Current Science International
Volume: 12 | Issue: 04| Oct. – Dec.| 2023

EISSN:2706-7920 ISSN: 2077-4435
DOI: 10.36632/csi/2023.12.4.43
Journal homepage: www.curresweb.com
Pages: 596-602

Predictive Factors for New-Onset Atrial Fibrillation in Patients with ST-Elevation Myocardial Infarction (STEMI) undergoing Primary Percutaneous Coronary Intervention

Muhammed A. A. Habba, Amr F. Al-Kassas, Mohamed N. Hussien and Magdy M. El-Masry

Cardiovascular Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Received: 10 Oct. 2023 **Accepted:** 11 Nov. 2023 **Published:** 20 Nov. 2023

ABSTRACT

Atrial fibrillation (AF) is the predominant cardiac arrhythmia seen in humans, regardless of the presence or absence of underlying structural heart disease. The increasing incidence of AF may be attributed mostly to the progressive aging of the population. AF is shown to be present in around 35% of those diagnosed with stable coronary artery disease (CAD), making it the second most common co-morbidity in patients with AF. Episodes AF have the potential to trigger the onset of an acute coronary syndrome (ACS) due to the heightened myocardial oxygen demand associated with increased tachycardia. Cardiac damage and atrial remodeling caused by ACS have been shown to directly cause AF. Percutaneous coronary intervention (PCI) is often used to treat individuals with AF who also have CAD due to the same risk factors between the two conditions. The development of AF in this setting may be effected by various factors, including elevated atrial pressure, ischemia, high left ventricular end-diastolic pressure, reduced atrial perfusion, glycolytic anaerobic pathways, inflammation, abnormalities in autonomic regulation, neurohumoral factors and other relevant factors. These factors have been observed to contribute to the development of AF in other critical illnesses as well. It was hypothesized that the prognostic and prevalence significance of AF after AMI would shift as a result of improvements in reperfusion methods and modern treatment with statins, antiplatelet medication and ACE inhibitors.

Keywords: Atrial fibrillation (AF), heart disease, Cardiac damage, cardiac arrhythmia, Percutaneous coronary intervention

Introduction

In the progression of acute myocardial infarction (AMI), pallor of the myocardium is the initial observable change. It manifests itself no earlier than 12 hours after the initiation of irreversible ischemia (Burke and Virmani 2007). AF is the most prevalent arrhythmia of the sustained ventricle (Kea *et al.,* 2016). The increasing prevalence of AF may be ascribed to the growing population of older individuals and the widespread occurrence of comorbidities (Garg *et al.,* 2018). PCI is often used in patients with both AF and CAD due to the existence of similar risk factors between these two conditions (Sutton *et al.,* 2016).

Pathophysiology of Atrial fibrillation AF

Complex atrial abnormalities are attributed to several factors, including hypo contractility, stretch-induced fibrosis, lipid infiltration, vascular remodeling, ischemia, ion-channel failure calcium instability and inflammation. All contribute to the exacerbation of ectopy and conduction disturbances, the promotion of atrial hypercoagulability associated with AF, and an increased propensity to maintain and develop AF. Hypo contractility decreases the magnitude of local endothelial shear stress, leading to an upregulation of plasminogen activator inhibitor expression. Conversely, inflammation

Corresponding Author: Muhammed A. A. Habba, Cardiovascular Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt. E-mail: thebright.sword1@gmail.com

induced by ischaemia either stimulates the shedding of endothelial cells or augments the expression of endothelial adhesion molecules, ultimately exposing tissue factors to the bloodstream. Many of these mechanisms are exacerbated by AF, which could potentially account for its progressive nature (Hindricks *et al.,* 2020).

Patterns of AF

1. **The first diagnosis of Atrial fibrillation AF:** AF that has not been previously diagnosed, regardless of the arrhythmia's duration or the severity of symptoms associated with AF (Kirchhof *et al.,* 2016).
2. **Paroxysmal AF** is often characterized by episodes that spontaneously resolve within a duration of forty-eight hours. Some episodes of AF may last for up to a duration of seven days. Episodes of AF that undergo cardioversion should be categorized as paroxysmal within a period of seven days (Kirchhof *et al.,* 2016).
3. **Persistent AF:** AF persisting for a duration exceeding 7 days, encompassing episodes terminated via cardioversion (either with medications or direct current cardioversion) after at least 7 days (Kirchhof *et al.,* 2016).
4. **Long-standing persistent AF** refers to a condition in which it is anticipated that AF would continue for a minimum duration of one year. In such cases, a rhythm management approach is initiated (Kirchhof *et al.,* 2016). **Permanent AF:** AF that is recognized by the doctor and the patient (Kirchhof *et al.,* 2016).

Incidence of AF in STEMI

The prevalence of AF ranges from 2% to 23% according to a study cited as González-Pacheco *et al.,* (2015). Additionally, individuals who have had a myocardial infarction have a 60% to 77% higher probability of developing new-onset AF, as shown in reference (Krijthe *et al.,* 2013). Furthermore, AF itself has been associated with an increased susceptibility to ST-STEMI or non-STEMI ACS. The user's text is already academic and does not require any rewriting.

The treatment approaches for patients diagnosed with AMI have undergone substantial changes over the last three decades. This transformation may be attributed to the widespread use of reperfusion therapy, which includes the administration of fibrinolytic drugs, as well as the increasing utilization of primary PCI as a treatment modality. Currently, the latter is regarded as the gold standard of treatment for AMI in centers that possess the necessary infrastructure, logistics, and expertise. However, in regions where transport delays are substantial, thrombolysis is the preferred initial treatment followed by transfer (Armstrong, 2006; Ting *et al.,* 2007).

Comparable rates of AF were observed in patients with AMI who underwent primary PCI. As an illustration, Kinjo *et al.* (2003) published results from the Osaka Acute Coronary Insufficiency Study (OACIS), which comprised 2475 patients who underwent PCI treatment within a 24-hour period. Atrioventricular failure was observed in 12% of the patients in this study.

Particular attention was paid by the Cooperative Cardiovascular Project to the incidence of AF in elderly patients with AMI (Rathore *et al.,* 2000). Achieving a cumulative incidence of 22.1%, AF was present in these patients, with nearly half of the patients developing the condition during their hospitalization and the remaining half presenting with AF upon admission. Several epidemiological studies have documented a higher prevalence of AF in the elderly, which is consistent with the high incidence of AF among senior AMI patients (Nantsupawat *et al.,* 2013).

It has been reported that AF incidence ranges from 2.3% to 21% when impeding AMI. Significantly reduced incidence of AF has been linked to the widespread implementation of interventional coronary revascularization (PCI), particularly in the acute phase. As anticipated, clinical trials assessing the impact of ACE, AT II-inhibitors, or b-blockers on mortality and morbidity in patients with AMI observed that these pharmacological therapies caused the least incidence of AF in the context of AMI. However, the late onset of AF remained the most significant consequence of this therapeutic approach. Anticipated is the continued prevalence and challenge of AF as a consequence of AMI, given the aging of our population (Schmitt *et al.,* 2009).

Mechanism of Atrial fibrillation AF During AMI

ACS can be precipitated by AF paroxysms, and ACS-related myocardial damage and atrial remodeling can induce AF (Dzeshka *et al.,* 2015). AMI can be predisposed to in the absence of atherosclerotic plaque rupture due to two mechanisms: thromboembolic event-induced coronary occlusion or an imbalance between myocardial oxygen delivery and demand resulting from an irregular and tachycardic heart rate (Li-Saw-Hee *et al.,* 2001; Thygesen *et al.,* 2018).

The pathogenesis of AF that arises after AMI has several components. Several factors may lead to the development of atrial ischemia, inflammation (pericarditis), and abnormalities in hemodynamics (atrial strain and dilation) (Andrade *et al.,* 2014). Following substantial ventricular damage, there is an increase in end-diastolic volume and pressure, leading to higher atrial pressure and wall strain. This elucidates the intimate association between heart failure and AF within the framework of MI, hence amplifying the susceptibility to AF (Schmitt *et al.,* 2009).

The results of the angiographic examination indicated that the occurrence of AF was more likely to happen in cases of inferior myocardial infarction when there was an occlusion in the proximal left circumflex artery, regardless of the presence of right coronary artery disease. Additionally, the presence of impaired perfusion in the AV nodal artery further increased the likelihood of AF recurrence (Alasady *et al.,* 2011).

Among a cohort of 266 patients, it was shown that the occurrence of atrial arrhythmias was only seen in all 12 persons who had inferior infarction. In the majority of these patients, it was seen that the sinus node artery was situated distal to the site of blockage in the right coronary artery. This finding suggests that sinus node ischemia might potentially play a role as a contributing cause (January *et al.,* 2014).

AF may be caused by infarction or ischemia of the left atrium. Furthermore, considering that the sinus node artery emerges in nearly 90% of cases from the AV nodal artery and 55% from the right coronary artery, respectively, their potential contribution to the development of atrioventricular arrhythmias during RV infarction cannot be disregarded. Similar to ill sinus syndrome, bouts of tachycardia can be induced by sinus node ischemia and dysfunction, which increases the likelihood of atrial flutter, junctional rhythms, and ectopic activity (Siu *et al.,* 2007).

The onset of AF during myocardial infarction (AMI) may also be predicted by PR-segment displacement on a 12-lead electrocardiogram (ECG) (Pizzetti *et al.,* 2001). Other risk factors that might contribute to the development of the condition include older age, the existence of congestive heart failure, blockage of the right coronary artery (RCA), three-vessel coronary disease, anterior Q-wave myocardial infarction, previous myocardial infarction, and prior coronary artery bypass graft (Schmitt *et al.,* 2009).

Consequences of AF During AMI

The progression of AF leads to the absence of atrial contraction and the occurrence of fast, irregular cardiac rhythms. Consequently, this condition results in compromised diastolic filling and heightened demand for myocardial oxygen. The contraction of the atria plays a significant role in the process of ventricular filling, especially in hearts that are experiencing failure. In the context of the ischemic canine heart, the experimental induction of AF was seen to result in a decrease in cardiac output, a decline in mean aortic pressure, and a drop in mean myocardial blood flow (Saglietto *et al.,* 2022). As AF worsens heart failure, the cycle may continue, increasing the likelihood of a further downward spiral. Both contribute to an elevated risk of ventricular arrhythmias and ischemia load. Patients with AF who have an AMI have a much greater in-hospital death rate compared to those without AF (Jons *et al.,* 2011). Some evidence suggests that AF may increase the likelihood of VF (Sankaranarayanan *et al.,* 2008). Patients with heart failure symptoms and greater infarcts are more likely to develop AF. The detrimental effects of AF have been shown in large-scale experiments to be unrelated to any other factors (Schmitt *et al.,* 2009, Crenshaw *et al.,* 1997).

AF in STEMI guidelines

Patients with AF are more likely to suffer from many medical conditions at once (Batra *et al.,* 2016). Most people may live with the arrhythmia without any special therapy beyond anticoagulation. Acute hemodynamic instability need immediate medical attention. There is minimal evidence demonstrating preferences for rate control over rhythm control in this context (Nilsson *et al.,* 2010).

Although AF should be treated with electrical cardioversion, it often returns soon after. Amiodarone is the only antiarrhythmic medication effective for controlling rhythm in the acute setting (Schmitt *et al.,* 2009). Beta-blockers are effective in controlling heart rate (Gorenek *et al.,* 2014). Rate control is more safely obtained with intravenous digoxin with or without simultaneous intravenous amiodarone therapy in individuals with substantial myocardial injury or severe LV dysfunction (Gorenek *et al.,* 2014) .

The co-administration of intravenous digoxin with amiodarone requires careful monitoring due to the potential for increased digoxin blood concentrations, which may lead to digoxin toxicity. Several studies have been conducted to investigate the possible impact of beta-blockers, ACE inhibitors/ARBs, and early-onset statin medication on the risk of developing new-onset atrial fibrillation. However, it is important to note that the findings of these studies are not uniformly consistent (Schmitt *et al.,* 2009). It is important to provide effective and consistent oral anticoagulation to patients who have AF and are at risk for thromboembolism. The prognosis of patients who are diagnosed with AF subsequent to a STEMI is comparatively worse when compared to those who maintain a normal sinus rhythm. This holds true for both the immediate and extended periods of time (Batra *et al.,* 2016, Jabre *et al.,* 2011). Increased rates of reinfarction, stroke, heart failure, and perhaps sudden cardiac death have all been linked to the presence of AF (Schmitt *et al.,* 2009; Batra *et al.,* 2016). Stroke rates are considerably greater during long-term follow-up in patients who have transitory, self-terminating AF after a STEMI (Batra *et al.,* 2016).

The care of patients with AF after ACS and/or PCI in the post-procedural period.

When making a decision about the appropriateness of using combination antithrombotic medication in individuals with AF who are experiencing ACS or having PCI, it is crucial to carefully consider the advantages and disadvantages associated with this treatment approach. Specifically, one must evaluate the potential benefits in terms of reducing the risk of ischemic stroke or systemic embolism, coronary ischemia events, as well as the potential drawbacks linked to bleeding caused by antithrombotic treatment (Lip *et al.,* 2018). There is a considerable reduction in heavy bleeding (and ICH) with dual antithrombotic treatment consisting of an OAC (ideally a NOAC) and a P2Y12 inhibitor (preferably clopidogrel). However, current data shows that certain AF patients following a recent ACS or undergoing PCI, particularly those at elevated risk of ischemic episodes, might benefit from at least a brief term of triple treatment (e.g., 1 week) (Gargiulo *et al.,* 2019, Potpara *et al.,* 2020).

For the first 12 months after PCI for ACS, or the first 6 months following PCI in patients with CCS, dual therapy with OAC plus an antiplatelet medication (ideally clopidogrel) is indicated (Neumann *et al.,* 2018). After then, if there have been no more ischemic episodes, OAC monotherapy should be maintained (regardless of the kind of stent used). OAC monotherapy is also advised for individuals with AF and CAD who have been symptom-free for 1 year without intervention (i.e., "stable") (Yasuda *et al.,* 2019).

In patients diagnosed with AF who have surgical coronary revascularization, it is recommended to promptly reinstate oral anticoagulant (OAC) medication if bleeding is well managed. This may be accompanied by the addition of clopidogrel, while the administration of triple therapy should be avoided (Yasuda *et al.,* 2019). Myocardial ischaemia symptoms may be made worse by uncontrolled ventricular rate in AF, which may lead to or aggravate the development of HF. A beta-blocker or a rate-limiting calcium antagonist might be effective medications. Acute cardioversion may be necessary in cases of hemodynamic instability. Rhythm management with vernakalant, flecainide, or propafenone is contraindicated in individuals with established CAD (Hindricks *et al.,* 2020).

Abbreviations

AF	Atrial fibrillation
CAD	Coronary artery disease
ACS	Acute coronary syndrome
PCI	Percutaneous coronary intervention
AMI	Acute myocardial infarction
OACIS	Osaka Acute Coronary Insufficiency Study
OAC	Oral anticoagulant

References

Alasady, M., W.P. Abhayaratna, D.P. Leong, H.S. Lim, H.S. Abed, A.G. Brooks, et al., 2011. Coronary artery disease affecting the atrial branches is an independent determinant of atrial fibrillation after myocardial infarction. Heart Rhythm, 8:955-60.

Andrade, J., P. Khairy, D. Dobrev, S. Nattel, 2014. The clinical profile and pathophysiology of atrial fibrillation: relationships among clinical features, epidemiology, and mechanisms. Circulation research, 114:1453-68.

Armstrong, P.W., 2006. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. European heart journal, 27:1530-8.

Batra, G., B. Svennblad, C. Held, T. Jernberg, P. Johanson, L. Wallentin, et al., 2016. All types of atrial fibrillation in the setting of myocardial infarction are associated with impaired outcome. Heart, 102:926-33.

Burke, A.P., and R. Virmani, 2007. Pathophysiology of acute myocardial infarction. Medical Clinics of North America., 91:553-72.

Crenshaw, B.S., S.R. Ward, C.B. Granger, A.L. Stebbins, E.J. Topol, R.M. Califf, et al., 1997. Atrial fibrillation in the setting of acute myocardial infarction: the GUSTO-I experience. Journal of the American College of Cardiology, 30:406-13.

Dzeshka, M.S., R.A. Brown, and G.Y. Lip, 2015. Patients with atrial fibrillation undergoing percutaneous coronary intervention. Polskie Archiwum Medycyny Wewnętrznej, 125:172-80.

Garg, L., S. Agrawal, M. Agarwal, M. Shah, A. Garg, B. Patel, et al., 2018. Influence of atrial fibrillation on outcomes in patients who underwent primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. The American Journal of Cardiology, 121:684-9.

Gargiulo, G., A. Goette, J. Tijssen, L. Eckardt, T. Lewalter, P. Vranckx, et al., 2019. Safety and efficacy outcomes of double vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of non-vitamin K antagonist oral anticoagulant-based randomized clinical trials. European heart journal, 40:3757-67.

González-Pacheco, H., M.F. Márquez, A. Arias-Mendoza, A. Álvarez-Sangabriel, G. Eid-Lidt, A. González-Hermosillo, et al., 2015. Clinical features and in-hospital mortality associated with different types of atrial fibrillation in patients with acute coronary syndrome with and without ST elevation. Journal of cardiology, 66:148-54.

Gorenek, B., C. Blomström Lundqvist, J. Brugada Terradellas, A.J. Camm, G. Hindricks, K. Huber, et al., 2014. Cardiac arrhythmias in acute coronary syndromes: position paper from the joint EHRA, ACCA, and EAPCI task force. EP Europace, 16:1655-73.

Hindricks, G., T. Potpara, N. Dagres, E. Arbelo, J.J. Bax, C. Blomström-Lundqvist, 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) The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. European heart journal. 2021, 42:373-498.

Jabre, P., X. Jouven, F. Adnet, G. Thabut, S.J. Bielinski, S.A. Weston, et al., 2011. Atrial fibrillation and death after myocardial infarction: a community study. Circulation, 123:2094-100.

January, C.T., L.S. Wann, J.S. Alpert, H. Calkins, J.E. Cigarroa, J.C. Cleveland, et al., 2014. AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology. 2014;64:e1-e76.

Jons, C., U.G. Jacobsen, R.M. Joergensen, N.T. Olsen, U. Dixen, A. Johannessen, et al., 2011. The incidence and prognostic significance of new-onset atrial fibrillation in patients with acute myocardial infarction and left ventricular systolic dysfunction: a CARISMA substudy. Heart rhythm, 8:342-8.

Kea, B., V. Manning, T. Alligood, and M. Raitt, 2016. A review of the relationship of atrial fibrillation and acute coronary syndrome. Current emergency and hospital medicine reports, 4:107-18.

Kinjo, K., H. Sato, H. Sato, Y. Ohnishi, E. Hishida, D. Nakatani, et al., 2003. Prognostic significance of atrial fibrillation/atrial flutter in patients with acute myocardial infarction treated with percutaneous coronary intervention. The American journal of cardiology, 92:1150-4.

Kirchhof, P., S. Benussi, D. Kotecha, A. Ahlsson, D. Atar, B. Casadei, et al., 2016. ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Kardiologia Polska (Polish Heart Journal). 74:1359-469.

Krijthe, B.P., M.J. Leening, J. Heeringa, J.A. Kors, A. Hofman, O.H. Franco, et al., 2013. Unrecognized myocardial infarction and risk of atrial fibrillation: the Rotterdam Study. International journal of cardiology, 168:1453-7.

Lip, G.Y., J.-P. Collet, M. Haude, R. Byrne, E.H. Chung, L. Fauchier, et al., 2018. Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a joint consensus document of the European heart rhythm association (EHRA), European Society of cardiology Working group on thrombosis, European association of percutaneous cardiovascular interventions (EAPCI), and European association of acute cardiac care (ACCA) endorsed by the heart rhythm Society (HRS), Asia-Pacific heart rhythm Society (APHRS), Latin America heart rhythm Society (LAHRS), and cardiac arrhythmia Society of southern Africa (CASSA). Ep Europace. 2019, 21:192-3.

Li-Saw-Hee, F., A. Blann, D. Gurney, and G. Lip, 2001. Plasma von Willebrand factor, fibrinogen and soluble P-selectin levels in paroxysmal, persistent and permanent atrial fibrillation. Effects of cardioversion and return of left atrial function. European heart journal, 22:1741-7.

Nantsupawat, T., K. Nugent, and A. Phrommintikul, 2013. Atrial fibrillation in the elderly. Drugs & aging, 30:593-601.

Neumann, F.-J., M. Sousa-Uva, A. Ahlsson, F. Alfonso, A.P. Banning, U. Benedetto, et al., 2018. ESC/EACTS Guidelines on myocardial revascularization. European heart journal. 2019; 40:87-165.

Nilsson, K.R., S.M. Al-Khatib, Y. Zhou, K. Pieper, H.D. White, A.P. Maggioni, et al., 2010. Atrial fibrillation management strategies and early mortality after myocardial infarction: results from the Valsartan in Acute Myocardial Infarction (VALIANT) Trial. Heart, 96:838-42.

Pizzetti, F., F. Turazza, M. Franzosi, S. Barlera, A. Ledda, A. Maggioni, et al., 2001. Incidence and prognostic significance of atrial fibrillation in acute myocardial infarction: the GISSI-3 data. Heart, 86:527-32.

Potpara, T.S., N. Mujovic, M. Proietti, N. Dagres, G. Hindricks, J.-P. Collet, et al., 2020. Revisiting the effects of omitting aspirin in combined antithrombotic therapies for atrial fibrillation and acute coronary syndromes or percutaneous coronary interventions: meta-analysis of pooled data from the Pioneer Af-Pci, Re-Dual Pci, and Augustus trials. EP Europace, 22:33-46.

Rathore, S.S., A.K. Berger, K.P. Weinfurt, K.A. Schulman, W.J. Oetgen, Gersh B.J., et al., 2000. Acute myocardial infarction complicated by atrial fibrillation in the elderly: prevalence and outcomes. Circulation, 101:969-74.

Saglietto, A., M. Fois, L. Ridolfi, G.M. De Ferrari, M. Anselmino, and S. Scarsoglio, 2022. A computational analysis of atrial fibrillation effects on coronary perfusion across the different myocardial layers. Scientific reports, 12:841.

Sankaranarayanan, R., M.A. James, B. Nuta, M. Townsend, S. Kesavan, S. Burtchaell, et al., 2008. Does atrial fibrillation beget ventricular fibrillation in patients with acute myocardial infarction? Pacing and clinical electrophysiology, 31:1612-9.

Schmitt, J., G. Duray, B.J. Gersh, S.H. Hohnloser, 2009. Atrial fibrillation in acute myocardial infarction: a systematic review of the incidence, clinical features and prognostic implications. European heart journal, 30:1038-45.

Siu, C.-W., M.-H. Jim, H.-H. Ho, R. Miu, S.W. Lee, C.-P. Lau, et al., 2007. Transient atrial fibrillation complicating acute inferior myocardial infarction: implications for future risk of ischemic stroke. Chest.,132:44-9.

Sutton, N.R., M. Seth, C. Ruwende, and H.S. Gurm, 2016. Outcomes of patients with atrial fibrillation undergoing percutaneous coronary intervention. Journal of the American College of Cardiology, 68:895-904.

Thygesen, K., J.S. Alpert, A.S. Jaffe, B.R. Chaitman, J.J. Bax, D.A. Morrow, et al., 2018. Fourth universal definition of myocardial infarction (2018). Circulation, 138:e618-e51.

Ting, H.H., C.S. Rihal, B.J. Gersh, L.H. Haro, C.M. Bjerke, R.J. Lennon, et al., 2007. Regional systems of care to optimize timeliness of reperfusion therapy for ST-elevation myocardial infarction: the Mayo Clinic STEMI Protocol. Circulation, 116:729-36.

Yasuda, S., K. Kaikita, M. Akao, J. Ako, T. Matoba, M. Nakamura, et al., 2019. Antithrombotic therapy for atrial fibrillation with stable coronary disease. New England Journal of Medicine, 381:1103-13.