitivity and specificity of PHT for severe PR were 0.86 (95% CI 0.70-0.94) and 0.57 (95% CI 0.36-0.75) respectively.

**Conclusion:** PHT has good sensitivity and specificity in diagnosing hemodynamically significant PR in patient with rToF. Thus, PHT can be used as a screening modality to monitor the progression of PR in patient with rTOF.

**Keywords:** tetralogy of fallot, pulmonary regurgitation, pressure half time, echocardiography, cardiac magnetic resonance

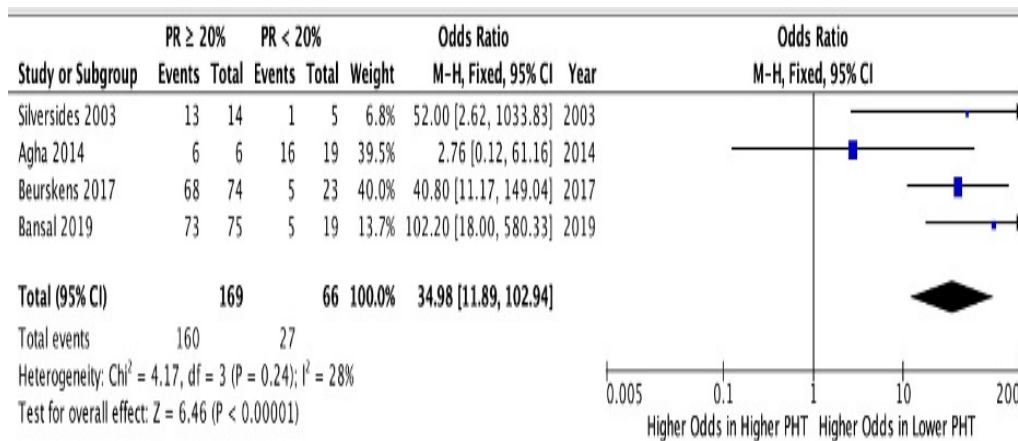
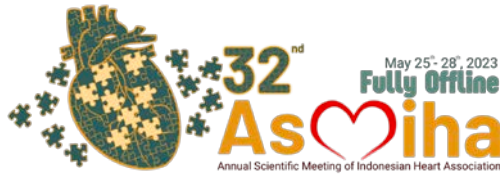


Figure 1. Pooled DOR of PHT in evaluating hemodynamically significant PR (PRF $\geq$  20%).



## Uncover The Potential Cardio-Vascular Risk Among Woman With Polycystic Ovarian Syndrome : A Meta-Analysis Of Cohort Studies

A.A. Rezquila<sup>1</sup>, T. Tarigan<sup>2</sup>, D.S. Maulida<sup>3</sup>, R. Triatmaja<sup>4</sup>, K.C. Prasadha<sup>5</sup>  
Mitra Paramedika Hospital, Yogyakarta<sup>1</sup>  
Happy Land Medical Center, Yogyakarta<sup>2</sup>  
Faculty of Medicine, Nursing and Public Health, Gadjah Mada University<sup>3</sup>  
Muhammadiyah Yogyakarta University<sup>4</sup>  
Yogyakarta Regional General Hospital<sup>5</sup>

**Background:** Since the risk of metabolic syndrome events is greater in PCOS-affected women, it's reasonable to speculate that PCOS women may have a higher Cardiovascular disease (CVD) risk. Various studies comparing CVD risk in PCOS women vs. control have been conducted, which yielded varied results. A recent study found women with PCOS have an increased risk of CVD and Cerebrovascular disease (CeVD). However, there was no difference in all-cause nor mortality-related CVD observed. Therefore, we performed this meta-analysis to uncover the cardiovascular risk and mortality among women with PCOS.

**Method:** We gathered 21 publications from Pubmed, ScienceDirect, Scholar, and Proquest searching for studies reporting the association between PCOS and CVD events from 1992 to 2022. The main outcomes were CVD i.e. coronary heart disease (CHD), myocardial infarction (MI), and mortality-related CVD. Other considerable outcomes including CeVD, and all-cause mortality, were extracted from the identified literature. We presented the results in odds ratios (OR).

**Results:** A total of 117.923 subjects from 11 cohort studies that met the inclusion criteria were included. The analysis compared the risk of CHD events in PCOS women to the control (OR: 1.29, 95%CI: 0.88-1.90). In addition, the risk for MI (OR: 1.14, 95%CI: 0.92-1.42), CeVD or stroke (OR: 1.15, 95%CI: 0.63-2.10), CVD mortality (OR:1.08, 95% CI: 0.89-1.32) and all-cause mortality (OR: 2.09, 95%CI: 0.52-8.37) were observed. All of the results' funnel plots are approximately symmetric, and no discernible publication bias was discovered.

**Conclusions:** Compared to the control, we found no statistically significant either CVD events or mortality-related CVD. There were also no discernible differences in the other observed outcomes, i.e. CeVD or stroke, and all-cause mortality. This is consistent with some earlier studies' findings PCOS women have no increased propensity for CVD than their non-PCOS counterparts. Nevertheless, independent CVD risk in PCOS women remains unclear and required additional large-scale studies.

**Keywords:** PCOS, Cardiovascular disease (CVD), Coronary Heart Disease (CHD), Myocardial infarct (MI), Mortality



## Is Staged Revascularization of Non-Infarct-Related Artery Chronic Total Occlusion Beneficial in Patients with Acute Myocardial Infarction? A Systematic Review and Meta-analysis

M. Yusuf<sup>1</sup>, L.A. Chandra<sup>1</sup>, M.F.A. Zaky<sup>1</sup>, A.D. Subali<sup>1</sup>, Y. Waranugraha<sup>2</sup>

Medical Profession Program, Faculty of Medicine, Brawijaya University, Malang<sup>1</sup>

Department of Cardiology and Vascular Medicine, Faculty of Medicine, Brawijaya University, Malang<sup>2</sup>

**Background and aims:** Coronary chronic total occlusion (CTO) is defined as a complete occlusion of a coronary artery without any antegrade blood flow. In the recent guidelines, uncertainty remains for the treatment of CTO concurrent with acute myocardial infarction (AMI). This study aims to investigate the outcomes of undergoing CTO-PCI for AMI patients in several comparison settings.

**Methods:** A systematic review based on PRISMA guidelines was carried out through PubMed, ScienceDirect, ProQuest, and EuropePMC. Randomized controlled trials (RCTs) and cohort studies that compared the cardiac death and major adverse cardiac events (MACE) of performing versus not performing PCI on coexisting non-infarct-related artery (non-IRA) CTO of AMI patients were included. The risk of bias was assessed using Cochrane RoB 2.0 for RCTs and Newcastle Ottawa Scale (NOS) for cohort studies. The pooled effect was reported as a random odd ratio (OR) and 95% confidence interval (CI).

**Results:** Initially, 11,261 articles were identified from the electronic scientific databases. After the detailed screening, one RCT and ten cohort studies were included. Six studies only included patients with STEMI, whereas the other included both STEMI and NSTEMI patients. A total of 2,274 patients with AMI divided into CTO-PCI (n=1186) or non-CTO-PCI (n=1088) were involved in the analysis. The risk of bias was low and the follow-up duration ranged from 1 year to 6 years in all studies. Cardiac death and MACE were significantly lower in the CTO-PCI group (OR [95%CI] = 0.29 [0.19-0.46] and 0.45 [0.34-0.59], respectively), especially in STEMI populations. The positive effect mainly arose from the comparison of successful CTO-PCI versus either failed CTO-PCI or the combination of failed CTO-PCI/no CTO-PCI attempted. Publication bias was not found.

**Conclusion:** Successful CTO revascularization is associated with more favorable clinical outcomes in AMI patients.

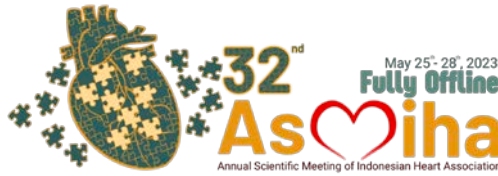
**Keywords:** chronic total occlusion, myocardial infarction, percutaneous coronary intervention, revascularization

Table 2. Summary of Follow up Outcomes Comparing CTO-PCI and No CTO-PCI

Outcome or Subgroup	Studies	Participants	OR	95% CI	P	I <sup>2</sup> (%)	Effect model
<b>1. Cardiac death</b>	11	2274	<b>0.29</b>	<b>0.19-0.46</b>	<b>&lt; 0.00001</b>	<b>40</b>	Random
Based on clinical diagnosis. Test for subgroup differences: Chi <sup>2</sup> = 0.86, df = 1 (P = 0.35), I <sup>2</sup> = 0%							
1.1 Cardiac death in AMI	5	812	0.24	0.14-0.41	< 0.00001	6	Random
1.2 Cardiac death in STEMI	6	1462	0.37	0.18-0.77	0.007	57	Random
Based on comparison groups. Test for subgroup differences: Chi <sup>2</sup> = 1.97, df = 2 (P = 0.37), I <sup>2</sup> = 0%							
1.3 Successful CTO-PCI vs Failed CTO-PCI	2	318	0.30	0.13-0.69	0.004	0	Random
1.4 CTO-PCI vs No CTO-PCI	2	518	1.82	0.10-33.34	0.69	63	Random
1.5 Successful CTO-PCI vs No CTO-PCI or Failed CTO-PCI	7	1438	0.24	0.17-0.35	< 0.00001	0	Random
<b>2. MACE</b>	8	1760	<b>0.45</b>	<b>0.34-0.59</b>	<b>&lt; 0.00001</b>	<b>24</b>	Random
Based on clinical diagnosis. Test for subgroup differences: Chi <sup>2</sup> = 0.18, df = 1 (P = 0.67), I <sup>2</sup> = 0%							
2.1 MACE in AMI	2	262	0.52	0.27-1.01	0.05	0	Random
2.2 MACE in STEMI	6	1441	0.44	0.32-0.62	< 0.00001	44	Random
Based on comparison groups. Test for subgroup differences: Chi <sup>2</sup> = 6.69, df = 2 (P = 0.04), I <sup>2</sup> = 70.1%							
2.3 Successful CTO-PCI vs Failed CTO-PCI	2	318	0.44	0.25-0.77	0.004	0	Random
2.4 CTO-PCI vs No CTO-PCI	1	302	1.05	0.52-2.10	0.90	NA	Random
2.5 Successful CTO-PCI vs No CTO-PCI or Failed CTO-PCI	5	1083	0.39	0.30-0.51	< 0.00001	0	Random

CTO-PCI, chronic total occlusion percutaneous coronary intervention; OR, odds ratio; CI, confidence interval; AMI, acute myocardial infarction; STEMI, ST-elevation myocardial infarction; MACE, major adverse cardiovascular event.

Summary of Follow up Outcomes Comparing CTO-PCI and No CTO-PCI



## Effect of Ramadan fasting on lipoprotein (a), apolipoproteins A-I, and B levels: a systematic review and meta-analysis

A. Adhyatma<sup>1</sup>, N.M. Nastiti<sup>1</sup>

Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Indonesia<sup>1</sup>

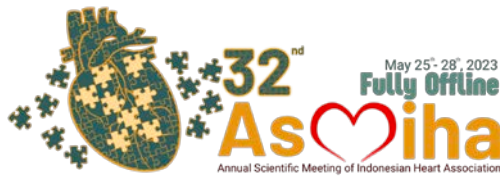
**Backgrounds and aims:** High levels of lipoprotein (a) [Lp(a)] is an independent risk factor for developing atherosclerotic cardiovascular diseases. Also, apolipoprotein A-I (apoA-I) and apolipoprotein B (apoB) have been suggested as predictors of cardiovascular events. Recent studies showed that intermittent fasting has been associated with an improved lipid profile. In this study, we aimed to investigate the effect of Ramadan fasting on Lp(a), apoA-I, and apoB levels.

**Methods:** PubMed and Google Scholar databases were searched for eligible studies up to February 2023. Observational studies comparing the levels of Lp(a), apoA-I, and apoB between the pre- and post-Ramadan fasting periods were included. The mean difference estimates were pooled by random-effect models with a 95% confidence interval (CI).

**Results:** We included 8 studies in this meta-analysis. At the post-Ramadan fasting period, we found a significant decrease in Lp(a) serum levels by 2.65 mg/dL (95% CI = -5, -0.31,  $I^2 = 0\%$ ,  $p = 0.03$ ) and apoB serum levels by 4.84 mg/dL (95% CI = -9.17, -0.51,  $I^2 = 53\%$ ,  $p = 0.03$ ), compared to the pre-Ramadan fasting period. Further, we also found a reduction in apoA-I serum levels at the post-Ramadan fasting period by 2.54 mg/dL, however, it was not statistically significant (95% CI = -19, 13.93,  $I^2 = 87\%$ ,  $p = 0.76$ ).

**Conclusions:** This study suggests that Ramadan fasting may be associated with a protective cardiovascular effect by lowering Lp(a) and apo B serum levels. However, there are a very limited number of participants included in this meta-analysis. Thus, further studies with a larger number of cohorts are warranted to elaborate more on this association.

**Keywords:** Ramadan fasting, lipoprotein (a), apolipoprotein A-I, apolipoprotein B



## Diurnal Variation Effect of Acetylsalicylic Acid Intake on Blood Pressure: A Systematic Review, Meta Analysis and Meta Regression of Randomized Controlled Trial

I. Ivan<sup>1</sup>, M.E. Ananta<sup>2</sup>, F. Budiman<sup>1</sup>, B. Widyantoro<sup>3</sup>

Faculty of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia<sup>1</sup>

Faculty of Medicine, Alumnus of Universitas Indonesia, Jakarta, Indonesia<sup>2</sup>

Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of Indonesia, National Cardiovascular Center of Harapan Kita, Jakarta, Indonesia<sup>3</sup>

### BACKGROUND

Evidence from chronotherapy studies suggested that acetylsalicylic acid may improve blood pressure. This systematic review aims to investigate the diurnal variation effect of acetylsalicylic acid intake in reducing blood pressure and other modifying factors that influence its outcome.

### METHODS

This systematic review followed PRISMA 2020 guidelines. We searched Cochrane Library, EBSCO, ProQuest, and PubMed for randomized-controlled trials published from inception until 17 March 2023. We include studies comparing the systolic/diastolic blood pressure (SBP/DBP) reduction effect after morning versus bedtime acetylsalicylic acid intake in hypertension patients. The mean difference of BP reduction between groups was pooled using random effects meta-analyses. Meta-regression was performed to examine potential confounders: age, sex, SBP/DBP pre-treatment, aspirin intake duration, diabetes mellitus (DM), coronary artery disease (CAD), stroke, type of prevention, and sample size. The quality of studies was evaluated using Cochrane RoB 2. Certainty of evidence was explored using the GRADE approach.

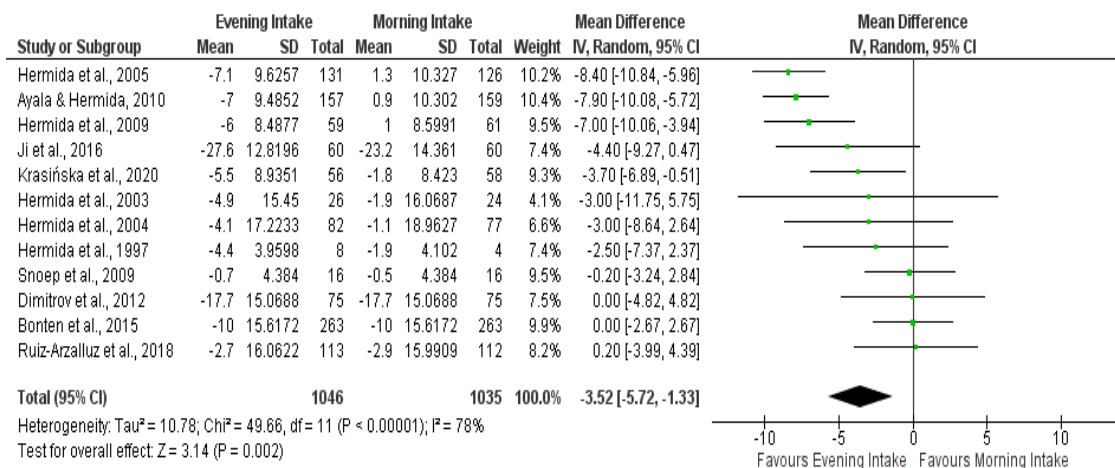
### RESULT

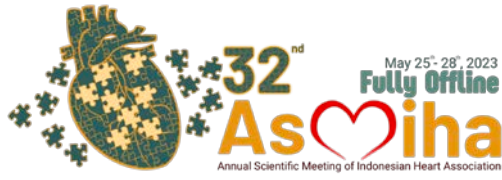
Search strategy identified 727 articles. Twelve randomized-controlled trials with 2081 patients met inclusion criteria. Cochrane RoB 2 showed some concerns for performance and attrition bias in 8 studies and 1 study, respectively. Bedtime acetylsalicylic acid intake has a significant SBP reduction (MD:-3.52;95%CI,-5.72 - -1.33;p<0.00001;I<sup>2</sup>=78%) and DBP reduction (MD: -2.5;95%CI,-3.82 - -1.18;p=0.001;I<sup>2</sup>=64%) compared to morning intake. No publication bias based on Egger's test (p=0.16) and rank correlation test (p=0.8). GRADE approach showed low and moderate certainty of evidence for SBP and DBP reduction, respectively. Meta-regression showed that a smaller magnitude of BP reduction was influenced by older age (p<0.0001), shorter aspirin intake duration (p=0.0196), male sex (p<0.0001), DM (p=0.0451), CAD (p=0.0301), and stroke history (p=0.0342).

### CONCLUSION

Acetylsalicylic acid intake during bedtime contributes to more blood pressure reduction compared to the morning. However, the effect magnitude is influenced by age, aspirin intake duration, sex, and comorbidities such as DM, CAD, and stroke history.

**Keywords:** acetylsalicylic acid, hypertension, chronotherapy, meta-analysis, meta-regression





## Indonesian Journal of Cardiology

Indonesian J Cardiol 2023;44:suppl\_A  
pISSN: 2830-3105 / eISSN: 2964-7304  
doi: 10.30701/ijc.1536

Forest Plot for Mean Difference of Systolic Blood Pressure Reduction after Acetylsalicylic Acid Evening Intake  
Compared to Morning Intake



## Comparison of Different Furosemide Regimens as Acute Decompensated Heart Failure Treatment – An Updated Systematic Review and Meta-Analysis

A. Alamsyaputra<sup>1</sup>, I.P. Farissa<sup>1</sup>, Safir<sup>1</sup>, L.D. Pradipta<sup>1</sup>  
RSUP Dr. Kariadi Semarang / Universitas Diponegoro<sup>1</sup>

### Background and aims

In patients with acute decompensated heart failure (ADHF), loop diuretics continue to play important role as component of the pharmacological treatment. It would be very advantageous to improve the management of such patients if we had a better understanding of the more efficient form of administration of loop diuretics. This meta-analysis set out to compare the efficacy of continuous versus bolus furosemide in treating patient with ADHF.

### Methods

We searched PubMed, ScienceDirect, and Scopus for studies that examined the efficacy of continuous versus intermittent of furosemide in acute decompensated heart failure patients between 2017 to March 2023. The primary endpoints included all-cause mortality, total length of stay, 48-hour reduction of body weight, 48-hour total urine output, 48-hour sodium-potassium level change, and the increase of 48-hour creatinine serum.

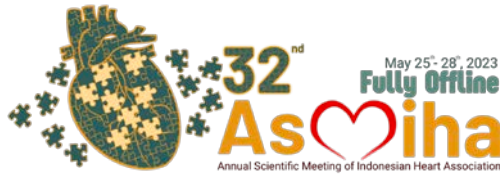
### Results

There were total of 7 studies with 732 participants, comprising 369 patients who received continuous furosemide administration and 363 patients who received intermittent furosemide administration. The analysis results showed no significant differences in all-cause mortality (OR = 0.84, 95% CI (0.42 – 1.7), p = 0.63); total length of stay (MD = -0.27, 95% CI (-3.54 – 3.0), p = 0.87); reduction of body weight (MD = -0.48, 95% CI (-1.34 – 0.38), p = 0.28); total urine output (MD = -0.43, 95% CI (-0.92 – 0.06), p = 0.08); hyponatremia (MD = 0.54, 95% CI (-0.57 – 1.65), p = 0.34); hypokalemia (MD = -0.05, 95% CI (-0.21 – 0.11), p = 0.54), increase of creatinine (MD = -0.00, 95% CI (-0.15 – 0.14), p = 0.96) between the 2 groups.

### Conclusion

There were no differences between two furosemide administration methods with regard to mortality, length of stay, reduction of body weight, urine output, incidence of hyponatremia-hypokalemia, and the raised of creatinine serum.

### Keywords:



## The Determinants of Slow/No-Reflow Phenomenon After Percutaneous Coronary Intervention in Patient with Acute Coronary Syndrome – A Systematic Review and Meta-Analysis

A. Alamsyaputra<sup>1</sup>, I.P. Farissa<sup>1</sup>, Bahrudin<sup>1</sup>, Y. Herry<sup>1</sup>, L.D. Pradipta<sup>1</sup>  
RSUP Dr. Kariadi Semarang / Universitas Diponegoro<sup>1</sup>

### Background and aims

The slow/no-reflow phenomenon is the most prominent example of clinical failure associated with cardiac reperfusion particularly in the setting of acute coronary syndrome (ACS). Patients who have slow/no-reflow have much greater chance of developing problems such as decreased systolic function, remodeling of the heart muscle, dilatation, left ventricular aneurysm, and death. In this meta-analysis, we sought the possibility of predisposition for slow/no-reflow which could be related with both local and systemic factors.

### Methods

Multiple databases including *PubMed*, *Scopus*, and *ScienceDirect* database were searched for relevant studies from 2010 – 2023. Seventeen screened literatures were assessed further for its variables which could increase or reduce risk of slow/no-reflow phenomenon after intervention in patient with ACS. RevMan 5.4 software was used to compile and show the summary of included studies through a random or fixed effect model. The quality of research methods was evaluated using Newcastle Ottawa Scale tool.

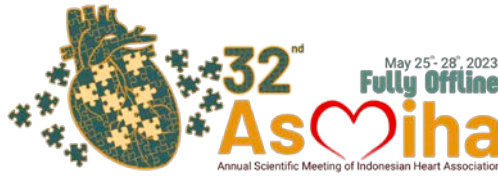
### Results

Of 17 studies, with total 14.001 patients, we found that increasing risks of slow/no-reflow were associated with advanced age, hypertension, family history of coronary artery disease, cerebrovascular disease, left anterior descending artery as culprit, direct stenting, low ejection fraction (EF) on admission, high creatinine level, initial TIMI flow <3, Killip class >1 at presentation, longer stent implantation, and thrombus grade >3. While balloon predilatation, thrombus aspiration, and GPIIb-IIIa usage could reduce the risk. Moreover, initial TIMI flow <3, longer stent implantation, and low EF on admission had the greater impact on slow/no-reflow phenomenon (OR95%CI = 3.7 [2.32 – 5.88],  $p < 0.0001$ , OR95%CI = 3.35 [1.5 – 7.35],  $p = 0.01$ , and OR95%CI = 3.3 [1.2 – 5.0],  $p < 0.0001$ , respectively).

### Conclusion

Our meta-analysis shows that initial TIMI flow <3, longer stent implantation, and low EF on admission are the strongest predictors of slow/no-reflow risk factors.

### Keywords:



## Factors Associated with the Development of Stent Thrombosis Following Primary Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis

A. Alamsyaputra<sup>1</sup>, I.P. Farissa<sup>1</sup>, S. Herminingsih<sup>1</sup>, L.D. Pradipta<sup>1</sup>  
RSUP Dr. Kariadi Semarang / Universitas Diponegoro<sup>1</sup>

### Background and aims

Stent thrombosis is an uncommon but dangerous complication of primary percutaneous coronary intervention (PPCI). In recent years, the development of stent thrombosis has been associated with an abundance of predictive and prognostic value. This study aims to examine each component that could predict the occurrence of stent thrombosis in patients who successfully underwent PPCI.

### Methods

Several databases, including PubMed, Scopus, and ScienceDirect, were queried for relevant research published before March 2023. Eleven literatures were evaluated further for characteristics that could increase the likelihood of stent thrombosis following PPCI procedure. RevMan 5.4 was utilized to build and display a summary of the included research using a random or fixed effect model. Using the Newcastle-Ottawa Scale, the quality of research methodologies was determined.

### Results

From a total of 11 research, we drew the conclusion that an increasing risk of stent thrombosis was related with advanced age (OR = 1.95, 95% CI (1.2 – 2.93),  $p < 0.0001$ ), diabetic mellitus (OR = 1.2, 95% CI (1.05 – 1.72), chronic kidney disease (OR = 2.11, 95% CI (1.45 – 3.07),  $p < 0.0001$ ), previous PCI (OR = 2.57, 95% CI (1.29 – 5.12),  $p = 0.007$ ), and Killip class >1 on presentation (OR = 1.88, 95% CI (1.2 – 3.5),  $p = 0.04$ ).

### Conclusion

Advanced age, history of diabetic mellitus, history of chronic kidney disease, previous PCI, and Killip class more than 1 on presentation, were associated with increased risk of stent thrombosis in patient who underwent PPCI.

### Keywords:



## **Low-Dose Colchicine Reduce Future Ischemic Cardiovascular Events in Coronary Artery Disease : A Systematic Review**

F.H. Ahmad<sup>1</sup>, A. Octaxena<sup>2</sup>, V. M. Arthacya<sup>1</sup>, R.H. Wibowo<sup>1</sup>

Department of Cardiology and Vascular Medicine, Cibabat General Hospital, Cimahi, Indonesia<sup>1</sup>

Department of Cardiology and Vascular Medicine, Sumedang General Hospital, Sumedang, Indonesia<sup>2</sup>

### **Background**

Colchicine is a widely available, safe, and low-cost drug in Indonesia. Colchicine acts through the inhibition of adhesion molecules and cytokines, and the pyrin domain-containing protein 3 inflammasome, an intracellular innate receptor that its activation results in release of the pro-inflammatory cytokines IL-1 $\beta$  and IL-18 which known to drive atherosclerotic plaque progression and increase the risk for instability. We performed a systematic review to determine the benefit of using low dose colchicine to reduce ischemic cardiovascular events in patients with coronary artery disease.

### **Method**

A systematic search in electronic databases of Science Direct were carried out to identify eligible studies. We search with the keywords of "[chronic coronary syndrome OR stable angina) AND (prior acute coronary syndrome OR unstable angina OR myocardial infarction)] AND Colchicine AND (recurrent unstable angina or myocardial infarction OR re-ischemic cardiovascular event)". Only randomized controlled trials evaluating the cardiovascular effects of colchicine in coronary artery disease were included

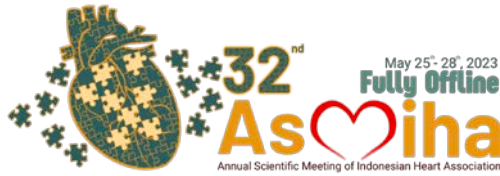
### **Result**

We sorted 732 titles from both search engine and 103 titles were accepted through thorough screening. The sorted 103 abstracts were screened and we finally included 8 controlled trials that meet our criteria. Study by Tardif et al, Nidorf et al, and Bouabdallaoui et al finds that low dose colchicine significantly reduce future myocardial infarction or ischemia. Study by Opstal et al shows that the benefits of colchicine are consistent to reduce myocardial infarction, or ischemia-driven coronary revascularization. The safety of using low-dose colchicine showed by Opstal et al was not associated with an adverse effect on any specific cause of death.

### **Conclusion**

Colchicine should be considered as adjuvant therapy for coronary artery disease considering its benefits and safety, although its evidence to reduce all-cause mortality in patients with coronary artery disease should undergo more investigation in the future.

**Keywords:** low-dose colchicine, coronary artery disease



## The Role of Ivabradine in Heart Failure Therapy: A Systematic Review

R.R. Dewi<sup>1</sup>, R.A. Siburian<sup>1</sup>, F.D. Atikah<sup>1</sup>, M.S. Tiyantara<sup>1</sup>, W. Nirwana<sup>1</sup>, A. Kurniawan<sup>1</sup>, R.A. Hidayat<sup>1</sup>, L.G. P. Rinjani<sup>1</sup>, R.E. Intan<sup>1</sup>, S.F. Karundeng<sup>1</sup>, A.K. Ratri<sup>1</sup>  
Cardiology and Vascular Medicine Department, Faculty of Medicine, Airlangga University<sup>1</sup>

**Background:** Ivabradine has been recommended as an adjuvant therapy for heart failure (HF) and should be considered in patients already on beta-blockers with sinus rhythm and heart rate > 70 beats per minute. However, the effect of ivabradine on cardiovascular outcomes is still unclear. We conducted a systematic review to investigate the effectiveness and safety of ivabradine in HF individuals.

**Method:** We searched PubMed, Cochrane Library, ScienceDirect, Scopus, and ProQuest databases in March 2023. We systematically reviewed twenty-five studies divided into the ivabradine, combination ivabradine and beta-blockers, and control groups. We analyzed its effect directly on cardiovascular outcomes, such as its effect on left ventricular ejection fraction (LVEF), heart rate, etc. We also assessed its impact on mortality, hospitalization time during follow-up, quality of life, and safety.

**Result:** This systematic review involved twenty-five studies with a subject of 33.010 patients. The results of the studies showed a promising trend in the outcome of the ivabradine combination group. All the studies stated improved cardiovascular and all-cause mortality and hospitalization. For the New York Heart Association (NYHA) functional class, exercise capacity, and quality of life, the study consistently showed improvement in the group of ivabradine add-on in the standard therapy. The addition of ivabradine showed significant improvement in left ventricular ejection fraction and diastolic function (i.e. e/e' ratio, deceleration time). A study showed that the ivabradine or the ivabradine add-on with the beta-blockers group improved LVEF better than the beta-blockers group alone. Better heart rate reduction without blood pressure alteration was demonstrated in the studies with the addition of ivabradine.

**Conclusion:** Ivabradine treatment in HF individuals improved cardiovascular outcomes and quality of life. Also, ivabradine decreased heart rate, improved exercise capacity, and was safe to be used.

**Keywords:** ivabradine, beta-blockers, heart failure, cardiovascular outcomes

## Efficacy of Acetazolamide to Ameliorate Congestion in Heart Failure: A Systematic Review and Meta-Analysis

T.F. Duta<sup>1</sup>, P.O. Zulfa<sup>1</sup>, M. Alina<sup>1</sup>, N. Henira<sup>1</sup>, G. Tsurayya<sup>1</sup>

Medical Research Unit, School of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia 23111<sup>1</sup>

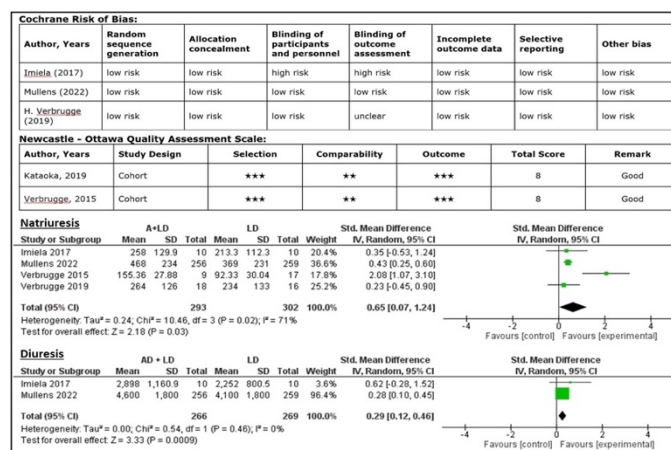
**Background :** High risk in developing congestion during heart failure (HF) urges the discovery of more efficacious treatment, of which is the use of acetazolamide as the adjunct therapy. Herein, we aimed to investigate the effectiveness of acetazolamide in ameliorating diuresis and natriuresis among HF patients with congestion by means of systematic review and meta-analysis.

**Method :** Randomized controlled trials (RCTs) and cohort studies were searched on PubMed, Scopus, and Embase on 7 March 2023 by using combinations of ‘acetazolamide’, ‘heart failure’ and along with their respective synonyms. The studies must investigate the effect of oral acetazolamide as the add-on to loop diuretic (LD) therapy with control (LD only) to be included. Successful decongestion, natriuresis and diuresis were set as the primary outcomes. Non-English records were excluded. Quality appraisal was performed on the included studies, where Cochrane ‘risk-of-bias’ tool was used for randomized controlled trials and Newcastle Ottawa Scale – for observational studies. Records screening and selection (M.A. & N.H.) and quality appraisal (M.A. & T.F.D.) were performed by two independent reviewers. Continuous variables were calculated and expressed as standardized mean differences (SMD) with 95% confidence intervals (CI). Statistical significance and heterogeneity were judged based on *p*-value and *I*<sup>2</sup>, respectively.

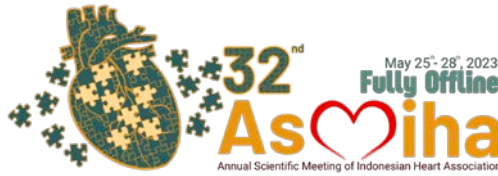
**Result :** We identified 1176 titles in the initial search, and further reduced to five studies (3 RCTs and 2 cohort studies) after in-depth screening. A total of 625 patients were recruited in the included studies published from 2015 to 2022. The overall quality of evidence was rated as moderate. Results from meta-analysis revealed that acetazolamide ameliorated natriuresis (n=4; SMD=0.65; 95%CI: 0.07–1.24; *p*=0.02) and diuresis (n=2; SMD=0.29; 95%CI: 0.12–0.46; *p*=0.46) when adjunct to loop diuretics.

**Conclusion :** Acetazolamide is efficacious in alleviating congestion in HF patients.

**Keywords:** Acetazolamide, efficacy, heart failure, loop diuretics, decongestion



Results from quality appraisal and meta-analysis on studies reporting the efficacy of acetazolamide in ameliorating congestion in heart failure



## The Effect of Levosimendan on Mortality and New York Heart Association (NYHA) Functional Class in Patients with Advanced Heart Failure: An Updated Meta-Analysis

P.A. Pratama<sup>1</sup>, I.C.S. Putra<sup>1</sup>, H.S. Prameswari<sup>1</sup>

<sup>1</sup>Department of Cardiology and Vascular Medicine, Faculty of Medicine Universitas Padjadjaran, Bandung, Indonesia<sup>1</sup>

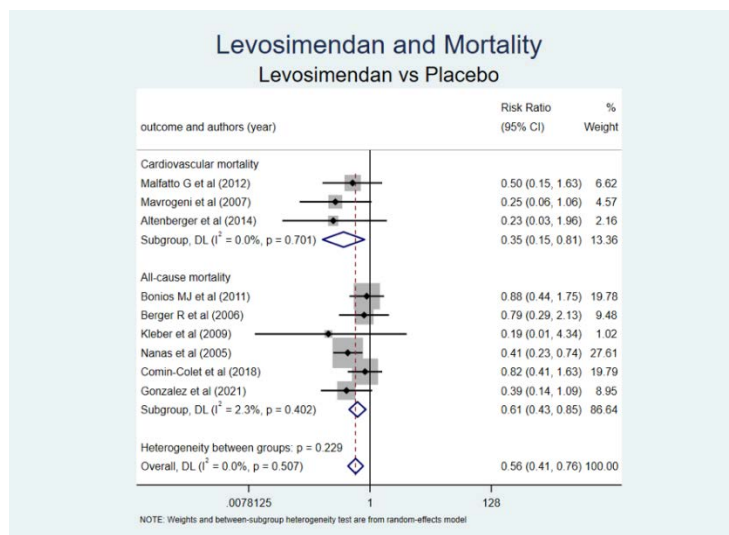
**Background and Aims** Studies have shown levosimendan has promising benefits for advanced heart failure (AdHF) patients in reducing mortality and rehospitalizations, hemodynamic improvements, and cardiovascular events. Previous meta-analyses showed positive results on the effect of levosimendan infusions on mortality and other parameters in AdHF patients; however, we arranged a more updated and comprehensive meta-analysis, including the most recent and extensive trials on levosimendan in AdHF patients and included NYHA functional class and blood pressure in the analysis.

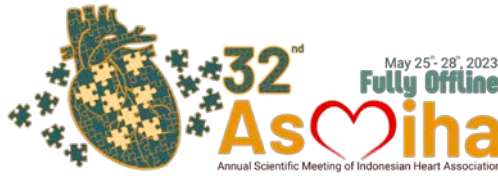
**Methods** PubMed, Scopus, the Cochrane Library of Clinical Trials, and the Europe PMC were searched for randomized clinical trials investigating the effect of intermittent levosimendan in AdHF patients. The literature search strategy identified 14 qualified studies. A meta-analysis was performed to analyze the impact of levosimendan on mortality, NYHA functional class, and blood pressure.

**Results** Levosimendan significantly reduced the risk of all-cause mortality (RR=0.61 (95% CI=1.43–0.85); P=0.003; I<sup>2</sup>=2.3%, P-heterogeneity=0.402) and cardiovascular mortality (RR=0.35 (95% CI=0.15–0.81); P=0.014; I<sup>2</sup>=0%, P-heterogeneity=0.701) compared to the control group. Levosimendan was also substantially associated with lower NYHA functional class compared to the control group (SMD=-1.14 (95% CI=(-1.84) – (-0.45)); P=0.001; I<sup>2</sup>=88.7%, P-heterogeneity<0.001). Upon a sensitivity analysis by excluding two studies, the heterogeneity was significantly reduced to 42% without altering its significance. However, Levosimendan was not correlated with systolic blood pressure (SMD=-0.02 (95% CI=(-0.26) – 0.21); P=0.839; I<sup>2</sup>=0%, P-heterogeneity=0.540) and diastolic blood pressure (SMD=-0.1 (95% CI=(-0.42) – (0.22)); P=0.530; I<sup>2</sup>=0%, P-heterogeneity=0.587).

**Conclusion** The meta-analysis supports the evidence that intermittent or repetitive levosimendan infusion is associated with mortality reduction and NYHA functional class improvement in patients with advanced chronic heart failure.

**Keywords:** levosimendan, advanced heart failure, mortality, NYHA





## Efficacy and Safety of Magnesium Sulfate as Adjunctive Therapy in Managing Atrial Fibrillation with Rapid Ventricular Response: A Systematic Review and Meta-Analysis

D.Sukmadja<sup>1</sup>, T. Tarigan<sup>2</sup>, K.C. Prasiddha<sup>3</sup>, S. Hayon<sup>4</sup>  
Hermina Hospital, Yogyakarta, Indonesia<sup>1</sup>  
Happy Land Medical Center, Yogyakarta, Indonesia<sup>2</sup>  
Yogyakarta Regional General Hospital, Yogyakarta, Indonesia<sup>3</sup>  
Sitnala General Hospital, Tangerang, Indonesia<sup>4</sup>

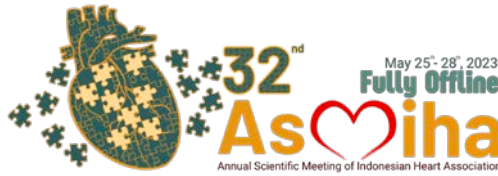
**Background and aims:** Atrial fibrillation (AF) is one of the most common arrhythmias that can cause significant morbidity and mortality. Magnesium sulfate (MgSO<sub>4</sub>) has been proposed as a potential treatment for AF in emergency settings, but its efficacy and safety remain debatable. This study aims to evaluate the efficacy and safety of magnesium sulfate in treating atrial fibrillation with a rapid ventricular response (AFRVR) in emergency settings.

**Methods:** Randomized controlled trials (RCTs) and observational studies were searched from Pubmed, Proquest, Google Scholar, and Cochrane Library databases. All studies that observed the efficacy of intravenous MgSO<sub>4</sub> as adjunctive to standard therapy in treating AFRVR patients in emergency department settings were included. The primary endpoints were mean ventricular rate reduction, successful rate control therapy, and conversion to sinus rate. The safety parameters were hypotension and bradycardia events.

**Results:** This study included 1899 AFRVR patients from 9 RCTs and 3 observational studies. When compared to placebo, the addition of intravenous MgSO<sub>4</sub> to standard therapy showed a greater reduction of ventricular rate (mean difference: 8.06; p < 0.001; 95% CI: 4.28-11.58), more successful rate control to below 100 bpm (RR: 1.43; p: 0.02; 95% CI: 1.05-1.95) and higher sinus conversion rate (RR: 1.80; p: 0.02; 95% CI: 1.02-1.37). There was no significant difference in safety parameters, including hypotension (RR 2.40; p: 0.25; 95% CI: 0.53-10.81) and bradycardia events (RR 1.57; p: 0.67; 95% CI: 0.20-12.70).

**Conclusion:** MgSO<sub>4</sub> as adjunctive therapy provided better outcomes in rate and rhythm management of AFRVR in the emergency department settings with similar safety profiles.

**Keywords:** magnesium sulfate, atrial fibrillation, rate control, cardioversion



## **Bempedoic Acid for Hypercholesterolemia, The Efficacy and Its Effect in Statin-intolerance Patients : Systematic Review of Randomized Controlled Trials**

C.F. Jhoputri<sup>1</sup>, L. Julian<sup>1</sup>, E. Vinsky<sup>1</sup>, W.S. Atmaja<sup>1</sup>, V.A. Damay<sup>2</sup>, V. Fernhandho<sup>1</sup>  
Faculty of Medicine, University of Pelita Harapan<sup>1</sup>

Department of Cardiology and Vascular, Faculty of Medicine, Pelita Harapan University, Banten, Indonesia<sup>2</sup>

### **Background**

Statins are the cornerstone of atherosclerotic cardiovascular disease prevention and the primary treatment for hypercholesterolemia. Statin intolerance, which describes a range of negative side effects and symptoms related to statins, has been observed in 5% to 30% of people with hypercholesterolemia. Additional treatment options needed for patients who are unable to achieve desired lipid levels with statin therapy. Bempedoic acid—an ATP citrate lyase inhibitor that prevents cholesterol biosynthesis—is one of the choices. However, there has not been much study done on its effectiveness and safety. This study evaluate the efficacy and safety of bempedoic acid therapy in patients with hypercholesterolemia and statin intolerance.

### **Method**

All studies were derived from PubMed, PMC, and Science Direct by keyword “*Hypercholesterolemia*” and “*bempedoic acid*” and “*statin*”. The search was occurring from March 5<sup>th</sup>, 2023 until March 10<sup>th</sup>, 2023. Three authors searched, extracted, and evaluated the studies with inclusion criteria as RCTs within the last five years. We excluded studies on patients under 18 years old, animal studies and irretrievable full text articles. The NewCastle Ottawa Scale (NOS) was used to determine the quality of the included studies.

### **Result**

Six RCTs were included after screening with a total of 8494 Hypercholesterolemia patients with statin-intolerance aged 18-75 years. All six studies showed bempedoic acid compared with placebo present as a safe and effective therapeutic option for significantly lowering LDL-C level among statin-intolerant hypercholesterolemia patients without resulting higher incidence of overall adverse event. During quality assessment using NOS, five studies showed to be in good quality and one study is fair in quality.

### **Conclusion**

Bempedoic acid is recommended as a treatment option due to its effect on lowering LDL-C levels in hypercholesterolemia patients with statin intolerance.

**Keywords:** Bempedoic Acid, Hypercholesterolemia, Hydroxymethylglutaryl-CoA Reductase Inhibitors.



## **Predictors of In-Stent Restenosis After Percutaneous Coronary Intervention Using Drug Eluting Stent: A Systematic Review and Meta-Analysis**

A. Alamsyaputra<sup>1</sup>, I.P. Farissa<sup>1</sup>, I. Uddin<sup>1</sup>, L.D. Pradipta<sup>1</sup>  
RSUP Dr. Kariadi Semarang / Universitas Diponegoro<sup>1</sup>

### **Background and aims**

In-stent restenosis (ISR) may still occur in as many as 2–10% of percutaneous coronary interventions (PCI), even though drug-eluting stents (DES) are used. Individuals with ISR are considerably more likely to present with symptoms of unstable angina pectoris as compared to individuals with de novo stenosis. In this study we sought to determine predictors of ISR after coronary stenting.

### **Method**

Multiple databases including *PubMed*, *Scopus*, and *ScienceDirect* database were searched for relevant studies in English from 2012 – 2023. Full-text articles of studies are used to compare the various risk factors of ISR after DES stenting. Review Manager 5.4 was used to estimate the effects of those risk factors among eligible articles. The quality of research methods was evaluated using Newcastle Ottawa Scale.

### **Results**

There were total of 9 studies with 19853 participants, comprising 5040 patients with ISR and 14813 patients without ISR. The analysis results showed the increase risk of restenosis in patient with: diabetic mellitus (OR = 1.39, 95% CI (1.24 – 1.5),  $p < 0.0001$ ), hypertension (OR = 1.13, 95% CI (1.05 – 1.21),  $p = 0.0006$ ), previous PCI (OR = 1.8, 95% CI (1.22 – 2.66),  $p = 0.003$ ), previous CABG (OR = 1.36, 95% CI (1.22 – 1.53),  $p < 0.0001$ ), low EF (OR = 2.2, 95% CI (1.2 – 4.2),  $p = 0.04$ ), multivessel disease (OR = 2.48, 95% CI (2.3 – 2.7),  $p < 0.0001$ ), chronic total occlusion (OR = 1.91, 95% CI (1.65 – 2.2),  $p < 0.0001$ ), ACC/AHA type B2/C lesion (OR = 1.6, 95% CI (1.4 – 1.7),  $p < 0.0001$ ), and left main lesion (OR = 1.88, 95% CI (1.5 – 2.4),  $p < 0.0001$ ).

### **Conclusion**

Our meta-analysis shows that diabetic mellitus, hypertension, previous PCI, previous CABG, low EF, multivessel disease, CTO, ACC/AHA type B2/C lesion, and left main lesion are the predictors of in-stent restenosis.

### **Keywords:**

## Analysis of C-Reactive Protein and BNP Levels in Peripartum Cardiomyopathy Patient for Recovery and Prognostic Evaluation: A Systematic Review

R.A. Rianda<sup>1</sup>, E.P.B. Mulia<sup>2</sup>, N.N. Humaera<sup>1</sup>

Dompu Regional General Hospital, West Nusa Tenggara, Indonesia<sup>1</sup>

Department of Cardiology and Vascular Medicine Dr. R. Soetrasno General Hospital, Rembang, Indonesia<sup>2</sup>

**Background and Aims.** Recent studies suggested potential C-Reactive Protein and BNP Level as a predictor outcome for Peripartum Cardiomyopathy (PPCM) patients. We performed a systematic review to evaluate the capability of C-Reactive Protein and BNP level as an evaluating marker in patient with PPCM.

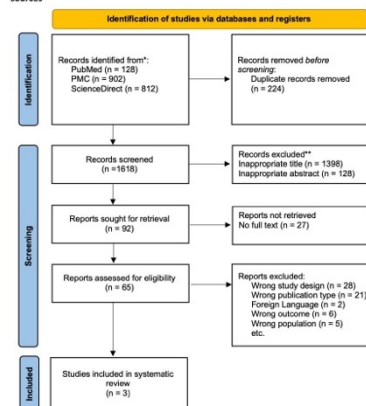
**Methods.** This study was performed according to PRISMA2020. We included articles from January 2013-March 2023. A systemic literature search using PubMed, PMC, and ScienceDirect was performed. We used terms “Peripartum Cardiomyopathy”, “C-Reactive Protein”, “BNP”, “Severity”, and “Prognosis” as keywords combined by using OR and AND operators. These studies looked at correlation between CRP and BNP with patient’s recovery and prognosis status.

**Result.** There are 1618 articles from all databases. 3 study were included with 134 of total sample was diagnosed with PPCM, with 47 patients had an uncomplete recovery. We found patients who had uncomplete recovery had CRP levels above the normal limit in direct proportion with BNP and CRP levels. Weping Li, et.al (2015) reported there was a positive correlation between elevated BNP and unrecovery condition ( $r=0.559$ ;  $p<0.001$ ). In uncomplete recovery group 7 patients increase their BNP level about 101-100pmol/L, and 24 patients had BNP level  $>1000$  pmol/L, with CRP level was reported 11-100mg/L in 28 patients. Other study showed that 6<sup>th</sup> month evaluation of BNP levels were significantly higher in patients who died compared to patients who survived ( $5.9\pm0.8$  vs  $4.7\pm1.1$ ,  $p=0.002$ ) with CRP comparison between recovery and non-recovery group in 6<sup>th</sup> month follow-up ( $2.4\pm1.7$  vs  $3.0\pm2.4$ ,  $p=0.031$ ). Wang et.al (2018) was reported same result which compare between PPCM patient with control sampling (CRP, mg/L  $38.8\pm12.8$  vs  $11.8\pm8.9$   $p<0.001$ ) and (BNP, pg/mL  $710.6\pm285.4$  vs  $102.2\pm42.7$   $p<0.001$ ).

**Conclusions.** The elevated levels of BNP and CRP were associated with non-recovery condition and mortality in PPCM patient.

**Keywords:** Peripartum Cardiomyopathy, C-Reactive Protein, Brain Natriuretic Peptide, Recovery, Prognostic

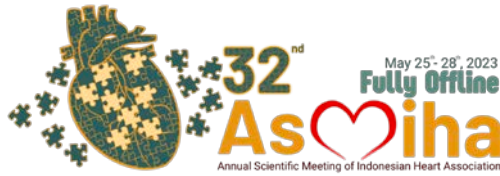
PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources



\*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

\*\*If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi:10.1136/bmj.n71. For more information, visit: <https://www.prismastatement.org>



**Clinical Outcome of Fractional Flow Reserve-Guided Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting in Patients with Left Main or Multivessel Disease: A Systematic Review and Meta-Analysis: A Systematic Review and Meta-analysis**

D. Sukmadja<sup>1</sup>, S. Hayon<sup>2</sup>, R. Triatmaja<sup>3</sup>, K.C. Prasiddha<sup>4</sup>  
Hermina Hospital, Yogyakarta, Indonesia<sup>1</sup>

Sitanala General Hospital, Tangerang, Indonesia<sup>2</sup>

Faculty of Medicine and Health Science, Universitas Muhammadiyah Yogyakarta, Yogyakarta, Indonesia<sup>3</sup>  
Yogyakarta Regional General Hospital, Yogyakarta, Indonesia<sup>4</sup>

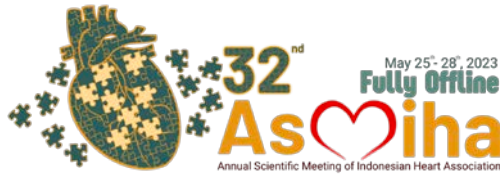
**Background and aims:** Fractional Flow Reserve-Guided Percutaneous Coronary Intervention (FFR PCI) has shown beneficial effects in treating left main and multivessel disease. However, its efficacy compared with coronary artery bypass grafting (CABG) is still not determined. This meta-analysis aims to compare the clinical outcome of FFR PCI and CABG in patients with left main or multivessel disease.

**Methods:** Studies from Pubmed, Proquest, Google Scholar and Cochrane Library databases which compare the clinical outcome of FFR PCI and CABG in patients with left main or multivessel disease were included. The primary outcome parameters were all-cause death, cardiovascular death, target vessel revascularization, stroke and myocardial infarction events.

**Results:** 2978 left main and multivessel disease patients from 3 randomized controlled trials were included in this study. It was found that CABG provide lower target vessel revascularization events (RR: 2.15; p: 0.005; 95% CI 1.26-3.67) than FFR PCI in the left main or multivessel patients. There was no significant difference between the two groups in all cause death (RR: 1.13; p: 0.53; 95% CI 0.77-1.65), cardiovascular death (RR: 1.01; p: 0.96; 95% CI 0.70-1.47), stroke (RR: 0.84; p: 0.57; 95% CI 0.47-1.53), and myocardial infarction (RR: 1.17; p: 0.49; 95% CI 0.76-1.80) events.

**Conclusion:** FFR PCI showed similar numbers from most of the clinical outcome compared with CABG in left main or multivessel patients. However, target vessel revascularization event was lower in CABG patients.

**Keywords:** FFR, PCI, CABG, multivessel



## Effects of Tolvaptan in Hospitalized Patient with Heart Failure : Systematic review

N.B.S.A. Purushotama<sup>1</sup>, C.J. Budiarto<sup>1</sup>, Y.P. Yogobi<sup>1</sup>, M.G. Setiawan<sup>1</sup>, M.Z. Sabran<sup>1</sup>  
Faculty of Medicine, Universitas Pelita Harapan<sup>1</sup>

### Background and aim

Heart failure is a medical condition that arises due to a heart disorder that affects the filling or pumping of blood throughout the body. This syndrome is complex and widespread, affecting over 23 million people worldwide. Tolvaptan is a new medication that can be taken orally and functions as a vasopressin V2 receptor antagonist, promoting the excretion of free water from the body. The aim of this study is to evaluate the efficacy of tolvaptan in hospitalized patients with heart failure.

### Methods

Studies were systematically extracted from databases such as PubMed, PMC, Scencedirect, Elsevier, and Euro PMC using the keywords "Tolvaptan" AND "Heart Failure". Extracted studies were then analyzed and selected according to our inclusion and exclusion criteria. Inclusion criteria were cohort, randomized controlled trial, and retrospective study within the last ten years. Our exclusion criteria consisted of case report, case series studies, animal studies, meta analysis, systematic review, children, and unfull paper. All eligible studies were assessed using the New-Castle Ottawa Scale (NOS).

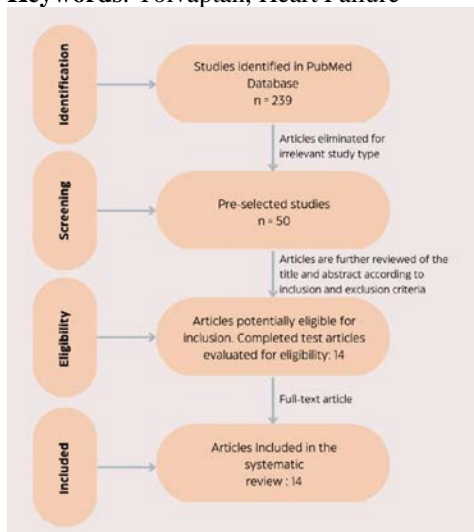
### Result

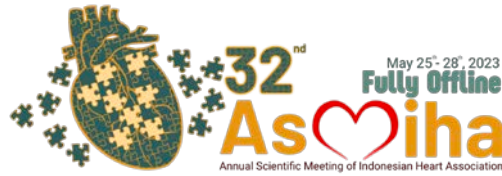
Through several inclusion criteria, A total of 14 (8 RCT, 4 CT, and 2 Cohort) out of 52 eligible studies were extracted. The studies included 6,653 patients, with heart failure, of age groups ranging from 55-90 years old. Based on our analysis, we found that in 7 studies, Tolvaptan is associated with significant reduction in heart failure complications; in-hospital use scenarios. However 7 studies also show no significant improvement after the use of Tolvaptan. All of the studies have been assessed to be of good quality based on the NOS criteria.

### Conclusion

Our study does not show significant improvement in patient with hospitalized heart failure. Further studies are still needed to support this study on Tolvaptan.

**Keywords:** Tolvaptan, Heart Failure





## Fluid Therapy in Cardiogenic Shock: Is It Appropriate?

H. Susilo<sup>1</sup>, C.D.K. Wungu<sup>2</sup>, C.E.C.Z. Multazam<sup>3</sup>, W. Widiarti<sup>3</sup>, D.S. Octaviana<sup>3</sup>

Department of Cardiology and Vascular Medicine, Universitas Airlangga Hospital, Surabaya, Indonesia<sup>1</sup>

Department of Physiology and Medical Biochemistry, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia<sup>2</sup>

Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia<sup>3</sup>

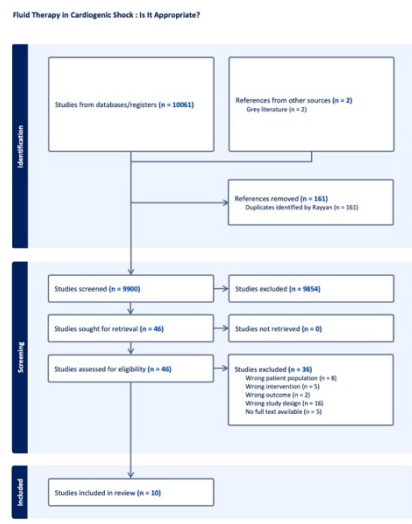
**Background and aims:** In the management of cardiogenic shock, fluid therapy plays an essential role in restoring intravascular volume and improving tissue perfusion. However, the application of fluid therapy in cardiogenic shock remains controversial because it must achieve sufficient volume to maintain adequate perfusion without inducing fluid overload. Thus, this systematic review aimed to analyze the outcome of fluid therapy in cardiogenic shock.

**Methods:** We conducted computerized data searching through PubMed, Scopus, and EBSCOHost. All related studies about fluid therapy in cardiogenic shock published in the last 10 years were screened. Quality assessment was conducted to minimize the risk of bias.

**Results:** 10 studies were reviewed. Various concomitant cardiovascular diseases were found, including ACS, HF, Takotsubo cardiomyopathy, and arrhythmia. Several studies demonstrated hemodynamic improvement after fluid administration, while others demonstrated otherwise. Numerous parameters can be utilized to evaluate fluid responsiveness through echocardiography including EVLWI, ITBVI, GEDVI, and VTI. Studies that did not demonstrate the advantage of fluid therapy in cardiogenic shock involved patients with exceptional comorbidities that required particular medical treatment based on its etiology.

**Conclusions:** The majority of studies exhibited positive outcomes of fluid therapy in cardiogenic shock patients. Several parameters should be monitored thoroughly to avoid fluid overload. Future studies are required to gather further evidence regarding fluid therapy in cardiogenic shock.

**Keywords:** cardiogenic shock, fluid therapy, hemodynamic



Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Chart



## COMPARING THE RISK OF THROMBOEMBOLIC EVENTS IN PATIENTS WITH ATRIAL FIBRILLATION ASSOCIATED WITH HYPERTHYROIDISM VERSUS PRIMARY ATRIAL FIBRILLATION: A SYSTEMATIC REVIEW

A. Parawangsa<sup>1</sup>, S.A. Nasution<sup>2</sup>

Faculty of Medicine, Universitas Indonesia<sup>1</sup>

Cardiology Division, Internal Medicine Department, Cipto Mangunkusumo National General Hospital, Faculty of Medicine, Universitas Indonesia<sup>2</sup>

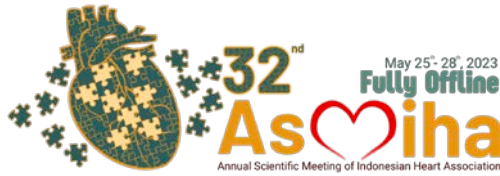
**Background:** Atrial fibrillation is a prominent type of arrhythmia with various complications, one of which is thromboembolic events that can occur mainly in the cardiovascular and cerebrovascular systems. Hyperthyroidism is a condition in which the thyroid produces more hormones than usual. Hyperthyroidism is one of the triggers for atrial fibrillation. Still, no studies conclude whether atrial fibrillation associated with hyperthyroidism differs in thromboembolic events compared to atrial fibrillation without hyperthyroidism.

**Methods:** A literature search was conducted on August 29, 2022, from three databases based on clinical questions and eligibility criteria. Then, the validity, importance, and application are assessed. The included studies were further ranked according to the level of evidence (LOE).

**Result:** There were seven included studies, three of which showed an increased risk of thromboembolism in patients with atrial fibrillation related to hyperthyroidism, two studies showed no significant difference, and two studies showed a lower risk.

**Conclusion:** There is no significant trend between thromboembolic events in patients with atrial fibrillation related to hyperthyroidism compared to non-thyroid atrial fibrillation.

**Keywords:** thromboembolism, atrial fibrillation, hyperthyroidism, risk factors, embolism



## Assessing the effect of azithromycin on the incidence of QTc prolongation in hospitalized COVID-19 patients

A. Parawangsa<sup>1</sup>, M.D. Darmawan<sup>1</sup>, R.M.R. Hadyansyah<sup>1</sup>, R.R. Felim<sup>1</sup>, T.A. Salsabila Djajasasmita<sup>1</sup>, M. Louisa<sup>2</sup>  
Faculty of Medicine, Universitas Indonesia<sup>1</sup>  
Department of Pharmacology and Therapeutics, Faculty of Medicine Universitas Indonesia<sup>2</sup>

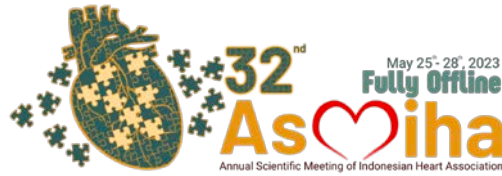
**Background:** Coronavirus disease 2019 (COVID-19) is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) and has been declared a worldwide pandemic. Azithromycin is one of the antibiotics of choice for treating COVID-19 patients with bacterial coinfections. However, several studies pointed out that using azithromycin with the standard therapy for hospitalized COVID-19 patients may lead to increased QTc prolongation, leading to cardiac arrhythmias. In the present review, we investigated the effect of azithromycin on top of COVID-19 standard treatment medications on the incidence of QTc prolongation.

**Method:** A literature search was conducted using four databases (PubMed, Scopus, Cochrane, and EBSCOhost) based on predetermined clinical questions and eligibility criteria. A critical appraisal of selected studies was done to assess each study's validity and importance using the CEBM Oxford Harm/Etiology worksheet.

**Results:** Eight studies were included, all considered valid after appraisal. All eight studies found no significant effect of adding azithromycin in standard therapy on the incidence of QTc prolongation.

**Conclusion:** The administration of combination therapy with COVID-19 standard treatment in the respective studies and azithromycin did not significantly associate with increased incidence of QTc prolongation.

**Keywords:** azithromycin, arrhythmia, COVID-19, adverse effects, QTc prolongation



## Electrocardiographic Left Ventricular Hypertrophy as Predictor of Coronary Heart Disease in Hypertensive Patients: A Meta-analysis

M.B. Rachmanadi<sup>1</sup>, S.M. Reza<sup>1</sup>, J. Rosa<sup>1</sup>, T. Kristianto<sup>1</sup>  
Rumah Sakit Umum Daerah Cabangbungin, Bekasi Regency, West Java, Indonesia<sup>1</sup>

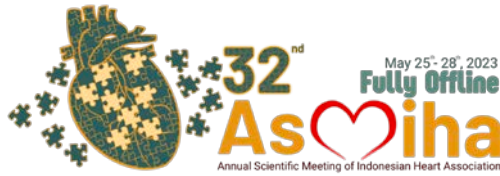
**Background and aims:** Electrocardiogram is commonly used to diagnose left ventricular hypertrophy (LVH) in clinical practice. LVH can be used to predict adverse prognoses in hypertensive patients. This meta-analysis aimed to investigate the association between electrocardiographic LVH and coronary heart disease in patients with hypertension.

**Methods:** We comprehensively searched PubMed databases until March 2023 to identify observational studies evaluating the association between electrocardiographic LVH (Sokolow-Lyon voltage, Cornell voltage, or Cornell product) and the risk of coronary heart disease among hypertensive patients. We calculated the pooled risk ratio (RR) using random or fixed effect and generic inverse variance methods. We used the Q test and  $I^2$  statistics to quantify and evaluate the heterogeneity. Data were analyzed using Review Manager 5.3.

**Results:** Five studies involving 48,212 hypertensive patients were enrolled. In comparison, with and without electrocardiographic LVH, the pooled RR of coronary heart disease was 1.49 (95% CI 0.87-2.54,  $I^2=67%$ ) for the Sokolow-Lyon voltage criteria, 1.34 (95% CI 1.16-1.55,  $I^2=0%$ ) for the Cornell voltage criteria, and 1.47 (95% CI 1.08-2.01,  $I^2=38%$ ) for the Cornell product criteria. Sensitivity analysis by omitting one study by turns showed no marked changes in the pooled risk estimates. Pooled RR of Cornell voltage and Cornell product were statistically significant.

**Conclusion:** Left Ventricular Hypertension detected by Cornell voltage or Cornell product can predict coronary heart disease among hypertensive patients. Detection of LVH using Cornell product appears to have better predictive value in the prediction of coronary heart disease in hypertensive patients.

**Keywords:** Electrocardiogram, Left Ventricular Hypertrophy, Coronary Heart Disease, Hypertension, Meta-analysis



## A Bibliometric Analysis of Global Publication and Trends in Cardiovascular Disease Research over the Last 5 Years

R. Mulawarman<sup>1</sup>, M. Trifitriana<sup>1</sup>, H. Mulawarman<sup>1</sup>, M.S. Ramadhan<sup>1</sup>  
Faculty of Medicine, Sriwijaya University, Palembang, South Sumatra, Indonesia<sup>1</sup>

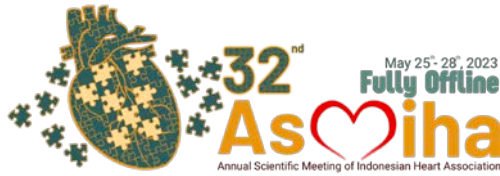
**Background and Aim:** Cardiovascular disease (CVD) is a leading cause of mortality worldwide. To gain insights into the current state of CVD research and identify emerging trends, we conducted a bibliometric analysis of publications on CVD over the last five years. This study aimed to analyze the global trends and publication activity related to CVD research over the last five years through bibliometrics analysis.

**Methods:** A systematic search was performed using the Web of Science Core Collection database to identify relevant publications on the trends of CVD over the last five years. Statistical analyses were performed using Excel and VOSviewer software. Various bibliometric indicators were analyzed to evaluate the publication trends, research topics, and collaboration networks.

**Results:** A total of 7510 articles with an H-index of 90 and 9,51 citations per paper related to the trends in CVD were identified over the last five years. The annual publication output showed an upward trend, peaking in 2022. The United States (2394) had the highest number of publications, followed by China (1579) and England (650). The most common research topics are divided into 4 clusters, including the mortality of CVD, risk factors for CVD, the prevalence of CVD, and prevention for CVD. Hypertension and outcomes of the CVD showed the highest for promising hotspots, followed by epidemiology, coronary heart disease, and metabolic syndrome.

**Conclusion:** Our bibliometric analysis provides a comprehensive overview of trends in CVD research over the last five years. By understanding the current state of CVD research and identifying emerging trends, researchers and policymakers can make informed decisions about where to focus their efforts to reduce the burden of CVD on global health.

**Keywords:** Cardiovascular disease research, trends, publication, bibliometrics



## Comparison of Management and Outcomes of STEMI in Asia and Europe During Covid-19 Pandemic Era: a Systematic Review and Meta-Analysis

P. Siahaan, R.N. Anjaswanti, D.F. Adani, H. Siahaan, M.J. Al-Farabi, Y.H. Oktaviono

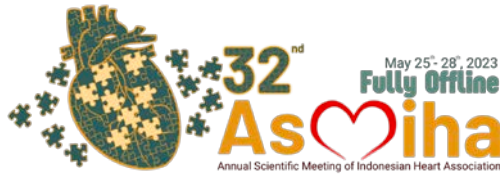
**Background:** COVID-19 pandemic impact STEMI management worldwide. This meta-analysis compares STEMI management and outcomes in Asia and Europe during COVID-19 pandemic.

**Methods:** 24 studies analysed for STEMI management and its outcomes (mortality, door to balloon time, symptom to first medical contact) during Covid-19 pandemic.

**Results:** A total of 98,494 STEMI patients were enrolled with 86,536 patients in the before pandemic and 11,958 patients in the during pandemic. Our study revealed that STEMI (RR = 1.00, 95% CI 1.00 – 1.00, I<sup>2</sup> = 0%, p = 1.00), PCI (RR = 1.39, 95% CI 1.21 – 1.73, I<sup>2</sup> = 100%, p < 0.00001), Mortality (RR = 1.06, 95% CI 0.88 – 1.28, I<sup>2</sup> = 36%, p = 0.10), Door To Balloon Time (RR = 0.72, 95% CI 0.58 – 0.89, I<sup>2</sup> = 95%, p < 0.00001) and Symptom to First Medical Contact (RR = 1.03, 95% CI 0.88 – 1.20, I<sup>2</sup> = 92%, p < 0.00001) in hospitals in Asia. Meanwhile, in Europe, STEMI (RR = 1.00, 95% CI 0.99 – 1.01, I<sup>2</sup> = 96%, p < 0.00001), PCI (RR = 1.39, 95% CI 1.21 – 1.73, I<sup>2</sup> = 100%, p < 0.00001), Mortality (RR = 0.86, 95% CI 0.73 – 1.03, I<sup>2</sup> = 18%, p = 0.28), Door To Balloon Time (RR = 0.57, 95% CI 0.34 – 0.95, I<sup>2</sup> = 98%, p < 0.00001) and Symptom To First Medical Contact (RR = 0.57, 95% CI 0.28 – 1.14, I<sup>2</sup> = 99%, p < 0.00001).

**Conclusion:** Asia showed significant differences for Door to Balloon time, while in Europe, PCI variable have significant differences during the Covid-19 Pandemic.

**Keywords:** COVID, STEMI, STEMI Management, PCI

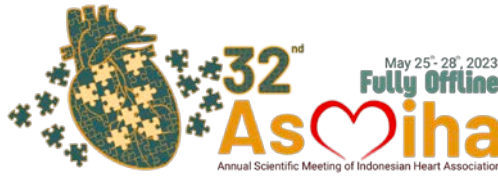


### Mortality of Heart Failure Patients in Rural vs Urban Area: a Meta Analysis

J.N. Arnindita<sup>1</sup>, P.B. T. Saputra<sup>2</sup>, S.D. Rasti<sup>1</sup>, A.D. Lamara<sup>2</sup>, M.E. Saputra<sup>2</sup>, D. Pasahari<sup>2</sup>, Y.H. Oktaviono<sup>2</sup>  
Faculty of Medicine University of Airlangga<sup>1</sup>  
Department of Cardiology and Vascular Medicine, Dr. Soetomo General Hospital, Faculty of Medicine,  
University of Airlangga<sup>2</sup>

**Background and aims:** Almost half of the world's population lives in rural areas. Challenges in social determinants of health, fewer hospitals, farther referral sites, and scarce specialists in rural areas may hinder medical care thus resulting in poorer outcomes. Heart failure (HF) patients are more likely to suffer from this rural-urban gap, as optimum care is only available in urban settings. This meta-analysis is conducted to assess the difference in mortality and other clinical outcomes of HF patients between rural and urban areas. **Methods:** A systematic search for eligible studies was done in PubMed, Embase, Medline, Science Direct, and Scopus databases until March 7, 2023. Odds ratios (ORs) or adjusted OR (aORs) and mean difference (MD) from each study were analyzed using Review Manager 5.4. **Results:** A total of 12 studies with 19,732,730 participants were included. HF patients in rural areas showed greater 1-year mortality (aOR= 1.06; 95% CI: 1.02-1.11; I<sup>2</sup>= 0%), 30 days mortality (OR= 1.14; 95% CI: 1.12-1.15; I<sup>2</sup>= 26%), and in-hospital mortality (aOR= 1.15; 95% CI: 1.04-1.27; I<sup>2</sup>= 90%). Hospitalizations in rural areas resulted in shorter length of stay (MD= -0.95; 95% CI: -1.17(-0.74); I<sup>2</sup>= 32%). Rural patients had more frequent 1-year readmission (OR= 1.19; 95% CI: 0.95-1.48; I<sup>2</sup>= 61%), 1-year ER visit (OR= 1.34; 95% CI: 1.03-1.76; I<sup>2</sup>= 91%), and 1-year physician/cardiologist visit (OR= 1.21; 95% CI: 0.88-1.66; I<sup>2</sup>= 84%). **Conclusion:** HF patients in the rural area demonstrated poorer outcomes compared to urban areas which may be related to shorter length of stay and suboptimal health service. Further, a large and systematic prospective study is needed to confirm the attributable factors to these results.

**Keywords:** heart failure, rural, mortality



## Association between Vitamin D Receptor Gene Polymorphism and Essential Hypertension: A Systematic Review and Meta-analysis

M.F. Adda<sup>1</sup>, I. Ivan<sup>2</sup>, R. Maulana<sup>3</sup>, B. Widyantoro<sup>1</sup>, I. Dakota<sup>1</sup>, R. Sukmawan<sup>1</sup>

National Cardiovascular Center Harapan Kita, Jakarta, Indonesia<sup>1</sup>

Universitas Atma Jaya<sup>2</sup>

1National Cardiovascular Center Harapan Kita, Jakarta, Indonesia<sup>3</sup>

**Background and aims:** Recent publications reported that the association between Vitamin D Receptor (VDR) gene polymorphism (FokI, BsmI, TaqI, ApaI, and other related SNP) and essential hypertension (EH) remains controversial. Thus, we conducted this study to investigate the relationship between these gene polymorphism and EH.

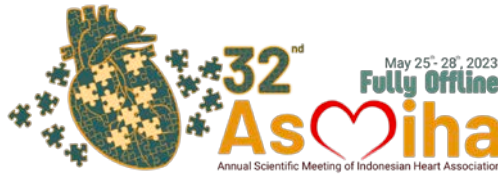
**Methods:** Major medical databases (EMBASE, PUBMED, Science Direct, Cochrane, Springer, Scopus, ProQuest, and Lilacs) were systematically searched for observational studies evaluating the impact VDR gene polymorphism on EH, published until March 19<sup>th</sup>, 2023 with predefined protocol and without language restriction regarding PRISMA guideline. Analysis was performed in RevMan 5.3 (fixed and random-effects model through heterogeneity test) to provide pooled measures for odds ratio (OR) under Hardy-Weinberg Equilibrium based on allele contrast, additive, dominant, and recessive genetic models. We also conducted meta-regression using method of moments to investigate the true causes of heterogeneity that explained I<sup>2</sup> statistic high value.

**Results:** Search strategy identified 1345 articles. Sixteen studies from 9 countries met inclusion criteria comprising 11.852 participants. Case-control, cross-sectional, and cohort studies have a score of 4 to 7, 9 to 10, and 8, respectively according to NOS. According to studies reporting hypertension susceptibility of patients with BsmI polymorphism, the allele model showed a higher risk of hypertension in patients with major allele (B) compared with minor (b) (OR: 1.16; 95%CI, 1.02 to 1.33; p = 0.03). Meanwhile, there were no significant association between FokI, ApaI, TaqI polymorphism and hypertension susceptibility. Meta-regression showed that methodological quality significantly influenced the pooled effect of hypertension risk in patients with FokI polymorphism based on all model (all p < 0.01).

### Conclusion:

We found that patients with BsmI polymorphism can significantly increase hypertension susceptibility. Currently, the role of FokI polymorphism to increase hypertension risk is still inconclusive due to low quality study. There is no association between ApaI, and TaqI polymorphism with hypertension. More studies with high methodological quality will be needed to elucidate known SNPs for hypertension susceptibility in the future.

### Keywords:



## Colchicine as Atrial Fibrillation Prophylaxis Post Cardiac Surgery: A Meta-analysis

M.B. Rachmanadi<sup>1</sup>, S.M. Reza<sup>1</sup>, J. Rosa<sup>1</sup>, T. Kristianto<sup>1</sup>

Rumah Sakit Umum Daerah Cabangbungin, Bekasi Regency, West Java, Indonesia<sup>1</sup>

**Background and aims:** Postoperative Atrial Fibrillation (POAF) is a common complication of cardiac surgery and a significant source of morbidity and mortality. Colchicine is an anti-inflammatory drug that has various cardiovascular benefits. This meta-analysis aims to evaluate the use of Colchicine as POAF prophylaxis post-cardiac surgery.

**Methods:** We searched PubMed, Cochrane, and Medline until March 2023 to identify randomized control trials (RCTs) using the terms Atrial Fibrillation, Colchicine, and Cardiac Surgery. The primary outcome is the occurrence of POAF in cardiac surgery that includes Coronary Artery Bypass Graft (CABG) surgery, valvular surgery, and other cardiac surgery. We calculated estimated odd ratios (OR) and 95% Confidence Interval using the Mantel-Haenszel formula. Data were analyzed using Review Manager 5.4.

**Results:** Eight studies enrolling a total of 1905 patients were included in this meta-analysis. The incidence of POAF post-cardiac surgery was significantly lower in the colchicine treatment group than in the control group (OR 0.59; 95%CI 0.47-0.74;  $p < 0.00001$ ,  $I^2=0\%$ ). Regarding the type of cardiac surgery, colchicine reduced the risk of POAF in the CABG group (OR 0.47; 95%CI 0.33-0.68;  $p < 0.0001$ ,  $I^2=0\%$ ) but no significant difference in the non-CABG or combined group (OR 0.71; 95%CI 0.38-1.32;  $p = 0.28$ ,  $I^2=0\%$ ). However, the use of colchicine is associated with an increased risk of diarrhea as an adverse event compared to placebo (OR 3.05; 95%CI 2.17-4.29;  $p < 0.00001$ ,  $I^2=5\%$ )

**Conclusion:** This meta-analysis showed that Colchicine decreased the occurrence of POAF post-cardiac surgery, especially in CABG surgery. Further studies are needed to figure out the optimal Colchicine dose, duration, and time administration to overcome the risk of diarrhea as an adverse event.

**Keywords:** Colchicine, Atrial Fibrillation, Cardiac Surgery, Coronary Artery Bypass Graft, Meta-analysis

**Optimal Timing of Ventricular Arrhythmia Ablation After Myocardial Infarction and Potential Role of Programmed Ventricular Stimulation: Systematic Review and Meta-analysis**

G.N.P. Jagannatha<sup>1</sup>, I.M.P.S. Antara<sup>2</sup>, A.M. Kosasih<sup>1</sup>

Faculty of Medicine Udayana University, Prof. Dr. I.G.N.G Ngoerah General Hospital, Denpasar, Bali, Indonesia<sup>1</sup>

Division of Cardiac Pacing and Electrophysiology, Department of Cardiology, Prof. Dr. I.G.N.G Ngoerah General Hospital, Denpasar, Bali, Indonesia<sup>2</sup>

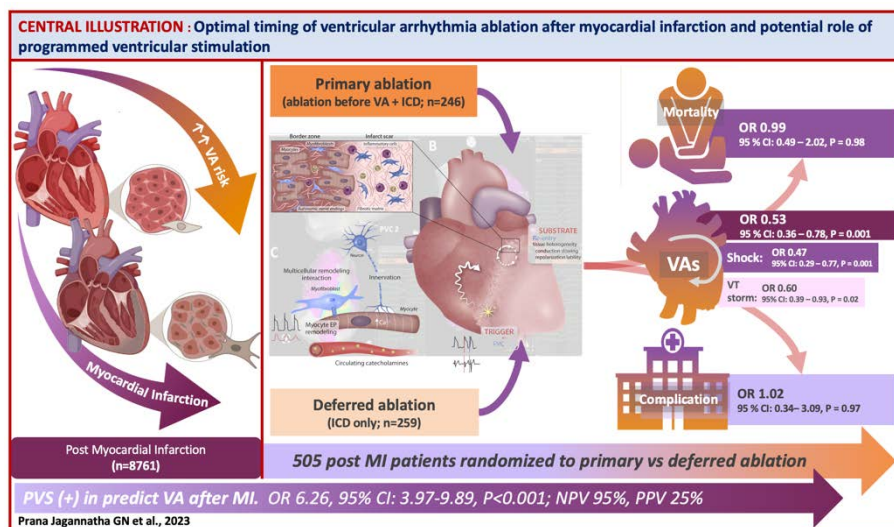
**Background and aims:** Ventricular arrhythmia (VA) are one of common complications after myocardial infarction (MI). Even though VAs ablation is promising, the perfect timing to carry this procedure become a knowledge gap and routine programmed ventricular stimulation (PVS) to predict upcoming VAs post-MI remains unclear. The aim of this research is to evaluate optimal timing of VAs ablation.

**Methods:** We conducted a systematic search on multiple databases in RCT study that compared the outcome of VAs ablation as a primary prevention and deferred ablation (secondary prevention after VAs) in MI patients. Primary outcomes included VAs incident (appropriate shock and anti-tachycardia pacing), appropriate shock, electrical storm, complication, and mortality. The secondary outcome was VAs event between positive and negative PVS from cohort studies. Data was analyzed using Review Manager 5.4 and R-studio.

**Results:** Thirty-seven studies with total 8761 patients with mean age 58.5 years old and mean LVEF 38.8% were included. After a mean of follow-up of 24 months, there was a correlation between preventive ablation and reduction of VAs events (OR 0.53, 95% CI: 0.36-0.78, P = 0.001), appropriate shocks (OR 0.47, 95% CI: 0.29-0.77, P = 0.001), and VT storm (OR 0.60, 95% CI: 0.39-0.93, P = 0.02) compared to deferred ablation. Similar benefits in the reduction of VAs events were also obtained based on LVEF subgroup analysis (OR 0.37, 95% CI: 0.19-0.72, P = 0.003). There was no significant difference in complications and mortalities. VAs inducibility during PVS on patient that was not undergo ablation correlated with VAs events during follow-up (OR 6.26, 95% CI: 3.97-9.89, P<0.001; Negative predictive value 95%, Positive predictive value 25%).

**Conclusion:** VAs ablation as primary prevention is proven beneficial for post-MI. Routine PVS also potentially provide in population stratification, whether the patient suitable for ablation after MI event.

**Keywords:** Myocardial infarction, Ventricular arrhythmia, Catheter ablation, Ventricular arrhythmia ablation, Programmed ventricular stimulation



**The Benefits and Safety of Supervised Exercise-based Cardiac Rehabilitation for Adults with Atrial Fibrillation: a Systematic Review and Meta-analysis of Randomized Controlled Trials**

E. Fukata<sup>1</sup>, K.A. A. P. Pramana<sup>1</sup>, R.B. Hardani<sup>1</sup>, Y. Pintaningrum<sup>2</sup>  
Universitas Mataram<sup>2</sup>

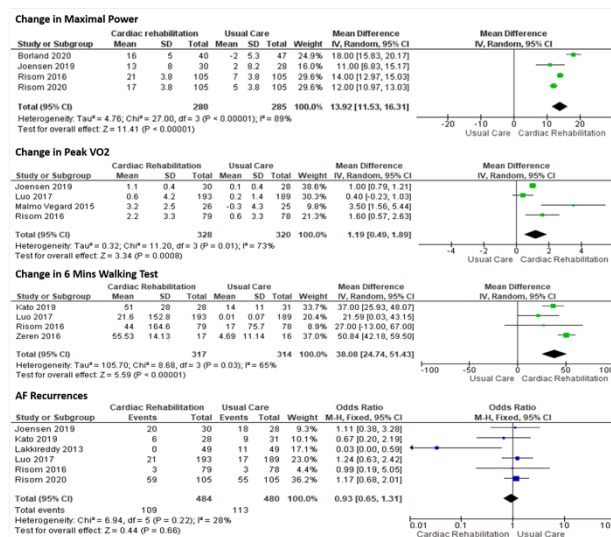
**Background and aims:** The benefits and safety of exercise-based cardiac rehabilitation (CR) following myocardial infarction and heart failure was already established. However, no such international nor national recommendation for cardiac rehabilitation is currently provided for patients with AF. This study aims to determine the impact of supervised exercise-based CR on physical capacity and AF recurrences in patients with AF.

**Methods:** Relevant studies from 2013-2023 were systematically searched in PubMed, ScienceDirect, and Cochrane Library to identify randomized controlled trials (RCT) assessing the effect of supervised exercise-based CR on adult patients with AF. RCT were included if they compared the effects of standard therapy of AF plus supervised exercise-based CR intervention to usual care control group. Meta-analysis with random-effect models was performed on included studies and odds ratio (OR), mean differences (MD), and 95% confidence interval (CI) were estimated using Review Manager v5.4. The primary outcome was physical capacity including maximal power (Watt), obtained by cycle ergometer, or by six minutes walking test (6MWT), or ergospirometry testing measuring peak VO<sub>2</sub>. The secondary outcome was AF recurrences during follow-up period.

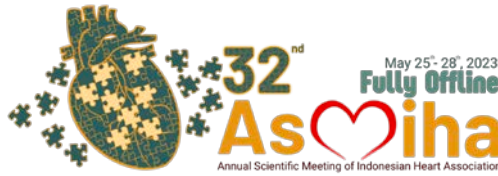
**Results:** We identified nine RCT involving 1198 patients with various types of AF. There were improvements in physical capacity (mean max power: 13.92 W, 95% CI, 11.53-16.31, p<0.00001; mean 6MWT: 38.08 m, 95% CI, 24.74-51.43, p<0.00001; mean peak VO<sub>2</sub>: 1.19 ml/kg/min, 95% CI, 0.49-1.89, p<0.0008). Besides, compared with control, pooled analysis showed no difference in AF recurrences (OR: 0.93; 95% CI, 0.65-1.31, p=0.66) following exercise-based CR.

**Conclusion:** Exercise-based cardiac rehabilitation improves physical capacity of patients with AF, while doesn't seem to increase the risk of AF recurrences.

**Keywords:** cardiac rehabilitation, atrial fibrillation, physical capacity



Forest Plot of Primary and Secondary Outcomes



## Paclitaxel-Eluting Stents versus Paclitaxel-Coated Balloons in Coronary Artery Disease: A Meta-Analysis of Randomized Controlled Trials

B.G. Liyis<sup>1</sup>, M.D.W. Aryaweda<sup>1</sup>, L.O. S. Suastika<sup>2</sup>

Faculty of Medicine, Udayana University, Denpasar, Bali, Indonesia<sup>1</sup>

Department of Cardiology and Vascular Medicine, Faculty of Medicine, Udayana University, Denpasar, Bali, Indonesia<sup>2</sup>

**Background and aims:** Research investigating the effectiveness of drug-coated balloons (DCB) compared to drug-eluting stents (DES) for the treatment of coronary artery disease (CAD) has yielded inconsistent findings. Despite paclitaxel being one of the most commonly used drugs in both DES and DCB, there is a significant lack of meta-analyses that specifically compare the use of paclitaxel-eluting stents (PES) and paclitaxel-coated balloons (PCB). This meta-analysis aims to equally evaluate and compare the clinical outcomes of DES and DCB using the same drug, paclitaxel.

**Methods:** A systematic literature search was performed in PubMed, Medline, and Cochrane databases from January 1st, 2009 to January 1st, 2023 which resulted in a total of six randomized controlled trials with a total of 951 patients at a 1:1 ratio meeting the inclusion criteria.

**Results:** The meta-analysis results showed that mortality (OR, 1.57; 95% CI, 0.67-3.66), target lesion vascularization (OR, 0.74; 95% CI, 0.37-1.48), myocardial infarction (OR, 1.76; 95% CI, 0.79-3.88), target vessel revascularization (OR, 0.76; 95% CI, 0.51-1.12), major adverse cardiovascular events (OR, 1.11; 95% CI, 0.48-2.58), in stent or in balloon binary stenosis (OR, 0.80; 95% CI, 0.34-1.87), in segment binary stenosis (OR, 1.16; 95% CI, 0.48-2.80), late luminal loss (MD, 0.03; 95% CI, -0.11-0.17), post minimal lumen diameter (MD, 0.04; 95% CI, -0.23-0.30), and post diameter stenosis (MD, -5.48; 95% CI, -13.88-29.2) did not significantly differ between the PES group and the PCB group in coronary artery disease.

**Conclusion:** These findings suggest that both DES and DCB may be similarly effective treatment options for CAD when using the same drug, paclitaxel. Both PES and PCB are equally efficacious and safe for the management of CAD.

**Keywords:** Coronary artery disease, Drug-coated balloons, Drug-eluting stents, Paclitaxel, Percutaneous coronary intervention

Endpoint	PES	PCB	Odds Ratio/ Difference [95% CI]	Mean <i>p</i>
Death	2.73% (13/477)	1.69% (8/474)	OR 1.57 [0.67, 3.66]	0.29
Target Lesion Revascularization	10.69% (51/477)	14.56% (69/474)	OR 0.74 [0.37, 1.48]	0.39
Myocardial Infarction	3.74% (16/428)	2.07% (9/434)	OR 1.76 [0.79, 3.88]	0.16
Target Vessel Revascularization	12.86% (53/412)	16.67% (68/408)	OR 0.76 [0.51, 1.12]	0.16
Major Adverse Cardiovascular Events	18.66% (89/477)	15.40% (73/474)	OR 1.11 [0.48, 2.58]	0.81
Binary Stenosis (in stent/in balloon)	12.43% (43/346)	13.65% (46/337)	OR 0.80 [0.34, 1.87]	0.60
Binary Stenosis (in segment)	14.83% (47/317)	12.62% (39/309)	OR 1.16 [0.48, 2.80]	0.74
Late Luminal Loss	-	-	MD 0.03 [-0.11, 0.17]	0.65
Minimal Lumen Diameter (Post)	-	-	MD 0.04 [-0.23, 0.30]	0.77
Diameter Stenosis (Post)	-	-	MD -5.48 [-13.88, 2.92]	0.20

PES=Paclitaxel Eluting Stents; PCB=Paclitaxel Coated Balloons.

Table 4. Forest plot results summary

Table 4. Forest plot results summary

**The Effect of Pulmonary Artery Denervation in Pulmonary Hypertension Patients**

A.H. Alamsyah<sup>1</sup>, A.Z. Alamsyah<sup>1</sup>, Y.M.P. Cardia<sup>1</sup>, M.S.Y. Dewangga<sup>2</sup>

Faculty of Medicine, Udayana University, Prof. I.G.N.G. Ngoerah General Hospital, Bali, Indonesia<sup>1</sup>

Department of Cardiology and Vascular Medicine, Faculty of Medicine, Udayana University, Prof. I.G.N.G. Ngoerah General Hospital, Bali, Indonesia<sup>2</sup>

**Background & Aims:** Pulmonary artery denervation (PADN) is a novel procedure/intervention in the management of pulmonary hypertension (PH). Previous studies have shown that PADN is safe and beneficial to be performed in patients with PH. However, studies comparing the effects between PADN and standard care are still very few with scattered results. Our study aims to elaborate on the effect of PADN compared to standard care in PH patients.

**Methods:** Several databases were searched on studies of PADN versus standard care in PH Patients. All articles were included until February 2023. The primary outcome is the mean pulmonary artery pressure (mPAP). The secondary outcomes are the other hemodynamic parameters (Pulmonary vascular resistance/PVR and pulmonary artery wedge pressure/PAWP) and the clinical state (6-minute walk distance/6MWD). The analysis was done using Review Manager v5.4.

**Results:** Seven studies were included with a total of 527 patients (245 in the PADN group). The mean age is 52.3±11.1 years old and 41.5% were male. the mean baseline mPAP score was 45.9±8 and 43.2±7.8 respectively in the PADN and the standard care group. On our primary outcome, the PADN group has significantly lower mPAP compared to the standard care group (WMD:-5.54; 95%CI:-8.48 to -2.60; p<0.01). The PADN group also showed a significantly lower PVR (WMD:-3.26; 95%CI:-5.48 to -1.05; p<0.01) and PAWP (WMD:-1.54; 95%CI:-2.29 to -0.78; p<0.01) compared to the control. The 6MWD was also significantly higher in the PADN group compared to the control group (WMD:56.88; 95%CI:7.51 to 106.24; p=0.02).

**Conclusion:** PH patients who underwent PADN significantly showed a lower mPAP, PVR, and PAWP and a higher 6MWD compared to standard care. These findings give a new insight that PADN had a significant beneficial effect compared to standard care in PH patients. A large randomized clinical trial was needed to validate our findings.

**Keywords:** Pulmonary Artery Denervation, Pulmonary Hypertension, mean pulmonary artery pressure

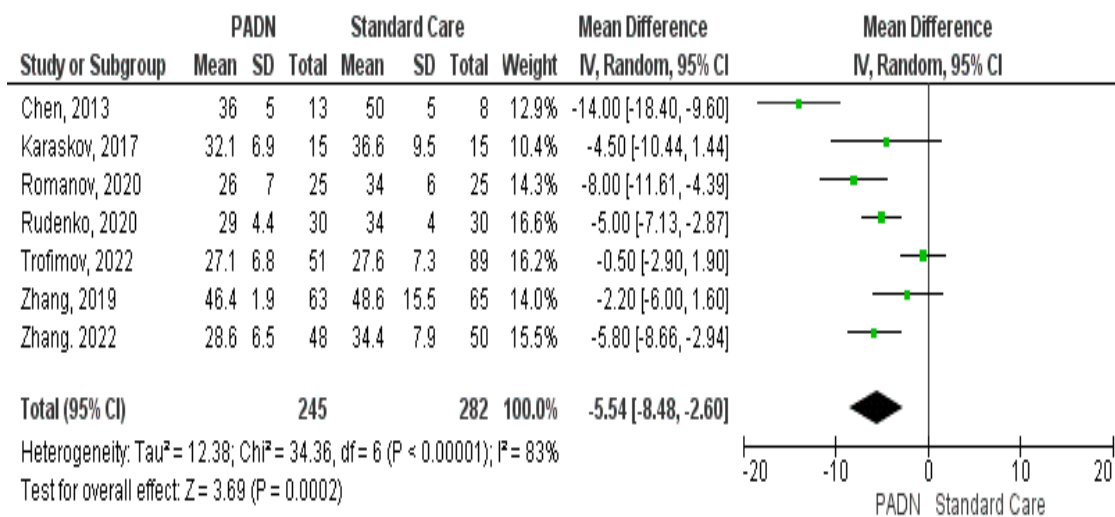


Figure 1. Forest plot of Pulmonary Artery Denervation versus Standard Care on mean Pulmonary Artery Pressure in Pulmonary Hypertension Patients.

## Comparison Between Novel Oral Anticoagulant and Vitamin K Antagonist After Transcatheter Aortic Valve Implantation in Patients with Concomitant Indication for Oral Anticoagulation: A Pooled Study-Level Meta Analysis

N.T. Labi<sup>1</sup>, V.N. Purnomo<sup>1</sup>, J. Nuralele<sup>2</sup>, S.H. Rampengan<sup>3</sup>, D. Rampengan<sup>1</sup>

Faculty of Medicine, Universitas Sam Ratulangi Manado<sup>1</sup>

Faculty of Medicine, Universitas Kristen Indonesia Jakarta<sup>2</sup>

Department of Cardiology and Vascular Medicine, Prof Dr. R. D. Kandou General Hospital Manado<sup>3</sup>

### Background and Aim

Transcatheter aortic valve implantation (TAVI) has emerged as a crucial treatment option for aortic stenosis (AS) patients with a high surgical risk. This procedure is often performed on patients with indication for oral anticoagulation (OAC), such as atrial fibrillation (AF). However, the best approach to anticoagulation in this group of patients is a matter of debate. We aimed to compare the efficacy and safety of novel oral anticoagulants (NOAC) and vitamin K antagonists (VKA) in patients undergoing TAVI with concomitant indication for OAC.

### Method

We comprehensively searched the databases of PubMed, ScienceDirect, and Cochrane Library from inception to January 2023. Included studies were published cohorts or randomized controlled trials (RCT) that compared clinical outcomes between NOAC and VKA after TAVI in patients with concomitant indication for OAC. Primary outcome is all-cause mortality. Secondary outcomes are major and/or life-threatening bleeding and stroke. Data from each study were combined using the fixed and random-effects model.

### Result

Our analysis included eleven studies with a total of 29,186 patients who underwent TAVI and required OAC (11,718 received NOAC and 17,468 received VKA). Most patients had AF as the indication for OAC. The all-cause mortality and stroke outcome showed no significant difference between the two groups ([OR] 0.82, 95% CI 0.61-1.11,  $I^2=87%$ ,  $p=0.20$  and [OR] 1.02, 95% CI 0.88-1.19,  $I^2=4%$ ,  $p=0.80$ , respectively). Furthermore, there was trend in lower incidence of major and/or life-threatening bleeding patients who received NOAC compared to VKA ([OR] 0.80, 95% CI 0.63-1.02,  $I^2=64%$ ,  $p=0.07$ ).

### Conclusion

Our findings indicate that, in patients who underwent TAVI and required OAC, NOAC was linked to a trend in lower incidence of major and/or life-threatening bleeding and similar rates of all-cause mortality and stroke compared to VKA.

**Keywords:** Transcatheter aortic valve implantation, novel oral anticoagulant, vitamin K antagonist

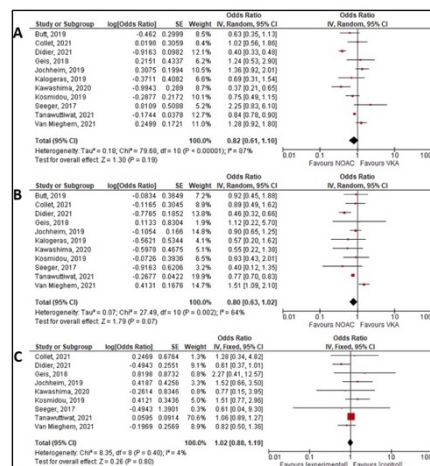
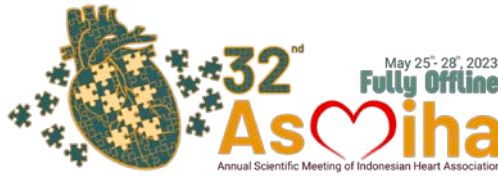


Figure 1. (A). Forest plots demonstrating the all-cause mortality risk between the NOAC and VKA groups in 11 studies. (B). Forest plots demonstrating the risk of major and/or life-threatening bleeding between the NOAC and VKA groups in 11 studies. (C). Forest plots demonstrating the risk of stroke between the NOAC and VKA groups in 9 studies.



## Unraveling The Efficacy, Thrombus Resolution and Bleeding Events of Utilizing Direct Oral Anticoagulant as an Alternative Therapy in Pediatric Vein Thromboembolism: A Meta Analysis

H.P. Megantara<sup>1</sup>, S. Imtiyaz<sup>1</sup>  
Faculty of Medicine, Universitas Indonesia<sup>1</sup>

**Background and aims:** Direct Oral Anticoagulant (DOAC) is a new class of anticoagulant, preceded by the Standard Oral Anticoagulant (SOC). The superiority of DOAC over SOC for venous thromboembolism (VTE) in adults has been reported. However, there are still lack of understanding and consensus for the use of DOAC in pediatric VTE. Hence, current research aims to determine the efficacy and adverse effects of DOAC as an alternative treatment of VTE in children.

**Methods:** The literature extraction was conducted in 5 databases (PubMed, Embase, WebofScience, EBSCOHost, and Cochrane). Studies of children <18 years diagnosed with VTE who received DOAC and SOC were included in this review. The DOACs used were apixaban, rivaroxaban, edoxaban, and dabigatran. The meta-analysis was done with a confidence interval (CI) of 95% in the literature with similar populations and outcomes through RevMan.5.4.1 application. Quality appraisal was assessed using the Joanna Briggs Institute questionnaire.

**Results:** Six studies were included; one was of fair quality and five of good quality. Three literatures were analysed with forest plots while the other three were reviewed of which had specific populations, namely children with cardiovascular disease, thrombophilia, and malignancy. The meta-analysis concluded that pediatrics receiving DOAC had lower VTE recurrence rate than SOC [RR: 0.43; CI-95% 0.20-0.93; p-value:0.03] and better thrombus resolution [RR:1.29; CI-95% 1.01-1.64; p-value: 0.04]. Although side effects of bleeding were minimal in DOAC group, no significant difference was found between the two types of anticoagulants [RR: 0.52; CI-95%: 0.14-1.89; p-value: 0.32].

**Conclusion.** DOAC provides better efficacy in pediatric VTE, depicted by lower recurrence and more thrombus resolution. Although, no difference in bleeding adverse effect was noticed. More extensive cohorts may be valuable to provide robust understanding of the use of DOAC in pediatric VTE.

**Keywords:** Vein thromboembolism, direct oral anticoagulant, standard oral anticoagulant, thrombus resolution, pediatric

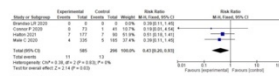


Figure 1. Forest plot of comparison between DOAC vs standard SOC in terms of VTE recurrence

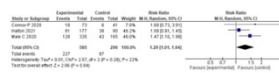


Figure 2. Forest plot of comparison between DOAC vs standard SOC in terms of thrombus resolution

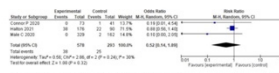
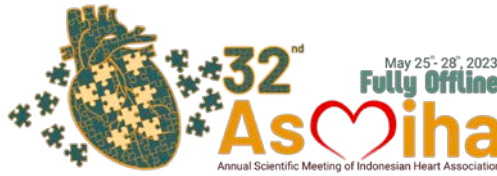


Figure 3. Forest plot of comparison between DOAC vs standard SOC in terms of bleeding events



## Incidence of Arrhythmia on Skeletal Myoblast Transplantation in Patients with Heart Failure : A Systematic Review and Meta-Analysis

I.H. Zahra<sup>1</sup>, E.T. Sinaga<sup>1</sup>, J.B. Simanjuntak<sup>1</sup>  
Gadjah Mada University<sup>1</sup>

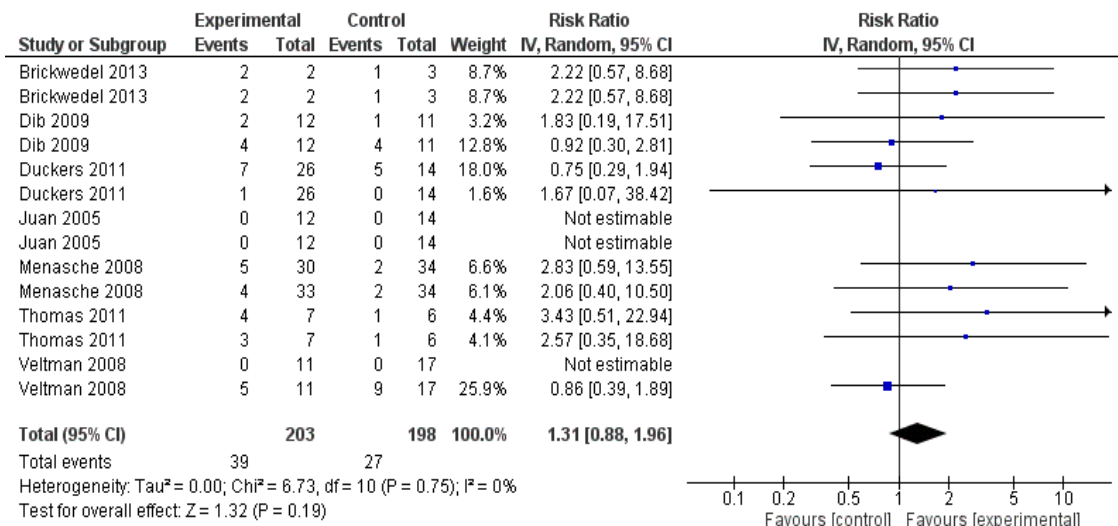
**Background and Aims:** In a post-myocardial infarction event there is significant loss of heart cells replaced by fibrotic tissue. In a clinical trial, Skeletal Myoblast (SkM) grafting into post-myocardial infarction scars has been proven to improve left ventricular function. But, some trials in transplantation of SkM for the Heart Failure (HF) patient showed arrhythmias. This study was aimed to assess the evidence of arrhythmia of the transplantation of autologous SkM in the patients with HF.

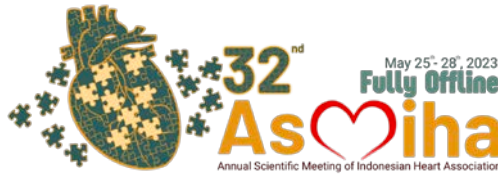
**Methods:** Three reviewers independently searched published studies from PubMed, Scopus, Sage, and Cochrane Library databases using pre-registered search strategies from inception to January 2023. Clinical trial examined the incidence of arrhythmia due to autologous SkM compared to placebo on HF patients. ROB2.0 tool was used to assess the risk of bias in the included studies. Results were described using a vote-counting analysis, then meta-analyses using random effects models were conducted. The quality of evidence was analyzed using GRADE and publication bias was examined using a forest plot.

**Results:** Vote-counting analysis from 7 records (201 participants) showed there is a tendency that patients receiving SkM have a higher risk of having arrhythmia than patients receiving standard treatment. However, the result from the meta-analysis did not reach a statistically significant threshold with a relative risk 1.31(95%CI 0.88-1.96) and I<sup>2</sup>=0% (Figure.1). This result was consistent even after subgroup analyses based on the dose of SkM. The quality of evidence is medium and publication bias was not detected.

**Conclusion:** Most studies favor that patients receiving SkM have higher risk of having arrhythmia than patients receiving standard treatment. Further studies with safety focused on SkM were still needed. To reduce the bias, the reason behind the inconsistent number of patients should be included and protocol-appropriate randomization methods should be applied.

**Keywords:** Skeletal Myoblast, arrhythmia, heart failure, safety-endpoint, stem-cell therapy





## **Cardioprotection Strategies to Prevent Cardiotoxicity of Breast Cancer Therapy: A Systematic Review**

N. Purnomo<sup>1</sup>, F.J. Purnomo<sup>2</sup>, J.K. Kurniawan<sup>3</sup>, I.K. Kurniawan<sup>4</sup>

Siloam Hospital TB Simatupang, Jakarta, Indonesia<sup>1</sup>

RSUD dr. Hj. Zainal Umar Sidiki, Gorontalo, Indonesia<sup>2</sup>

RST dr. Asmir, Jawa Tengah, Indonesia<sup>3</sup>

Resident of Internal Medicine, Sebelas Maret University, Surakarta, Indonesia<sup>4</sup>

### **Background and aims :**

Breast cancer cases has affected more than 2.1 millions of women each year and caused the highest number of cancer-related mortality. Cardiovascular effects is the most frequent cancer therapy-related side effects and may reduce the quality of life of breast cancer survivors. The use of chemotherapy and targeted-therapy increased the risk of cardiotoxicity or CTRCD (Cancer-Therapy Related Cardiac Dysfunction). Cardioprotective management and strategies are needed to minimize the CTRCD. This systematic review will discuss further about the efficacy and recommendations of prophylactic cardio-protection.

### **Methods:**

Systematic literature search was conducted based on PRISMA flow diagram from PubMed with keywords “cardioprotection”, “breast cancer therapy”, “cardiotoxic”, and “cardiac dysfunction.” Data extraction was done, thus we use Cochrane Risk of Bias tool for randomized trials (RoB 2) and Newcastle-Ottawa Scale (NOS) was used to assess the study quality.

### **Results:**

There are 19 selected publications that were included in this systematic review. All of the included studies have good quality. Eleven studies assessed the effect of cardio-protective drug on Anthracycline (Doxorubicin and Epirubicin) and nine studies assessed the impact on Trastuzumab. Cardioprotective interventions such as RAAS inhibitors, beta-blockers, statin, Dexrazoxane, and exercise play a role in reducing Left Ventricular Ejection Fraction (LVEF) decline, fewer interruption of the chemotherapy, lower the increase of cardiac enzyme, and reduce the Global Longitudinal Strain (GLS) decline.

### **Conclusion :**

Strategies and medications including RAAS inhibitor, Beta-blockers, Statins, Spironolactone, exercise, and Dexrazoxane could play a significant role in primary and secondary cardioprotection from Anthracycline and Trastuzumab-induced cardiotoxicity.

**Keywords:** Cardioprotection, Cancer-Therapy Related Cardiac Dysfunction, Anthracycline, Trastuzumab



## Efficacy of Rivaroxaban and Aspirin for Acute Limb Ischemia in Patients with Peripheral Artery Disease: A Systematic Review of Randomized Controlled Trials

V.A. Damay<sup>1</sup>, E.W. Mokalu<sup>1</sup>, J.I. X. Hasan<sup>1</sup>, P. Yossy<sup>1</sup>, W.S. Atmaja<sup>1</sup>  
Universitas Pelita Harapan<sup>1</sup>

### Background and Aims

Peripheral Artery Disease (PAD) is a narrowing or blockage of the arteries that carry blood from the heart to the extremities. Generally, the fatty plaque buildup promotes this condition. Infection, ulceration, heart attack, stroke, and even amputation are just a few of the consequences that PAD can lead to if addressed. For the treatment of symptomatic PAD, rivaroxaban and aspirin have been suggested together. The advantages of preventing additional complications are unclear, though. To evaluate the effectiveness of rivaroxaban and aspirin for the risk reduction in patients with PAD, we conducted a systematic evaluation of published trials.

### Methods

This study was conducted on 1st until 20th March 2023. Four researchers used the keywords "PAD," "Efficacy," "Aspirin," and "Rivaroxaban" to extract data from the Pubmed, Science Direct, and SpringerLink databases. The studies were culled and subjected to inclusion standards for RCTs conducted within the previous five years. Studies on patients under the age of 18, systematic reviews, meta-analyses, and animal research were all excluded. The caliber of the included studies was assessed using the NewCastle Ottawa Scale (NOS).

### Result

Five RCTs with a combined total of 32756 PAD patients with the age of 50 and above were included after evaluation. Despite increases bleeding, all studies that met the criteria for inclusion demonstrated the effectiveness of rivaroxaban and aspirin in reducing the occurrence of acute limb ischemia thrombosis in PAD patients, other condition such as major amputation for vascular causes, myocardial infarction, and ischemic stroke also decreased. Four studies were found to be of good quality using the NOS, while one study was found to be of fair quality.

### Conclusion

Rivaroxaban and aspirin together have been proven to lower the chances of acute limb ischemia thrombosis in patients with a PAD.

**Keywords:** Peripheral Artery Disease, Rivaroxaban, Aspirin

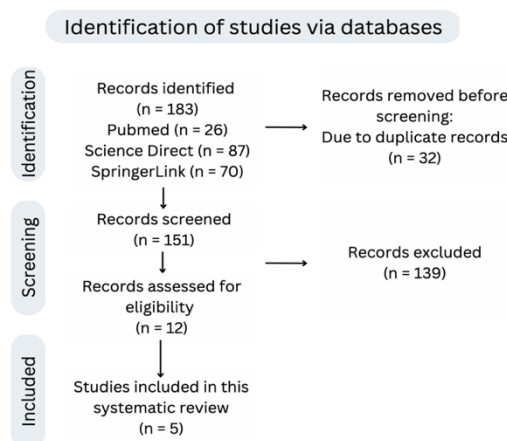
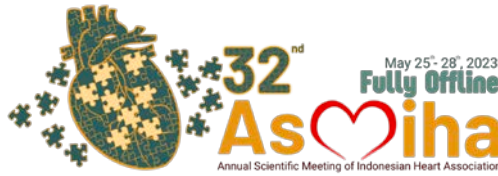


Figure 1. PRISMA Chart



## Angiogenesis Outcomes of Metformin Utilization in Diabetes Mellitus: A Systematic Review and Meta-Analysis

Y.H. Oktaviono<sup>1</sup>, A.D. Paramitha<sup>2</sup>, A.S. Hariftyani<sup>2</sup>, S.R. Desita<sup>2</sup>, F.A. Shabrina<sup>2</sup>, P.M. Harsoyo<sup>1</sup>, H.O. Hermawan<sup>1</sup>

Cardiology and Vascular Medicine, Faculty of Medicine, Airlangga University<sup>1</sup>  
Faculty of Medicine, Airlangga University<sup>2</sup>

**Background:** Metformin was proven to have other therapeutic effects such as improving blood vessel dilation and reducing inflammation. Exposing endothelial cells to metformin inhibits the expression of endothelial adhesion molecules from the inflammatory process to investigate the role of metformin in angiogenesis outcomes

**Methods:** We performed systematic review and meta-analysis conducted from MEDLINE, ScienceDirect, ProQuest, Web of Science, EBSCOhost, and Cochrane Library. The authors screened the articles based on inclusion criteria: (1) Diabetes mellitus type 2 patients; (2) Metformin as interventional therapy; (3) Human studies that have an angiogenesis endothelial marker as an outcome; (4) Written in English. Endothelial markers such as Vascular endothelial growth factor (VEGF), von-Wille-factor (vWf), plasminogen activator inhibitor-1 (PAI-1), soluble vascular adhesion molecule-1 (sVCAM-1), intercellular adhesion molecule-1 (ICAM-1), sE-selectin, tissue plasminogen activator (tPA), urinary albumin excretion (UAE), platelet endothelial cell adhesion molecule-1 (PECAM-1), and thrombin-activatable fibrinolysis inhibitor (TAFI) were assessed as angiogenesis outcomes.

**Result:** Seven randomized control trials (RCT) and one cross sectional study involving 1,119 patients were included. vWF (OR -0.28 [-0.50, -0.06]; p=0.01), sVCAM-1 (OR -0.33 [-0.46, -0.20]; p<0.00001), ICAM-1 (OR -0.25 [-0.38, -0.11]; p=0.0003), sE-selectin (OR -0.19 [-0.33, -0.05]; p = 0.007), and tPA (OR -0.62 [-0.88, -0.36]; p < 0.00001) were significantly reduced compared before and after metformin treatment using random effect methods. PAI-1 (OR -0.24 [-0.41, -0.08]; p=0.003) was significantly lower at the end of metformin treatment using random effect methods.

**Conclusion:** Metformin has additional benefits in the improvement of endothelial function, as demonstrated by reduced antiangiogenic levels such as vWF, PAI-1, sVCAM-1, ICAM-1, sE-selectin, and tPA, after metformin treatment.

**Keywords:** angiogenesis, metformin, diabetes mellitus, endothelial dysfunction

## Therapeutic Effect of Stem Cells Therapy In Left Ventricular Function, The Event of Arrhythmia, and Cardiac Arrest of Heart Failure Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

L.P. Suhandoko<sup>1</sup>, Z. Zuhra<sup>1</sup>, A.N. Fadila<sup>1</sup>, M.S. Tiyantara<sup>1</sup>, M.A. Ayuba<sup>1</sup>, R.R. Dewi<sup>1</sup>, F.D. Atikah S<sup>1</sup>, D. Satriojati<sup>1</sup>, W.I. T. Simatupang<sup>1</sup>, S.S. A. Sinaga<sup>1</sup>, H. Siringoringo<sup>1</sup>, R.E. Intan<sup>1</sup>, L.G. P. Rinjani<sup>1</sup>, Andrianto<sup>1</sup>  
Department of Cardiology and Vascular Medicine, Dr. Soetomo General Hospital, Surabaya Indonesia<sup>1</sup>

**Background and aims:** The prognosis of heart failure remains poor despite improvement in treatment strategies, partly because of irreversible myocardial damage. Stem cell-based therapies are expected to amend the condition through its regeneration property. This study aims to assess and investigate the therapeutic effect of stem cell therapy on left ventricular function, the event of arrhythmia and cardiac arrest of heart failure patients.

**Method:** The PubMed, Cochrane Library, Proquest, and Clinicaltrial.gov databases were searched for randomized controlled trials (RCT) in March 2023. We included 19 studies in this systematic review and 17 studies in the meta-analysis. The mesenchymal stem cells (MSC), bone marrow stem cells (BMC), CD34+, CD133+, c-kit+ cells, and cardiac progenitor cells (CPC) delivered through injection or direct transplantation were included in this study. The primary endpoints of this study are arrhythmia and cardiac arrest as adverse events, left ventricular functions, and six-minute walk test (6MWT). The analysis was done using Review Manager 5.1 Analyzer.

**Result:** Seventeen RCTs involving 818 patients were included in the meta-analysis. Compared to the control group, the stem cell therapy showed a statistically significant improvement of 6MWT (MeanDiff= 22.98, 95%CI=7.20, 38.76, **p=0.004**). It also showed a lower risk of arrhythmia and cardiac arrest adverse events, an increase of LVEF although statistically insignificant (RR=0.83, 95%CI=0.60, 1.17; p=0.29; RR=0.54, 95%CI=0.19, 1.48; p=0.23; MeanDiff=1.29, 95%CI=-1.15, 3.73, p=0.30). However, there is no significant increase for LVESV (MeanDiff=-1.44, 95%CI=-4.88, 2.00, p=0.41) and LVEDV (MeanDiff=-0.36, 95%CI=-4.16, 3.45, p=0.85).

**Conclusion:** Stem cell therapy in heart failure is associated with improved 6MWT. It also has a lower risk of arrhythmia and cardiac arrest adverse events, and a higher improvement of LVEF but statistically insignificant. Nevertheless, it does not have significant influence on LVEDV and LVESV.

**Keywords:** Stem Cells Therapy, Heart Failure, Left Ventricular Function, Arrhythmia, Cardiac Arrest

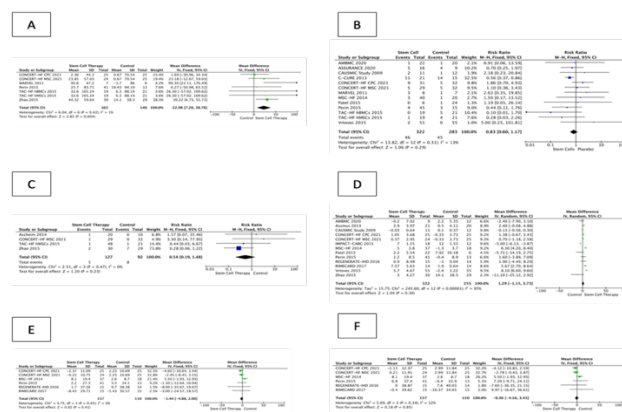
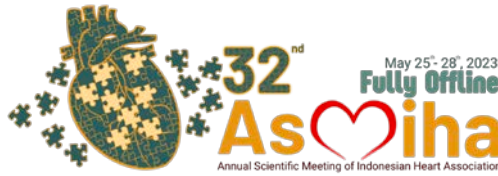


Figure 1. Forest Plot (A) 6MWT p= 0.004; (B) Arrhythmia Adverse Events p=0.29; (C) Cardiac Arrest p=0.23; (D) LVEF p=0.30; (E) LVESV p=0.41; (F) LVEDV p=0.85



## Therapeutic Potential of Ketone Body in Heart Failure Patient with Diabetes Mellitus Comorbid

H.O. Hermawan<sup>1</sup>, O.W. Firmansyah<sup>1</sup>, P.M. Harsoyo<sup>1</sup>, D. Ardiany<sup>1</sup>, Andrianto<sup>1</sup>  
Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia<sup>1</sup>

### Background and Aim:

Heart failure and Diabetes Mellitus (DM) are two diseases that could affect each other independently. The prevalence of DM in heart failure patients ranges from 10-47%. The presence of comorbid in heart failure certainly leads to worse clinical outcome. Evidence in metabolic changes and the use of ketone body in heart failure and DM has prompted researchers to conduct various studies to find ketone body potential as a therapeutic modality.

### Methods:

We retrieved all published studies in PubMed/MEDLINE and Cochrane Library on January 27, 2023, without time restriction using the following keywords: “Keton bodies” and “Heart Failure” and “diabetes mellitus”. In addition, relevant articles that were found during full text search were added. We identified 16 articles that were reviewed in this paper.

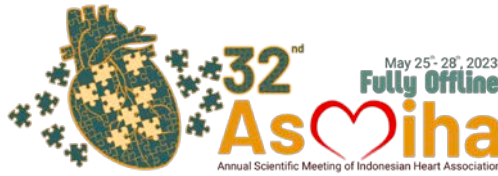
### Results:

The Preclinical studies reveal that triggering therapeutic ketosis and increasing ketone body distribution to myocardium can improve cardiac outcome in mice and other large animals. At clinical aspect, therapeutic ketone body supplementation has good potential in heart failure. Some of the approach include 3-hydroxybutyrate ketone body administration, and utilization of Sodium Glucose Co-Transporter-2 (SGLT2) inhibitor. However, questions regarding the treatment mechanism, long-term effect, its benefit in heart failure population with DM and HFpEF (Heart failure with preserved ejection fraction) need further investigation.

### Conclusion:

There is some evidence of changes in metabolism and the use of ketone body in the heart of heart failure and DM patients, making treatment using ketone body or by modifying systemic ketosis has promising potential. further research still needs to be carried out.

**Keywords:** Diabetes Mellitus, Heart failure, Ketone Body, systemic ketosis



## Dietary Intervention Improve Cardiorespiratory Fitness Outcomes in Patients with Heart Failure with Preserved Ejection Fraction: A Systematic Review and Meta-Analysis

R.R. Muhammad<sup>1</sup>, L.P. Suhandoko<sup>1</sup>, A. Lefi<sup>1</sup>

Department of Cardiology and Vascular Medicine, Faculty of Medicine Airlangga University – Dr. Soetomo General Hospital<sup>1</sup>

**Background and aims:** The incidence of Heart Failure with Preserved Ejection Fraction (HFpEF) is increasing worldwide. However, there has been lack of evidence in decreasing morbidity and mortality. Cardiorespiratory fitness (CRF), is associated with improved exercise capacity and quality of life. Peak oxygen consumption (VO<sub>2</sub>) on cardiopulmonary exercise testing (CPET) is a strong prognostic marker in HFpEF and increases in peak VO<sub>2</sub> are linked to reductions in mortality. This study aims to assess and investigate the cardiorespiratory fitness outcomes (peak VO<sub>2</sub>) of dietary intervention in patients with HFpEF.

**Method:** The PubMed, Proquest, and Cochrane databases were searched for randomized controlled trials (RCT) in March 2023. We included 10 studies in this systematic review and 3 RCTs in the meta-analysis. Study characteristics were summarized according to population, intervention, comparator, outcome categories, and intervention complexity was assessed. The analysis was done using Review Manager 5.1 Analyzer.

**Result:** Ten clinical trials involving 369 HFpEF patients were included in the systematic review and 3 RCTs involving 83 HFpEF patients were included in the meta-analysis. The dietary interventions are classified into prescribed diets targeting specific micronutrients (organic nitrate) (n=30%), macronutrient modification (n=40%), dietary pattern interventions (n=20%), and specific dietary supplements (n=10%). Compared to the control group, the organic nitrate intervention showed a statistically significant improvement in peak VO<sub>2</sub> (MeanDiff=-0.65 [-0.91, -0.39], **p<0.00001**). It also showed a statistically significant association between a fat-rich diet, specifically UFAs (MUFAs and PUFAs), and dietary pattern intervention with the improvement of CRF in HFpEF patients. However, there is no significant association between vitamin-D3 supplementary with CRF in HFpEF patients.

**Conclusion:** Organic nitrate intervention and other dietary manipulation are associated with improved CRF in HFpEF patients.

**Keywords:** Dietary Intervention, Cardiorespiratory Fitness, Heart Failure with Preserved Ejection Fraction, Peak VO<sub>2</sub>

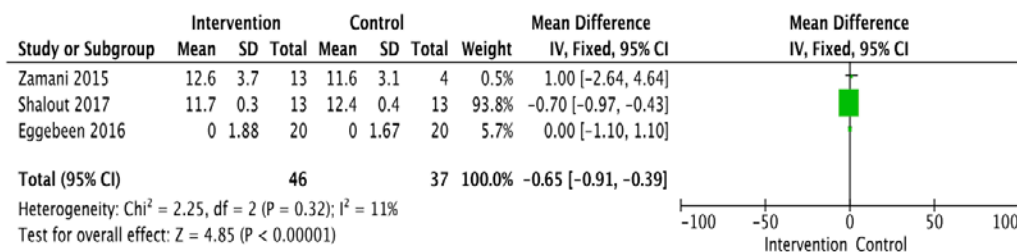


Figure 1. Forest plot of organic nitrate intervention vs control and change in peak VO<sub>2</sub> outcomes (p<0.00001)

## T-wave inversion and elevated level high sensitive troponin I are associated with poor outcomes in COVID-19 patients : A systematic review and meta-analysis

I.S. Pradisa<sup>1</sup>, M. Pramudyo<sup>1</sup>

Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of Padjadjaran, Bandung, Indonesia<sup>1</sup>

### Abstract

**Background and Aims :** Prior studies demonstrated that COVID-19 patients were reported to have Electrocardiogram (ECG) Abnormality. T-Wave inversion (TWI) is found in several case COVID-19 patients and associated with elevated level high sensitive troponin I (Hs Trop-I) as a predictor myocardial damage. Thus, our aim was to determine the prognostic utility of TWI and HS Trop-I in associated with poor outcome in COVID-19 patients.

**Methods :** We searched PubMed, ProQuest, Europe PMC, and Cochrane Library from conception to March 2023. Studies were eligible if they evaluated the relationship of TWI and Hs Trop-I with poor outcome in COVID-19 patients.

**Results :** A total of 7 studies involving 1965 patients met the inclusion criteria and were included in this meta analysis. Our study revealed significantly higher poor outcome in COVID-19 patients associated with new TWI on admission and elevated Hs Trop-I. regardless of the periods of outcomes, study population, or diverse cut-off values, moreover, both new TWI and elevated Hs Trop-I also can predicted poor outcome in COVID-19 patients.

**Conclusion.** This study illustrates the new TWI is common amongst COVID-19 patients and associated with elevated HS Trop-I. Our finding leads that new TWI and elevated Hs Trop I are significantly associated with poor outcome in COVID-19 patients. Given this growing body of evidence, as well as the fact that TWI and Hs Trop-I are very easily to used on admission.

**Keywords:** t wave inversion, high sensitive troponin i, covid-19, poor outcome

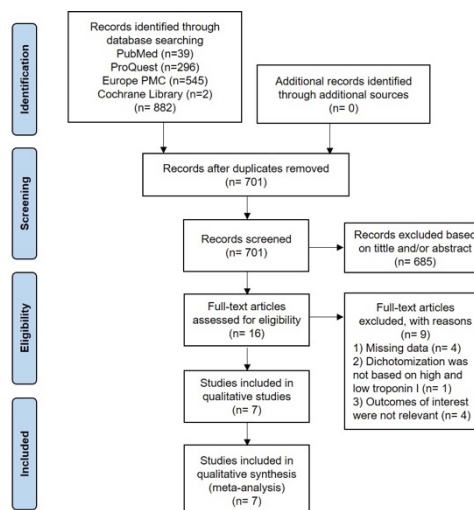


Figure 1. Flow chart of study selection

Flow chart of study selection