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Abstract: Review

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Prognostic Value of N-Terminal Pro-B-Type Natriuretic Peptide in Determining the Outcomes of Atrial Fibrillation Patients with or without Heart Failure: A Systematic Review

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Background: Atrial fibrillation (AF) and heart failure (HF) often coexists and predispose to each other. N-Terminal Pro-B-Type Natriuretic Peptide (NT-pro BNP) levels in predicting the outcomes of heart failure are already established. Meanwhile in patients with AF without heart failure, NT-pro BNP levels are still underused. Therefore, this study aimed to understand the clinical importance of NT-pro BNP measurement in determining the outcomes of AF patients with or without heart failure.
Methods: A comprehensive literature searching was conducted in five online databases including PubMed, EbscoHost, Cochrane, ScienceDirect, and ClinicalKey. Studies were selected using PRISMA diagram. Studies reported outcomes including stroke/embolism, cardiovascular death, and HF hospitalization were considered. Studies presented B-type natriuretic peptide (BNP) data, not converted to NT-pro BNP, were also included.
Results: Six studies were included in this systematic review, five of which were prospective cohorts and the remaining was retrospective cohort. NT-pro BNP and BNP measurement is important in risk assessment of AF patients regardless of HF status. Higher cutoff value of NT-pro BNP in AF with and without HF is associated with higher risk of cardiovascular outcome.
Conclusion: Elevated NT-pro BNP levels are associated with adverse clinical outcomes (stroke/systemic embolism [SE], cardiovascular death, and HF hospitalization) in AF patients with and without clinically diagnosed HF.

Keywords: Atrial fibrillation; NT-pro BNP; heart failure

Author	Year	Study Design	NT-pro BNP	Follow-up	Outcome
Kuronuma K, et al.	2020	Prospective observational cohort	508.2 (IQR 202.0-1094.8)	39.3 months	All cause death, stroke/SE, major bleeding
Hamatani Y, et al.	2020	Prospective observational cohort	488 (IQR 169–1015)	5.0 years	All cause death, stroke/SE, HHF
Brady PF, et al.	2022	Prospective observational cohort	607 (IQR, 217–1831)	4.3 years	HHF, CV death
Hayashi K, et al.	2018	Prospective observational cohort	BNP: 104 (IQR 52.1–199.9)	751 days	TE, death
Nakamura M, et al.	2013	Prospective cohort	BNP: 111 (IQR 67 - 170) pg/ml	5.1 years	Stroke, HF, AMI, sudden cardiac death
Hofer F, et al.	2022	Retrospective cohort	1167 (IQR 337–2963)	4.5 years	CV death, HHF

SE: systemic embolism; **HHF**: hospitalization of heart failure; **CV death**: cardiovascular death; **TE**: thromboembolism; **AMI:** acute myocardial infarction; **IQR:** interquartile range.

Table 1. Characteristic of studies

Prognostic Value of Fragmented QRS Complex in Patients with non-ST Elevation Myocardial Infarct: a literature review

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Background: Fragmented QRS (fQRS) is defined as the presence of one or more notches on R or S waves without any bundle branch block in two contiguous leads. Previous studies said it has a prognostic value for the major adverse cardiac event (MACE) in patients with acute coronary syndrome (ACS), but little is still known about its potential on non-ST elevation myocardial infarct (NSTEMI). This literature study aims to find out whether the fragmented QRS complex can be used to predict MACE in patients with NSTEMI.
Methods: A literature study searched three electronic databases (Pubmed, Science Direct, and Scholar Google) for previous studies using a cohort retrospective design published between 2016 and 2020. The CASP Checklist was used to assess the eligibility of the studies. Data tabulated and narration analysis for study findings were performed.
Results: We found 3 studies that met the inclusion criteria in this review. One study assessed short-time prognostic (≤6 months), one study evaluated long-time prognostic (>12 months), and the last study assessed both. More than a thousand patients participated in these studies. Each study divides patients with NSTEMI into two groups based on ECG findings that are with and without the fQRS complex. The Relation between the fQRS group and MACE, especially cardiovascular mortality has been analyzed. All studies explained that Cardiac mortality in the fQRS group is higher than non fQRS. Recurrent angina, recurrent myocardial infarction, revascularization, and heart failure are also more common happened in the fQRS group. There is a significant relation between NSTEMI with fQRS and late mortality but not in-hospital or 30-days mortality. Fragmented QRS NSTEMI patients were also found to have LVEF lower than non-fQRS. Fragmented QRS suggests a heterogenous depolarization of ventricle myocardium due to ischemic, scar, or fibrosis. This conduction disturbance can become a substrate for a reentrant ventricular arrhythmia that is potentially fatal. Moreover, fQRS finding increases the risk of triple vessel lesions indicating an advanced coronary artery disease which usually has cardiomyopathy.
Conclusion: The presence of fQRS can be used as a predictor for MACE in NSTEMI patients.

Keywords: NSTEMI; fQRS; prognosis; MACE.

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Catheter ablation versus rate control strategy in managing atrial fibrillation with heart failure patients: a systematic review and meta-analysis

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Background: Management of atrial fibrillation (AF) in heart failure (HF) patients remains challenging. It has been widely shown that catheter ablation is more superior than anti arrhythmic drugs due to proarrhythmic effect and increased mortality rates in the rhythm control drugs. However, there is still lack of evidence to determine the comparison of catheter ablation and rate control strategy in the outcome of AF with HF patients. This study aims to compare the effect of catheter ablation and rate control strategy in managing AF with HF patients.
Methods: Randomized controlled trials (RCTs) were obtained from Pubmed, Proquest, Cochrane Library dan Google Scholar databases, which were published in the year of 2000-2022. Studies that compared the outcome of catheter ablation and rate control strategy in AF with HF patients were included. We analyzed left ventricular ejection fraction (LVEF) and all-cause mortality as the primary endpoint with brain natriuretic peptide (BNP) level, Minnesota Living with Heart Failure Questionnaire (MLHFQ) score and 6-minute walk test result (6MWT) as the secondary outcome.
Results: 8 RCTs with 952 patients were included in this study. From primary endpoint, It was found that catheter ablation had no significant difference with rate control strategy to mortality (RR: 0.79; 95% CI: 0.52 to 1.51; p=0.28) and LVEF parameter (mean difference: 3.10; 95% CI: -0.11 to 6.31; p= 0.06). It was also showed that there was no significant difference in the BNP level (mean difference: -77.63; 95% CI: -240.33 to 85.07; p= 0.35) and 6MWT result (mean difference: 7.91; 95% CI: -22.04 to 37.86; p= 0.60) between the two groups. However, it was found that rate control strategy contributed to the higher score of MLHFQ score (mean difference: -13.38; 95% CI: -26.80 to 0.04; p= 0.05).
Conclusion: In most of outcome parameters, there was no significant difference between catheter ablation and rate control strategy. However, it was shown that rate control strategy provided a higher quality of life based on MLHFQ score. .

Keywords: Ablation, rate control; atrial fibrillation; heart failure .

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Comparison of Heart Failure with a Reduced Ejection Fraction (HFrEF) and Heart Failure with a Preserved Ejection Fraction (HFpEF) for Thromboembolisms Risk in Patient with Atrial Fibrillation: A Systematic Review

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Background: Atrial fibrillation (AF) frequently coexists with heart failure (HF) in many patients and they are tightly interrelated. AF patients who also have HF as their comorbidity, often predisposes to an increased risk of thromboembolisms, particularly for HF with reduced ejection fraction (HFrEF). While thromboembolisms risk in AF patient and HF with preserved ejection fraction (HFpEF) is more scarce and conflicting. HFpEF is defined by EF $\geq$ 50%, and HFrEF by EF $\leq$ 40% . However, whether HFrEF carries the same risk as HFpEF in AF patients or not, there is still not enough evidence to clarify this issue. In this systematic review, we aimed to know the comparison of HFrEF and HFpEF for thromboembolisms risk in AF patient.

Methods: A systematic review of interventional studies was performed. Five scientific databases (PubMed, EbscoHost, Cochrane, ClinicalKey, and ScienceDirect) were included in the literature searching strategy. Selected papers then explored by three independent authors regarding the comparison of HFrEF and HFpEF for thromboembolisms risk in patient with AF. Relevance studies further reviewed using the Centre for Evidence-based Medicine (CEBM) critical appraisal tool.

Results: Three studies that included in the review were published within five years between 2017 to 2022. Two of the three studies stated that there is no difference risk of thromboembolisms in HFrEF or HFpEF patients with AF. So, patients with HF and concomitant AF should be treated with anticoagulants irrespective of the EF. Meanwhile, the other one articles concluded that HFrEF in AF patient increases the risk of cardiovascular mortality but not the risk of thromboembolism events (such as stroke and systemic embolism).

Conclusion: Atrial fibrillation with HF has higher risk of thromboembolism events, whether the HF type is HFrEF or HFpEF. Further data needed to give a better understanding.

Keywords: Atrial Fibrillation; HFrEF; HFpEF; Thromboembolisms.

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The Outcome of Corticosteroids Therapy in Patients with Cardiac Arrest: A Systematic Review and Meta-Analysis

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Background: Cardiac arrest (CA) is the sudden loss of blood flow that has long been a dreaded condition for its high mortality rate. Epinephrine (EP) has been considered a main choice of life support for decades. It is an active sympathomimetic hormone that increases the likelihood of achieving the return of spontaneous circulation (ROSC). Moreover, ROSC as a series of pathophysiologic changes affecting the patient's stability ensues, one of which is low serum cortisol. It is useful for identifying corticosteroid impact in improving outcomes in patients with cardiac arrest. We aim to assess the latest evidence of corticosteroids use for adjunctive therapy in patients with cardiac arrest.
Methods: We performed a comprehensive search on topics that assesses corticosteroids use to increase ROSC and survival to hospital discharger in patiens with cardiac arrest from inception up until June 2022.
Results: There were a total of 8558 patients from 5 studies. Meta-analysis showed that corticosteroid was associated with increased ROSC (RR 1.40 [1.24, 1.57], $p<0.005$; I^2: 76%, $p<0.00001$) Pooled analysis also showed that corticosteroid was associated with patiens better survival to hospital discharge (RR 0.94 [0.92, 0.96], $p=0.003$; I^2: 75%, $p<0.00001$).
Conclusion: Corticosteroids is shown to be associated with increased ROSC and survival to hospital discharge in patients with cardiac arrest.

Keywords: Cardiac arrest, Corticosteroids, Meta-analysis.

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Exercise-Induced Premature Ventricular Complexes as a Predictor of Mortality in Asymptomatic Patients: A Systematic Review and Meta-analysis

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Background: It is widely known that exercise-induced premature ventricular complexes (EI-PVCs) in patients with coronary artery disease (CAD) was shown to be associated with mortality. However, the association between EI-PVCs and mortality in asymptomatic individuals remains equivocal. Therefore, the present meta-analysis has two primary objectives. Firstly, to evaluate the prognostic value of exercise and recovery-induced PVCs in increasing the risk of all-cause mortality (ACM) and cardiovascular mortality (CVM) in asymptomatic population. Secondly, to compare the diagnostic value of exercise and recovery-induced PVCs to determine which one is the better predictor of similar outcomes.

Methods: A comprehensive literature search was conducted utilizing the several online databases including PubMed, Europe PMC, and ScienceDirect from inception to April 2022. The study comprised cohort studies examining the relationship between EI-PVCs and ACM as well as CVM in asymptomatic populations. To provide diagnostic values across the statistically significant parameters, we additionally calculated sensitivity, specificity, and area under the curve (AUC).

Results: A total of 13 cohort studies with 82,161 patients were included. EI-PVCs were significantly associated with an increased risk of ACM (RR=1.30 (95%CI=1.18–1.42); P<0.001; I^2=59.6%, P-heterogeneity<0.001) and CVM (RR=1.67 (95%CI=1.40–1.99); P<0.001; I^2=7.5%, P-heterogeneity=0.373). Subgroup analysis based on the frequency of PVCs revealed that frequent PVCs were significantly related with a higher risk of ACM and CVM, but not infrequent PVCs. Moreover, diagnostic test accuracy meta-analysis showed that recovery phase EI-PVCs (specificity: 85% and 90%) have a higher overall specificity than exercise phase EI-PVCs (specificity: 66% and 85%) regarding ACM and CVM, respectively.

Conclusion: EI-PVCs in asymptomatic population are significantly correlated with higher risk of ACM and CVM. Nonetheless, only frequent PVCs were shown to be correlated with ACM and CVM. Furthermore, the specificity of PVCs elicited during recovery phase in predicting the interest outcomes is superior compared to the exercise phase. As a result, we propose that the exercise ECG should be utilized on a regular basis in the asymptomatic population to determine the incidence of frequent PVCs and thereby reduce the risk of mortality.

Keywords: Electrocardiography, premature ventricular complexes, exercise test, EI-PVCs, mortality.

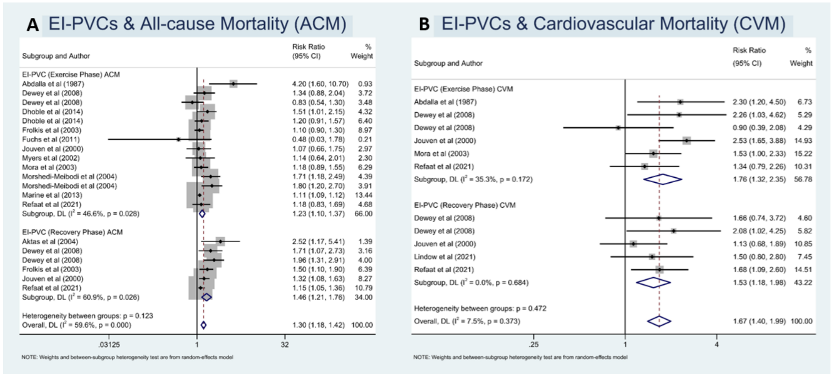

Figure 1. A meta-analysis of association between EI-PVCs and all-cause mortality (a), along with cardiovascular mortality (b).

EI-PVCs: exercise induced premature ventricular complexes; ACM: all-cause mortality; CVM: cardiovascular mortality.

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Widow Maker ECG pattern equivalent to high-risk Acute Coronary Syndrome: Literature Review

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Background: Cardiovascular Disease continues to increase as the leading cause of death in the world. Atherosclerotic cardiovascular disease (ASCVD) is a major disease with high mortality and morbidity rates globally, even in an era of revascularization with percutaneous coronary intervention (PCI). 12-lead electrocardiography (ECG) is a modality that is often used to help clinicians to detect abnormalities in the coronary arteries of the heart. There is a special ECG pattern called “Widow maker ECG” (WME) which is considered STEMI equivalent and features risk of complications and death similar to those of the STEMI and therefore require rapid and adequate coronary evaluation and management.

Methods: ECG examination is an initial investigation that requires a short time in diagnosing Acute Coronary Syndrome (ACS), where STEMI and WME are associated with a high risk of Major Adverse Cardiovascular Event (MACE) and require immediate coronary evaluation and revascularization. WME has a variety of clinical features in its patients and also the pattern on the ECG which is a challenge to detect these abnormalities. There are several WME forms have been reported, including Wellen's Syndrome, de Winter Sign, Shark fin Pattern, Lambda Wave, Tombstone Pattern. Each of these forms of WME has a distinctive clinical pattern and appearance, especially on the ECG pattern. Some WME also have a prognostic value for the occurrence of a complication such as ventricular dysfunction, arrhythmia or even death. Not all WME is a cardiac process and can be an extracardiac process, however, because WME has predictive value equivalent to STEMI special attention is needed in recognizing and treating WME which is basically the same as treatment for STEMI. Although WME has been widely reported in the literature, WME has not yet received a place in the existing guidelines and it is still a challenge to recognize this pattern due to its rare occurrence compared to typical STEMI patterns and the atypical clinical appearance that assuming to ACS.

Conclussion: ECG is still the main modality in recognizing cardiovascular disease such as ACS, especially in STEMI. WME is considered to be equivalent to STEMI and has predictive value for complications and poor prognosis.

Keyword: Widow Maker ECG, STEMI equivalent, Acute Coronary Syndrome

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RED BLOOD CELL DISTRIBUTION WIDTH AS THE COST EFFECTIVE MARKER FOR PREDICTING ATRIAL FIBRILLATION IN PATIENTS WITH HYPERTENSION

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Backgorund: Atrial fibrillation (AF) is the most common cardiac arrhythmia and increases the risk of morbidity and mortality. AF is very common in hypertension patients.
In the Framingham Heart Study, and hypertension induced a 1.7-fold higher risk of AF in the population-based estimates. Inflammation plays a crucial role in the pathophysiology of AF and increased red blood cell distribution width (RDW) associated with activated inflammatory state and oxidative stress. However, information about RDW as the simple parameters for predicting AF in patients with hypertension are limited. The aim of this study is to investigate the role of RDW as the simple and cost effective marker for predicting AF in hypertension patients.

Methods: We performed a systematic search in databases (PubMed, ScienceDirect, and Cochrane Library). We searched for original research articles that included patients with hypertension who had undergone for testing the RDW levels, electrocardiography (ECG) examination and distinguished which subjects had AF and which do not. Review Manager 5.4 was utilized to compute the summary of mean differences (MD) and 95% CI for the outcomes.

Results: We identified three observational studies involving 783 patients with hypertension. most of the study subjects had AF on ECG (65.7%). Pooled analysis showed that hypertension patients with AF was significantly had higher RDW levels by 0.76% compared with hypertension patients without AF [MD 0.76 (95% CI 0.19 - 1.34; p = 0.009)].

Conclusion: RDW levels examination can be considered as a simple and cost effective marker that can be measured anywhere especially in public health centre and covered by National Health Insurance to predicting AF in patients with hypertension. Regarding this examination, further research is needed as a predictor tool to predicting AF in hypertension patients.

Keywords: Red Cell Distribution Width, Hypertension, Atrial Fibrillation.

	AF (+)			AF (-)				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Sarikaya 2014	15.13	1.58	63	14.05	1.157	63	30.4%	1.08 [0.60, 1.56]
Vintila 2016	13.5	1.9	102	12.5	1.1	123	32.2%	1.00 [0.58, 1.42]
Zheng 2020	12.7	0.8	350	12.4	0.7	82	37.4%	0.30 [0.13, 0.47]
Total (95% CI)			**515**			**268**	**100.0%**	**0.76 [0.19, 1.34]**

Heterogeneity: Tau² = 0.22; Chi² = 16.03, df = 2 (P = 0.0003); I² = 88%
Test for overall effect: Z = 2.61 (P = 0.009)

Mean Difference IV, Random, 95% CI: -4, -2, 0, 2, 4 — Favours [AF (-)] Favours [AF (+)]

Figure 1. Forest plot of RDW levels in hypertension patients with AF compared without AF.

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The difference of clinical outcome of early rhythm control between antiarrhythmic drugs and catheter ablation for symptomatic atrial fibrillation: A systematic review

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Background: Atrial fibrillation (AF) increases the risk of mortality and morbidity even with optimal rate control treatment and anticoagulant. Many trials have shown that early rhythm control decreases risk mortality rate from stroke, recurrent AF and cardiovascular event in patient with early AF. This systematic review aims to discuss the comparison of first-line early rhythm control between antiarrhythmic drugs (AAD), catheter ablation (CA), or combination in symptomatic AF.

Methods: All the studies were searched by PubMed using PICO analyses (patients of symptomatic AF, Intervention [catheter ablation and/or antiarrhythmic drugs], not using comparator, Outcome included mortality, arrhythmia recurrence and stroke) and obtained 67 articles. Based on the predetermined inclusion and exclusion criteria, we got 13 articles.

Results: We found 2 meta-analysis randomized clinical trials (RCTs), 1 systematic review and meta-analysis, 2 RCTs, 2 prospective studies, 2 retrospective studies, 1 review, 2 observational studies, and 1 clinical investigation. From those articles that we had reviewed shows: CA is superior to AADs found in 7 articles (lower mortality shows in 5 articles, lower arrhythmia recurrence in 5 articles, and lower stroke in 1 articles); combination between AADs and CA in 4 articles (lower mortality shows in 1 articles, lower arrhythmia recurrence in 3 articles, and lower stroke in 2 articles); and 2 articles stated successful CA preceded by failure of AADs (lower arrhythmia recurrence appear in 2 articles).

Conclusion: Among patients with AF, CA seems to be superior to AADs. CA alone or CA combined with AADs is associated with lower mortality, lower arrhythmia recurrence and lower stroke. Whereas CA preceded by failure of AADs shows lower arrhythmia recurrence.

Keywords: Atrial fibrillation, catheter ablation, antiarrhythmic drug, mortality, arrhythmia recurrence, stroke.

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Association of Sleep Disturbance and Incidence of Atrial Fibrillation: A Systematic Review

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Background: Sleep disturbance, defined as various types of impaired sleep quality, is a health-threatening condition experienced by people from almost every age group in this digitized era. Impaired sleep quality has been linked to adverse cardiovascular outcomes. Atrial fibrillation (AF) is the most recorded dysrhythmias, frequently associated with impaired sleep quality with obstructive sleep apnea (OSA) and sleep duration as the most studied area. Our study aims to search for other sleep-related risk factors that contribute to atrial fibrillation.

Methods: A systematic review was conducted according to PRISMA 2020 guidelines. Four electronic databases (PUBMED, ScienceDirect, Cochrane Reviews, and Scopus) were used in the literature searching strategy. Studies focusing on adults with new-onset AF after reporting sleep disturbance other than OSA were included. The Joanna Briggs Institute Critical Appraisal tool is used to evaluate the risk of bias.

Results: A total of five eligible studies with 15.332.293 patients, composed of three retrospective cohorts and two prospective cohorts, were included in the review. Adjustments were made to other confounding factors such as age, gender, nutritional status, comorbidities, medication, and lifestyle. Two studies assessed insomnia, one showed that insomnia is associated with an increased risk of AF, and one showed that the insomnia group had the highest cumulative incidence of AF compared to other sleep disturbance groups. Two studies showed that frequent night-time awakening, decreased rapid eye movement, and short irregular sleep were associated with an increased risk of AF, and the last one showed that patients with healthy sleep scores had a lower association with AF incidence compared to patients with poor sleep scores.

Conclusion: Sleep disturbance other than OSA is associated with an increased risk of new-onset AF incident, independent of other confounding factors. Improved sleep quality is needed to prevent AF. Further research needs to be conducted with standardized measurement to increase accuracy.

Keywords: Sleep Disturbance, Atrial Fibrillation, Systematic Review.

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ARRHYTHMIA ASSOCIATED WITH DENGUE VIRUS INFECTION: A SYSTEMATIC REVIEW OF CASE REPORTS

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Background: The mosquito Aedes aegypti is responsible for transmitting the virus that causes dengue fever. Although they are rare, cardiac problems can occur in specific situations. Arrhythmias caused by dengue virus infection have developed into a serious health problem. They are essential in the diagnosis of the first symptom of acute myocarditis and acute cardiovascular event. To review the incidence of arrhythmias and dengue virus infection in several countries
Methods: We completed a descriptive systematic review of case reports according to PRISMA guidelines, including cases of children and adult patients with incident dengue virus infection and arrhythmia. We collected data on the clinical history, outcomes, and patient characteristics. then utilized a standardized tool to assess the quality of the cases.
Results: Search strategy in studies were terms for arrhythmia and dengue virus infection and systematically searched PubMed, SCOPUS, and ScienceDirect. Among 223 articles, we included 13 reports from 12 countries, comprising 25 patients consisting entirely of 61,9% children and 38,1% adults. We have identified a total of 16 patients with serology-positive dengue virus infection and arrhythmias 76,2% of patients. The mean platelet count of 60181 (57000 ± 44485,96) / mm^3, the mean Hb count of 13,28 (12,35 ± 2,15) g/dL, the mean Ht count of 32,01% (18 patient of 21), and WBC count of 6175 (4875 ± 3628,99) / mm^3. Tachyarrhythmia is the most common in this study (8 patients; 38,1%; consist of Supraventricular Tachycardia or Atrial Fibrillation). Additionally junctional rhythm (6 patients; 28,6%), atrioventricular block (7 patients; 33,3%), and ventricular arrhythmia (4 patients; 19%; consists of Ventricular Tachycardia).
Conclusion: Changes in electrocardiogram (ECG) are common during viral dengue infection. In patients with acute cardiovascular compromise, clinicians should have a high indicator of suspicion for dengue virus infection as an etiology.

Keywords: Arrhythmia, Dengue Virus Infection, Aedes aegypti.

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Adjunctive Left Atrial Posterior Wall Isolation Compared to Isolation of Pulmonary Veins Alone in Catheter Ablation of Atrial Fibrillation: A Meta-analysis

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Background: Atrial fibrillation (AF) is the most common heart rhythm disorder. One of the current recommendations in AF management is catheter ablation for rhythm control as well as symptoms management. However, even after ablation many patients still experience recurrent AF events. Posterior wall isolation (PWI) of the left atrium, in conjunction with pulmonary vein isolation (PVI) has shown to be a promising new method of better managing AF recurrence.
Methods: We systematically searched electronic medical databases including PubMed, ScienceDirect as well as Cochrane Library for studies comparing the effect of PVI with PWI versus PVI alone in AF ablation using the keywords “posterior wall isolation”, “catheter ablation” and “atrial fibrillation”. Included studies were assessed for quality, and relevant data were extracted. The primary outcome of interest was the recurrence of AF during the follow-up period. The secondary outcomes were total procedure time and procedural complications. Statistical analysis was performed in Review Manager 5.4 using a random-effects model.
Results: 10 studies (7 randomized trials, 3 prospective studies) with 1,234 AF patients were included in the final analysis. Overall, the addition of PWI to PVI resulted in a significant decrease in the recurrence of atrial arrhythmias (OR 0.62, 95% CI 0.42 – 0.93, p = 0.02). Subgroup analysis found significant difference between methods used (p = 0.02), suggesting a better outcome from studies which used cryoballoon ablation compared to radiofrequency ablation (OR 0.37, 95% CI 0.23 – 0.59 vs. 0.81, 0.52 – 1.27). However, no study directly compared these two methods in performing PWI. There was a significant mean increase in procedure time of 23.38 minutes (95% CI 12.36 – 34.49), with no difference in procedural complications.
Conclusion: PWI in conjunction with PVI is effective in reducing the recurrence of atrial fibrillation compared to PVI alone. Further studies should be conducted to determine the best method for performing PWI.

Keywords: Atrial fibrillation, catheter ablation, posterior wall isolation.

	PVI + PWI		PVI only			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
1.1.1 Radiofrequency Catheter						
Kim 2015	10	60	22	60	9.8%	0.35 [0.15, 0.81]
Lee 2019	27	102	25	105	12.4%	1.15 [0.61, 2.16]
Pak 2020	16	57	18	57	10.4%	0.85 [0.38, 1.89]
Tamborero 2009	27	55	27	54	11.0%	0.96 [0.46, 2.04]
Tokioka 2021	28	90	43	91	12.7%	0.50 [0.27, 0.93]
Yu 2016	16	54	11	59	9.6%	1.84 [0.76, 4.42]
Subtotal (95% CI)		**418**		**426**	**65.8%**	**0.81 [0.52, 1.27]**
Total events	124		146			
Heterogeneity: Tau² = 0.17; Chi² = 10.90, df = 5 (P = 0.05); I² = 54%						
Test for overall effect: Z = 0.91 (P = 0.36)						
1.1.2 Cryoballoon Catheter						
Ahn 2022	12	50	23	50	9.8%	0.37 [0.16, 0.87]
Aryana 2020	14	55	25	55	10.3%	0.41 [0.18, 0.92]
Bisignani 2020	3	30	6	50	5.2%	0.81 [0.19, 3.53]
Nishimura 2019	8	50	23	50	8.9%	0.22 [0.09, 0.57]
Subtotal (95% CI)		**185**		**205**	**34.2%**	**0.37 [0.23, 0.59]**
Total events	37		77			
Heterogeneity: Tau² = 0.00; Chi² = 2.28, df = 3 (P = 0.52); I² = 0%						
Test for overall effect: Z = 4.18 (P < 0.0001)						
Total (95% CI)		**603**		**631**	**100.0%**	**0.62 [0.42, 0.93]**
Total events	161		223			
Heterogeneity: Tau² = 0.22; Chi² = 20.76, df = 9 (P = 0.01); I² = 57%						
Test for overall effect: Z = 2.35 (P = 0.02)						
Test for subgroup differences: Chi² = 5.76, df = 1 (P = 0.02), I² = 82.6%						

Odds Ratio
M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours [PVI + PWI] Favours [PWI]

Figure 1. Forest plot demonstrating the efficacy of PWI in conjunction with PVI on preventing the recurrence of AF.

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Early Rhythm Control for Cardiovascular Outcomes in Patients with Atrial Fibrillation: A Meta-analysis and Systematic Review

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Background: Fibrillation (AF) is the most common cardiac arrhythmia worldwide. It increases the mortality and morbidity even for patients with optimal current guideline-based management. Recent Early Treatment of Atrial Fibrillation for Stroke Prevention Trial (EAST-AFNET 4) revealed that early rhythm control (≤1 year before enrollment) was associated with lower risk of primary cardiovascular outcome. Our study aims to assess the applicability of this trial in general practice after it had been published for two years.
Methods: A total of four observational studies were retrieved from PubMed and Google Scholar. It involves 101,542 atrial fibrillation patients consisting of 29,291 patients received early rhythm control and 71,621 patients underwent usual care therapy using rate control medication. Analysis was conducted to calculate hazard ratio for primary outcome containing a composite of death from cardiovascular causes, stroke, or hospitalization with worsening of heart failure and acute coronary syndrome; all-cause mortality; and risk of stroke using RevMan 5.4. application.
Results: Based on the analysis, early rhythm control reduces composite outcomes by 16% (HR 0.84 [95% CI: 0.77-0.92], p=0.0003; I^2: 0%, p=0.67) compared to usual care. In contrast, the result of all-cause mortality of early rhythm control was comparable to usual care group (HR 0.90 [95% CI: 0.79-1.02], p=0.10; I^2: 0%, p=0.82). The risk of stroke group can be decreased by 26% by early rhythm control (HR 0.74 [95% CI: 0.64-0.86], p<0.0001; I^2: 0%, p=0.81).
Conclusion: Early rhythm-control approach seems to be a promising treatment to reduce the risk of stroke and cardiovascular outcomes in atrial fibrillation patients.

Keywords: Early rhythm control; rate control; atrial fibrillation; cardiovascular outcomes.

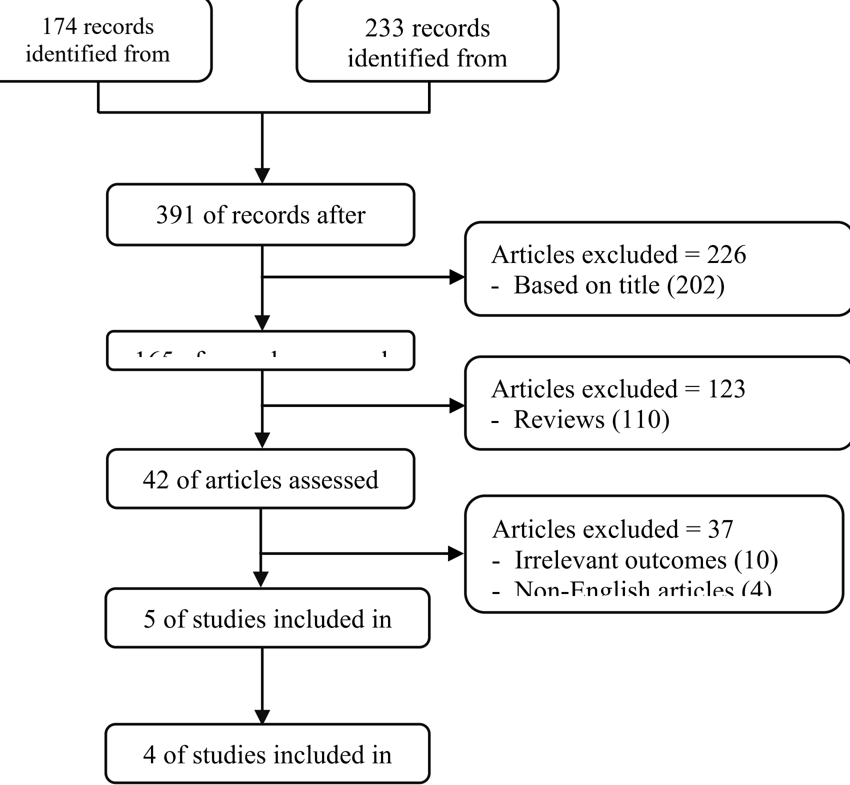

Figure 1. Summary of Included Studies

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Investigation of high-risk electrocardiographic markers as predictors of lethal arrhythmic events in Brugada syndrome: A systematic review and meta-analysis

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Background: Numerous studies have demonstrated that a history of syncope, prior sudden cardiac arrest, and previous documented ventricular tachyarrhythmias are still insufficient to stratify the risk of sudden cardiac death in Brugada syndrome. Several auxiliary risk stratification parameters are pursued to yield a better prognostic model. Various research have studied the prognostic usefulness of various electrocardiographic markers related to the electrophysiological nature of this entity, albeit with contradictory results. Our aim was to assess the association between several electrocardiographic (ECG) markers (e.g., wide QRS, fragmented QRS, S-wave in lead I, aVR sign, early repolarization pattern in inferolateral leads, and repolarization dispersion pattern) with the risk of developing poor outcomes in patients with Brugada Syndrome.

Methods: A systematic literature search from several databases (PubMed, Europe PMC, ScienceDirect) was conducted from inception up until August 17th, 2022. Studies were eligible if they investigated the relationship of the aforementioned ECG markers with the likelihood of acquiring lethal arrhythmic events.

Results: This meta-analysis comprised of 27 studies with a total of 6552 participants. Our study demonstrated that wide QRS, fragmented QRS, S-wave in lead I, aVR sign, early repolarization pattern in inferolateral leads, and repolarization dispersion ECG pattern were associated with the incremental risk of developing syncope, ventricular tachyarrhythmias, implantable cardioverter-defibrillator shock, and sudden cardiac death in the future, with the risk ratios ranging from 1.41 to 2.00. Moreover, diagnostic test accuracy meta-analysis indicated that repolarization dispersion ECG pattern had the highest overall area under curve (AUC) value amid other ECG markers regarding our outcomes of interest.

Conclusion: A multivariable risk assessment approach based on the aforementioned ECG markers has an excellent prognostic value and contains the ability to improve the current risk stratification models in Brugada syndrome.

Keywords: Electrocardiography, lethal arrhythmic events, Brugada syndrome, risk stratification.

ECG markers	Number of studies	Risk ratio (95% CI)	Heterogeneity	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
fQRS	17	1.84 (1.13-3.00) (P=0.014)	I^2=76.5% (P<0.001)	34% (19%-53%)	83% (74%-89%)	0.71 (0.67-0.75)
Wide QRS	8	1.50 (1.04-2.16) (P=0.031)	I^2=65.6% (P=0.005)	30% (13%-56%)	74% (55%-87%)	0.57 (0.53-0.61)
S-wave in lead 1	10	1.69 (1.08-2.64) (P=0.021)	I^2=68.4% (P=0.001)	61% (43%-76%)	63% (51%-73%)	0.66 (0.62-0.70)

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aVR sign	4	1.81 (1.02-3.22) (P=0.042)	I^2=45.1% (P=0.141)	48% (25%-71%)	78% (68%-85%)	0.74 (0.70-0.78)
ER pattern in inferolateral leads	15	2.00 (1.26-3.18) (P=0.003)	I^2=78.0% (P<0.001)	16% (10%-25%)	87% (81%-91%)	0.57 (0.52-0.61)
Repolarization dispersion	9	1.41 (1.21-1.65) (P<0.001)	I^2=91.8% (P<0.001)	63% (56%-69%)	83% (74%-90%)	0.77 (0.73-0.80)

AUC: area under curve; CI: confidence interval; ECG: electrocardiographic; ER: early repolarization; fQRS: fragmented QRS

Table 1. Summary results of several electrocardiographic markers in predicting lethal arrhythmic events in Brugada syndrome.

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The Safety of Discontinuation of Oral Anticoagulants in Patients with Atrial Fibrillation Following Ablation: A Systematic Review

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Background: The safety of discontinuing oral anticoagulants in patients with atrial fibrillation following ablation remains controversial. European Society of Cardiology stated that the long-term continuation of anticoagulants beyond two months following ablation should be based on the patient's stroke risk profile; however, the decision remains challenging considering the lack of explicit guidelines. Furthermore, a worldwide survey showed that some centers implement a policy of withdrawing OAT even in the majority of patients at high risk of thromboembolic events. To address this issue, we conducted a systematic review to investigate the safety of discontinuing oral anticoagulants in patients with atrial fibrillation following ablation.

Methods: A systematic review of cohort studies was performed. A comprehensive search for relevant literatures was conducted using predefined keywords in five scientific databases (PubMed, Cochrane, EBSCOhost, ClinicalKey, ScienceDirect). Studies published in the last ten years which compared the incidence of thromboembolic events in off-OAC group and on-OAC group were considered. Duplicated articles were removed.

Results: Eight studies were retained for the final review. Overall, there was no difference in the incidence of thromboembolic events between off-OAC and on-OAC groups, while higher bleeding rates in on-OAC groups were observed in three studies. One study revealed significantly higher rate of ischemic stroke in off-OAC subgroup with CHA_2DS_2-VASc scores ≥ 2 compared to on-OAC group (1.6% per year vs. 0.3% per year; p = .046). However, another study comprising of 108 patients with prior strokes (mean CHA_2DS_2-VASc score = 4.1 ± 1.4) showed no difference in thromboembolic events between off-OAC and on-OAC group, with higher bleeding instances in on-OAC group (8.3% vs. 0%; p = .027).

Conclusion: Patients who discontinued OAC after AF ablation generally had a similar incidence of TE to patients who remained on OAC. This systematic review indicates that the risk-benefit ratio favors the discontinuation of OAC in patients with successful AF ablation. Regarding the inconsistency between studies involving high-risk patients, further studies with larger sample size may be warranted to investigate factors which could predict thromboembolic events in those with high stroke risk profile.

Keywords: atrial fibrillation, ablation, anticoagulant discontinuation, thromboembolic event, bleeding