Pharmacological Treatment of Tachyarrhythmias in Acute Myocardial Infarction - a Review
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ABSTRACT
Acute myocardial infarction (AMI) causes severe metabolic and electrophysiological changes that induce silent or symptomatic life-threatening arrhythmias. Ventricular arrhythmias and atrial fibrillation are common during the early phase of AMI and are also important prognostic factors. Rapid identification and treatment of these arrhythmias can be life-saving, since in-hospital mortality rises dramatically in patients who develop arrhythmias with a fast ventricular rate following an AMI. Along with myocardial revascularization, adequate pharmacological therapy of hemodynamically relevant arrhythmias is generally useful. Since there are no controlled randomized trials comparing different antiarrhythmic drugs (AADs) in AMI, optimal decision making is based on medical societies guidelines recommendations and clinical judgement.

Keywords: atrial fibrillation, acute myocardial infarction, ventricular arrhythmias, antiarrhythmic drugs.

INTRODUCTION
Both atrial and ventricular arrhythmias may occur in the setting of acute myocardial infarction (AMI). Therapy for AMI and arrhythmia management are now based increasingly on invasive approaches, with early reperfusion therapy as paramount action. In addition to myocardial revascularization, a ‘wait and see’ strategy for arrhythmias with no or moderate haemodynamic relevance seems reasonable1. However, when arrhythmias result in hemodynamic instability, careful use of antiarrhythmic drugs is generally recommended and alternative treatment options such as electrical cardioversion or catheter ablation should be considered. Frequently, sustained ventricular tachyarrhythmias (VAs) may lead to hemodynamic collapse and warrant immediate treatment2. While the urgent treatment for VAs with haemodynamic instability remains direct current cardioversion (DCC), recurrent sustained VAs requires drug therapy. Atrial fibrillation (AF) may also require urgent treatment when it presents with a fast ventricular rate which results in hemodynamic deterioration2. The management of other arrhythmias is also based mainly on symptoms and their hemodynamic impact.

SUPRAVENTRICULAR ARRHYTHMIAS
AF is the most frequent supraventricular arrhythmia occurring in up to 21% of the patients presenting with
ST elevation acute myocardial infarction (STEMI)\textsuperscript{1,3}. AF occurring in STEMI patients is associated with a worse short- and long-term prognosis\textsuperscript{1}. Significant multivariable predictors of AF include three-vessel coronary artery disease and initial thrombolysis, advanced age, higher peak creatine kinase levels, worse Killip class and increased heart rate\textsuperscript{6}. Lower socioeconomic status seems to predict prevalence of AF in some populations in a similar fashion to other cardiovascular diseases\textsuperscript{5,6}.

In the acute setting, AF results in reduced cardiovascular performance through a variety of mechanisms. These include loss of atrioventricular synchrony and atrial systole, reduced ejection time due to high ventricular rates, and rhythm irregularity\textsuperscript{7,8}. Patients with AMI and AF have a more adverse clinical course of their disease due to older age, increased number of comorbidities, worse Killip class, severe LV dysfunction, more extensive coronary artery disease and poorer perfusion after thrombolysis or primary PCI\textsuperscript{9}. Moreover, the presence of AF adds a burden on the therapeutical decisions considering the need for anticoagulation.

Pathophysiology

The most common etiology of AF in the setting of AMI appears to be atrial stretching due to heart failure with elevation in left atrial pressures\textsuperscript{10}. In patients with AMI complicated with severely depressed left ventricle systolic function, AF is precipitated or exacerbated by on-going atrial ischemia or infarction, abnormalities of autonomic regulation, increased sympathetic tone\textsuperscript{11}, pericardial inflammation and by iatrogenic factors such as positive inotropic agents. One must also consider the reverse relationship between AF and AMI: AF with rapid ventricular response could also lead to a Type II MI. In this case, invasive therapy may not be warranted\textsuperscript{12}.

Acute pharmacological management of AF

Typically, recent onset AF is well-tolerated and no specific treatment is required, except anticoagulation. Episodes are often repetitive and may last from minutes to hours\textsuperscript{2}. However, when it leads to hemodynamic instability, urgent treatment is needed to ensure rate control or return to sinus rhythm\textsuperscript{1}. When the fast ventricular rate results in haemodynamic collapse, direct current cardioversion is generally required.

Parenteral anticoagulation

Parenteral anticoagulation is recommended in addition to antiplatelet therapy in all AMI patients undergoing PCI\textsuperscript{1}. AF may be only a transient arrhythmia accompanying an acute MI, in an anticoagulant-naive patient. Consequently, in the periprocedural setting, parenteral anticoagulation is indicated. Routine of unfractionated heparin (UFH) is recommended\textsuperscript{1}. As an alternative to UFH, routine use of enoxaparin i.v. should be considered\textsuperscript{1}.

Amiodarone

If an acute rhythm control strategy is pursued, amiodarone is the only pharmacological option\textsuperscript{1}. Intravenous amiodarone could facilitate electrical cardioversion and/or decrease the risk for early recurrence of AF after electrical cardioversion\textsuperscript{1}. Amiodarone may also be considered for rate control, if this strategy is chosen\textsuperscript{1,11}, with an initial dose of 5 mg/kg in 1 h followed by 50 mg/h\textsuperscript{12}.

Beta-blockers

Intravenous beta-blockers, including esmolol, propranolol and metoprolol are indicated for rate control and to reduce myocardial oxygen demands, if no clinical signs of acute heart failure (AHF) or hypotension are present\textsuperscript{13,14}. In these cases, the negative inotropic effect of \(\beta\)-blockers may result in further compromise of pump function. In the setting of AMI without AHF, short-acting beta blockers are preferred to allow rapid adjustment of the dose, based on the patient’s blood pressure and heart rate response. Close to the time of discharge, longer-acting beta blockers may be preferred.

Digoxin

In selected patients, intravenous digitalis should be considered for rate control when concomitant AHF and hypotension are present\textsuperscript{15}. Usual dosage is 0.25 mg each 2 h up to 1.5 mg\textsuperscript{2}. Digoxin is ineffective in converting recent onset AF to sinus rhythm\textsuperscript{16}. However, data from the ARISTOTLE AF trial showed that digoxin was independently associated with higher mortality rate in patients with AF regardless of HF\textsuperscript{17}. In these patients, the risk of death increased with higher serum digoxin concentrations\textsuperscript{17}. Among patients whose digoxin levels were greater than 1.2 ng/ml, the death rate increased by 56\%\textsuperscript{17}.

Nondihydropyridine calcium antagonists

Administration of nondihydropyridine calcium antagonists might be considered to slow a rapid ventricular response in patients with AMI and AF only in the absence of significant HF or hemodynamic instability\textsuperscript{11}.

Vernakalant, flecainide and propafenone should not be used for rhythm control in patients with AMI\textsuperscript{11}.
Post-procedural management of AF

Patients with AF and moderate-to-severe thromboembolic risk (CHA₂DS₂-VASc score ≥2) should be adequately treated with oral anticoagulants (either vitamin K antagonists or novel oral anticoagulants) to reduce the risk of stroke or systemic embolism. Consequently, patients with AMI and AF require combined antithrombotic therapy which results in a significant bleeding risk. Concomitant risks of cerebro-vascular and coronary ischemic events and bleeding need to be balanced when deciding the duration and the type of antithrombotic therapy. Generally, dual antithrombotic therapy with a novel oral anticoagulant (NOAC) and a P2Y12 inhibitor (preferably clopidogrel) is recommended for the first 12 months after percutaneous coronary intervention (PCI) for an acute coronary syndrome (ACS), since it results in less major bleeding than triple therapy. NOACs and the recommended doses are shown in Table 1.

However, in AF patients with AMI, at least a short course of triple therapy (e.g. ≤1 week) is desirable and should be continued up to one month when the bleeding risks are low and ischemic concerns prevail. These recommendations are based on the results of four RCTs which compared dual therapy with a P2Y12 inhibitor (mostly clopidogrel) plus a NOAC—dabigatran 110 mg or 150 mg b.i.d. (REDUALPCI)²⁰, rivaroxaban 15 mg o.d. (PIONEER AF-PCI)³¹, apixaban 5 mg b.i.d. ( AUGUSTUS)²² or edoxaban 60 mg o.d. (ENTRUST-AF PCI)²³—vs. triple therapy with a VKA in AF patients with a recent ACS or undergoing PCI. All trials have shown a significant reduction of major or clinically significant bleeding, comparable rates of ischemic stroke, AMI and stent thrombosis with dual (NOAC + P2Y12) vs. triple (VKA + P2Y12 + aspirin) therapy. Since patients with AMI who develop AF are usually frail, with severe cardiovascular diseases and multiple comorbidities, they frequently have a high risk for both thrombotic and bleeding events. Consequently, the duration of the triple antithrombotic therapy should always take into consideration the balance between these risks. Assessment of ischemic and bleeding risks should be done using validated risk predictors (e.g. CHA₂DS₂-VASc, ABC, and HAS-BLED) with a focus on modifiable risk factors.

For paroxysmal AF, long-term antiarrhythmic therapy is not indicated when moderate to severe left ventricular systolic dysfunction or HF are absent associated with increased in-hospital and long-term mortality rates. This notion is based on data collected before thrombolysis and additional modern methods of treatment became widely available, and no information is available on the significance of PAF in the general population with AMI in the thrombolytic era. The aim of the present study was to define the incidence, associated clinical parameters, and short- and long-term prognostic significance of PAF in patients with AMI in the thrombolytic era. Methods and Results - A prospective, nationwide survey was conducted of 2866 consecutive patients admitted with AMI in all coronary care units in Israel during January/February 1992, 1994, and 1996 (thrombolytic era [TE]). In patients with AMI complicated with LV dysfunction, angiotensin-converting enzyme inhibitors appear to reduce the incidence of AF. Statin therapy, possibly owing to an antiinflammatory effect, has been associated with a reduction in paroxysmal AF in patients with ischemic heart disease. In a retrospective study of over 3300 patients presenting with AMI and in sinus rhythm, early statin therapy (prescription within 48 hours of hospitalization) was associated with a reduced risk of AF.

In patients at risk of gastrointestinal bleeding, concomitant use of proton-pump inhibitors is reasonable.

**VENTRICULAR ARRHYTHMIAS**

Ventricular tachyarrhythmias (VAs) commonly appear early in ischemia and markedly increase the risk of mortality in patients with an AMI. The incidence of VAs has declined with the use of reperfusion strategies but they still occur in 6-8% of the AMI patients.

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**Table 1**

| NOAC       | CrCl>30mL/min-150mg b.d | CrCl=30-49mL/min-110mg b.d | CrCl=15-30mL/min-75 mg b.d | CrCl<15mL/min-Avoid |
|------------|-------------------------|---------------------------|---------------------------|---------------------|
| Dabigatran |                         |                           |                           |                     |
| Apixaban   | CrCl>15mL/min-5mg b.d    | Any 2 (>80yrs, <60kg, SCr>1,5mg/dl)-2,5mg b.d | CrCl<15mL/min-Avoid     |
| Rivaroxaban| CrCl>50mL/min-20mg o.d   | CrCl=15-50mL/min-15mg o.d | CrCl<15mL/min-Avoid     |
| Edoxaban   | CrCl>50mL/min-60mg o.d   | CrCl=30-49mL/min-30mg o.d | CrCl<15mL/min-Avoid     |

Note: CrCl = creatinine clearance as calculated by Cockcroft-Gault formula, AF = atrial fibrillation, BD = twice daily regimen, NOAC = non-vitamin K antagonist oral anticoagulant, OD = once daily regimen, VTE = venous thromboembolism.

Adapted from Paul David Morris, Karan Saraf, Pankaj Garg, Paul Sheridan, Robert Storey - Non-Vitamin K antagonist oral anticoagulants (NOACs): Clinical Evidence and therapeutic considerations
**Pathophysiology**

The mechanisms of arrhythmogenesis depend on the stage of evolution of an AMI. Acute ischemia results in harmful consequences on the myocardial metabolism causing anaerobic glycolysis leading to acidosis and accelerated potassium efflux from the myocytes. This generates electrolyte imbalance and electrical instabili-

ity, which facilitate VAs development in the early phase of AMI. Myocardial reperfusion may also result in abrupt changes in ionic and electrical balance promoting life-threatening VAs. Acute phase arrhythmias arise in the first 30 to 60 minutes and are attributed to reentry and abnormal automaticity. Chronic phase VAs appear after more than 48 hours following an AMI and are usually re-entrant and scar mediated, owing to a large MI resulting in a severely depressed LV function and LV remodeling. Monomorphic ventricular tachycardia (VT) is generally scar-related and is the typical presentation in patients with older fibrotic infarct areas in the myocardium.

**General management**

Management of VAs is dependent on whether the arrhythmia is sustained or non-sustained, and if it results in hemodynamic compromise or occurs in an otherwise stable patient. The timing of the VA relative to the AMI plays another important role in the therapeutic decision. AMI related VAs can occur in multiple instances: pre-reperfusion VAs, reperfusion-induced VAs, early post-reperfusion VAs (within 48 h), late post-reperfusion VAs (>48 h after reperfusion), post-discharge arrhythmias. Ventricular fibrillation (VF) is the most frequent mechanism of prehospital sudden cardiac death (SCD) and warrants immediate DCC. The development of VF in patients with an AMI, if occurring within the first 48 h, is associated with an increase in early mortality, but little or no increase in long term mortality after hospital discharge. Recurrent VF and/or polymorphic VT may be an indicator of incomplete reperfusion or recurrence of acute ischemia (e.g. acute stent thrombosis). Urgent coronary angiography should consequently be considered.

Generally, sustained VAs (monomorphic or polymorphic) which result in hemodynamic instability call for rapid treatment by DCC. Non-sustained, recurrent or well-tolerated VAs require correction of the underlying ischemic substrate, possible added triggers and should not be treated with anti-arrhythmic drugs before reperfusion.

If ongoing myocardial ischemia is suspected to be responsible for the VA, coronary angiography and prompt and complete revascularization is the mainstay of treatment. Correction of electrolyte imbalances (especially hypokalemia and hypomagnesemia) is recommended in patients with VT and/or VF. Hypokalemia during an AMI is a risk factor for VF. In the GISSI-2 trial, the probability of VF among patients with a serum potassium <3.6 mEq/L was almost twice as high as among patients with a higher serum potassium. Statin therapy has been shown to lower the incidence of premature ventricular complexes (PVCs) and non-sustained VT in patients with ACS. Drugs that inhibit the renin-angiotensin-aldosterone system, namely angiotensin converting enzyme (ACE) inhibitors also reduce the incidence of VAs in AMI. For the temporary management of malignant VT/VF refractory to usual treatment, deep sedation (preferably with benzodiazepines) is a viable therapeutic option which provides a reduction of the sympathetic drive associated with post-MI VAs. For patients with AMI without VAs, prophyllactic antiarrhythmic drug treatment, with the exception of beta-blockers is not indicated and may be harmful.

**Antiarrhythmic drugs**

The use of antiarrhythmic drugs (AAD) for VAs in AMI has been questioned and is largely based on observational data. Controlled randomized trials on the use of AAD for VAs in AMI are lacking. Prophylactic treatment with AADs is not indicated (with the possible exception of beta-blockers) and may be harmful. Useful antiarrhythmics, their classification, mechanisms of action, indications, dosing and possible side-effects are shown in Table 2.

**Beta-blockers**

Beta-blockers are first-line therapy in the management of VA in patients with AMI. Intravenous beta-blocker treatment is indicated for patients with VAs, in the absence of contraindications. VAs in the early or acute stages of an MI are in part related to enhanced automaticity, resulting from elevated catecholamines and beta receptor stimulation. At cellular level, the favorable electrophysiological effects of beta-blockers include decreased automaticity, which reduces the predisposition for triggered VA, and reduced conduction velocity, which impacts on the stability of re-entrant circuits. Beta-blocker use in the first 24 hours after AMI was associated with reduced in-hospital mortality in patients with sustained VT/VF. In the CAPRICORN trial, Carvedilol was shown to have significant anti-arrhythmic effects after AMI, suppressing both atrial and ventricular arrhythmias in these patients.
Furthermore, in patients with severe recurrent VAs such as VT/VF storm, an intravenous beta-blocker can be useful. The mortality reduction observed with beta-blockade in the first 24 hours after AMI suggested that patients with sustained VAs benefited from acute beta-blockade without an increase in worsening heart failure.

**Amiodarone**

Intravenous amiodarone is recommended for treatment of recurrent polymorphic VT. Amiodarone has a wide spectrum of action that includes blockade of depolarizing sodium currents and potassium channels that generate repolarizing currents. This results in prolongation of the refractoriness of the His-Purkinje system and ventricular contractile fibers thus preventing micro reentry. Consequently, amiodarone may inhibit or terminate VAs by decreasing automaticity and re-entry. Amiodarone (150–300 mg i.v. bolus) should be considered to acutely suppress recurrent VT or VF. However, over the long term, amiodarone...
ne treatment may result in increased mortality at 6 months. This outcome is most likely explained by confounding factors (e.g., patients with worse prognosis received amiodarone). It may also occur due to residual adverse effects from amiodarone, possibly by further reducing myocardial contractility in already severely depressed left ventricles. Intravenous amiodarone may cause phlebitis (it is advisable to use a large peripheral vein, avoid administration >24 h and use preferably volumetric pump) and arterial hypotension.

Lidocaine
Lidocaine may be used to treat recurrent VT with haemodynamic deterioration despite repetitive electrical cardioversion, if beta-blockers, amiodarone and overdrive stimulation are not effective or applicable. An observational study by Piccini et al suggested that lidocaine might be preferred over amiodarone for the treatment of sustained VT/VF complicating acute MI. In the first hours after VAs complicating acute MI, both amiodarone and lidocaine are associated with better survival. On longer term, amiodarone use was associated with a higher risk of death at 30 days and 6 months, while lidocaine use did not result in benefit or harm.

CONCLUSION
Both supraventricular and ventricular arrhythmias which occur in the setting of an AMI are associated with a worse short- and long-term prognosis, increasing the risk of mortality in these patients. Adequate use of antiarrhythmic drugs in the management of hemodynamically relevant arrhythmias is generally useful. At the same time, it is also challenging since, with the exception of beta-blockers, data derived from randomized clinical trials on antiarrhythmic drugs in the management of patients with AMI and life-threatening arrhythmias are scarce, outdated and inconclusive. In this setting, clinical judgement is mandatory.

Compliance with ethics requirements:
The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

References
1. B. Ibanez et al., “2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation,” Eur. Heart J., vol. 39, no. 2, pp. 119–177, 2018, doi: 10.1093/eurheartj/ehx393.
2. B. Gorenek et al., “Cardiac arrhythmias in acute coronary syndromes: Position paper from the joint EHRA, ACCA, and EAPCI task force,” Europace, 2014, doi: 10.1093/europace/euu208.
3. J. Schmitt, G. Duray, B. J. Gersh, and S. H. Hohnloser, “Atrial fibrillation in acute myocardial infarction: A systematic review of the incidence, clinical features and prognostic implications,” European Heart Journal, 2009, doi: 10.1093/eurheartj/ehn579.
4. B. S. Crenshaw, C. B. Granger, A. L. Stebbins, E. J. Topol, and R. M. Califf, “Atrial fibrillation in the setting of acute myocardial infarction: The GUSTO-I experience,” J. Am. Coll. Cardiol., vol. 30, no. 2, pp. 406–413, 1997, doi: 10.1016/S0735-1097(97)00194-0.
5. S. R. Lee, E. K. Choi, K. Han, M. J. Cha, and S. Oh, “Prevalence of non-valvular atrial fibrillation based on geographical distribution and socioeconomic status in the entire Korean population,” Korean Circ. J., vol. 48, no. 7, pp. 622–634, 2018, doi: 10.4070/kcj.2017.0362.
6. tefania Matei et al., “The Relationship Between Psychosocial Status and Hypertensive Condition,” Curr. Hypertens. Rep., vol. 20, no. 12, p. 102, Oct. 2018, doi: 10.1007/s11901-018-0902-y.
7. E. G. Daoud et al., “Effect of an irregular ventricular rhythm on cardiac output,” Am. J. Cardiol., 1996, doi: 10.1016/S0002-9149(97)89297-1.
8. J. P. Piccini and L. A. Allen, “Heart Failure Complicated by Atrial Fibrillation: Don’t Bury the Beta-Blockers Just Yet,” JACC: Heart Failure, 2017, doi: 10.1016/j.jchf.2016.12.003.
9. B. Gorenek and G. Kudaiberdieva, “Atrial Fibrillation in Acute STElevation Myocardial Infarction: Clinical and Prognostic Features,” Curr. Cardiol. Rev., 2012, doi: 10.2174/157340312803760857.
10. Ş. Çelik, C. Erdöl, M. Baykan, Ş. Kaplan, and H. Kasap, “Relation between paroxysmal atrial fibrillation and left ventricular diastolic function in patients with acute myocardial infarction,” Am. J. Cardiol., 2001, doi: 10.1016/S0002-9149(01)01611-3.
11. G. Hindricks et al., “2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS),” Eur. Heart J., 2020, doi: 10.1093/eurheartj/ehaa612.
12. Z. Kalarus et al., “Cardiac arrhythmias in the emergency settings of acute coronary syndrome and revascularization: An European Heart Rhythm Association (EHRA) consensus document, endorsed by the European Association of Percutaneous Cardiovascular Interventions (EAPCI), and,” Europace, 2019, doi: 10.1093/europace/euz163.
13. C. T. January et al., “2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation,” J. Am. Coll. Cardiol., 2019, doi: 10.1016/j.jacc.2019.01.011.
14. J. B. Segal et al., “The evidence regarding the drugs used for ventricular rate control,” Journal of Family Practice. 2000.
15. M. Metawe et al., “Digoxin and short term mortality after acute STEMI: Results from the MAGIC trial,” Int. J. Cardiol., 2016, doi: 10.1016/j.ijcard.2016.05.022.
16. S. P. Thomas et al., “Rapid loading of sotalol or amiodarone for management of recent onset symptomatic atrial fibrillation: a randomized, digoxin-controlled trial,” Am. Heart J., 2004, doi: 10.1016/s0002-8703(03)00526-x.
17. R. D. Lopes et al., “Digoxin and Mortality in Patients With Atrial Fibrillation,” J. Am. Coll. Cardiol., 2018, doi: 10.1016/j.jacc.2017.12.060.
18. J.-P. Collet et al., “2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation,” Eur. Heart J., pp. 1–79, 2020, doi: 10.1093/eurheartj/ehaa575.
19. K. Saraf, P. Morris, P. Garg, P. Sheridan, and R. Storey, “Non-Vitamin K antagonist oral anticoagulants (NOACs): Clinical evidence and therapeutic considerations,” Postgrad. Med. J., vol. 90, no. 1067, pp. 520–528, 2014, doi: 10.1136/postgradmedj-2014-132605.
20. C. P. Cannon et al., “Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation,” N. Engl. J. Med., 2017, doi: 10.1056/nenjmoa1708454.
21. C. M. Gibson et al., “Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI,” N. Engl. J. Med., 2016, doi: 10.1056/nenjmoa1611594.
22. R. D. Lopes et al., “Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation,” N. Engl. J. Med., 2019, doi: 10.1056/nejmoa1817083.

23. P. Vranckx et al., “Edoxaban in atrial fibrillation patients with percutaneous coronary intervention by acute or chronic coronary syndrome presentation: a pre-specified analysis of the ENTRUST-AF PCI trial,” Eur. Heart J., 2020, doi: 10.1093/eurheartj/ehaa617.

24. F. J. Neumann et al., “2018 ESC/EACTS Guidelines on myocardial revascularization,” European Heart Journal, 2019, doi: 10.1093/eurheartj/ehy394.

25. M. Eldar et al., “Significance of paroxysmal atrial fibrillation complicating acute myocardial infarction in the thrombolytic era,” Circulation, 1998, doi: 10.1161/01.CIR.97.10.965.

26. O. D. Pedersen, H. Bagger, L. Køber, and C. Torp-Pedersen, “The occurrence and prognostic significance of atrial fibrillation/flutter following acute myocardial infarction. TRACE Study group. TRAn-dolapril Cardiac Evaluation,” Eur. Heart J., 1999, doi: 10.1053/euhr.1998.1352.

27. N. Danchin et al., “Impact of early statin therapy on development of atrial fibrillation at the acute stage of myocardial infarction: Data from the FAST-MI register,” Heart, 2010, doi: 10.1136/ hrt.2010.201574.

28. R. D. Lopes et al., “Safety and Efficacy of Antithrombotic Strategies in Patients with Atrial Fibrillation Undergoing Percutaneous Coronary Intervention: A Network Meta-analysis of Randomized Controlled Trials,” JAMA Cardiol., 2019, doi: 10.1001/jamacardiol.2019.1880.

29. D. E. Thomas, N. Jex, and A. R. Thorley, “Ventricular arrhythmias in acute coronary syndromes–mechanisms and management,” Contin. Cardiol. Educ., vol. 3, no. 1, pp. 22–29, 2017, doi: 10.1002/ cce2.51.

30. J. P. Piccini et al., “Antiarrhythmic drug therapy for sustained ventricular arrhythmias complicating acute myocardial infarction,” Crit. Care Med., vol. 39, no. 1, pp. 78–83, 2011, doi: 10.1097/ CCM.0b013e3181f6ada7.

31. M. J. Janse and A. L. Wit, “Electrophysiological mechanisms of ventricular arrhythmias resulting from myocardial ischemia and infarction,” Physiological Reviews, 1989, doi: 10.1152/physrev.1989.69.4.1049.

32. M. Said et al., “Calcium-calmodulin dependent protein kinase II (CaMKII): A main signal responsible for early reperfusion arrhythmias,” J. Mol. Cell. Cardiol., 2011, doi: 10.1016/j.yjmcc.2011.08.010.

33. J. M. Di Diego and C. Antzelevitch, “Ischemic ventricular arrhythmias: Experimental models and their clinical relevance,” Hear. Rhythm, 2011, doi: 10.1053/j.hrrthm.2011.06.036.

34. N. KH, T. T, Stebbins A, T. Ej, and Califf, “Sustained ventricular arrhythmias in patients receiving thrombolytic therapy: incidence and outcomes. The GUSTO Investigators. Circulation nell’Infarto Miocardico (GISSI-2),” Circulation, 1998.

35. V. Barletta, I. Fabiani, C. Lorenzo, I. Nicastro, and V. Di Bello, “Sudden cardiac death: A review focused on cardiovascular imaging,” Journal of Cardiovascular Echography. 2014, doi: 10.4103/2211-4122.135611.

36. S. G. Priori et al., “2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death the Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the Europea,” Eur. Heart J., vol. 36, no. 41, pp. 2793-2867l, 2015, doi: 10.1093/eurheartj/ehv316.

37. C. J. Nalliah, S. Zaman, A. Narayan, J. Sullivan, and P. Kovoor, “Coronary artery reperfusion for ST elevation myocardial infarction is associated with shorter cycle length ventricular tachycardia and fewer spontaneous arrhythmias,” Europace, 2014, doi: 10.1093/europace/eus307.

38. A. Volpi, A. Cavalli, L. Santoro, and E. Negri, “Incidence and prognosis of early primary ventricular fibrillation in acute myocardial infarction results of the gruppo italiano per lo studio della sopravvivenza nell’infarto miocardico (GISSI-2) database,” Am. J. Cardiol., 1998, doi: 10.1016/s0002-9149(98)00336-1.

39. X. Z. He, S. H. Zhou, H. Y. Wan, H. Y. Wang, Q. H. Zhong, and J. F. Xue, “The effect of early and intensive statin therapy on ventricular premature beat or nonsustained ventricular tachycardia in patients with acute coronary syndrome,” Clin. Cardiol., 2011, doi: 10.1002/ clc.20818.

40. R. Latini, A. P. Magni, M. Flather, P. Sleight, and G. Tognoni, “ACE inhibitor use in patients with myocardial infarction: Summary of evidence from clinical trials,” Circulation. 1995, doi: 10.1161/01.CIR.92.10.3132.

41. J. S. Bundgaard et al., “Deep sedation as temporary bridge to definitive treatment of ventricular arrhythmia storm,” Eur. Hear. J. Acute Cardiovasc. Care, 2020, doi: 10.1177/2048872620903453.

42. J. Bhar-Amato, W. Davies, and S. Agarwal, “Ventricular arrhythmia after acute myocardial infarction: The perfect storm,” Arrhythmia Electrophysiol. Rev., vol. 6, no. 3, pp. 134–139, 2017, doi: 10.15420/ aer.2017.241.

43. H. V. Huikuri, A. Castellanos, and R. J. Myerburg, “Sudden Death Due to Cardiac Arrhythmias,” N. Engl. J. Med., 2001, doi: 10.1056/ nejmra0000650.

44. J. P. Piccini et al., “Relation of Mortality to Failure to Prescribe Beta Blockers Acutely in Patients With Sustained Ventricular Tachycardia and Ventricular Fibrillation Following Acute Myocardial Infarction (from the VALsartan In Acute myocardial Infarction trial [VAL-IANT]) Re,” Am. J. Cardiol., vol. 102, no. 11, pp. 1427–1432, 2008, doi: 10.1016/j.amjcard.2008.07.033.

45. H. J. Dargie, “Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: The CAPRICORN randomised trial,” Lancet, 2001, doi: 10.1016/S0140-6736(00)04560-8.

46. S. M. Al-Khatib et al., 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: Executive Summary, vol. 138, no. 13.

47. F. Mehraein, “A Review on Amiodarone as an Antiarrhythmic Drug,”

48. R. M. L. Colunga Biancatelli, V. Congedo, L. Calvosa, M. Ciacciarelli, A. Polidoro, and L. Iuliano, “Adverse reactions of amiodarone,” J. Geriatr. Cardiol., vol. 16, no. 7, pp. 552–566, 2019, doi: 10.11909/j.issn.1671-5411.2019.07.004.
