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EVALUATION OF RECENT UPDATES REGARDING MYOCARDIAL INFARCTION MANAGEMENT APPROACH

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Abstract:

Background: *ST-elevation myocardial infarction (STEMI) occurs due to acute occlusion of a coronary artery which require urgent intervention to avoid morbidity and mortality. In patients with acute STEMI, cardiogenic shock is the leading cause of death. STEMI outcomes has improved significantly in the past few decades due to the advancement of different methods of acute myocardial infarction management plans. Therefore, we aim in this review to discuss the management of STEMI and the controversies mentioned in literature.*

Objective: *A lot of literature have been done in order to provide better outcomes for patients presented with Myocardial Infarction, in our review we aim to discuss the recent literature that discussed Myocardial Infarction diagnosis and management.*

Methods: *A lot of literature have been done in order to provide better outcomes for patients presented with Myocardial Infarction, in our review we aim to discuss the recent literature that discussed myocardial infarction management.*

Conclusion*: Prompt and effective reperfusion therapy is the cornerstone of treatment for acute STEMI and is the only widely applicable acute treatment to diminish infarct size and major cardiac complications. Primary PCI is therefore the preferred strategy for patients with acute ST elevation MI. Fibrin-specific agents in combination with parenteral anticoagulants offer the highest level of efficacy in terms of short-term mortality reduction in patients with STEMI. Dual antiplatelet therapy reduced the 1-year incidence of cardiovascular events by approximately 20% compared with aspirin alone. Recent studies suggested that oxygen may do more harm than good and results in a greater infarct size and possibly increase the risk of mortality.*

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INTRODUCTION:

ST-elevation myocardial infarction (STEMI) occurs due to acute occlusion of a coronary artery and requires urgent reperfusion to avoid morbidity and mortality. STEMI is a syndrome of symptoms of myocardial ischemia with consequent ST-elevation on electrocardiography (ECG) and an associated rise in cardiac biomarkers (1,2).

In patients with acute STEMI, cardiogenic shock is the leading cause of death. Cardiogenic shock is a state of low cardiac output leading to end-organ hypo-perfusion. It complicates approximately 5–8% of STEMIs and is associated with a mortality rate approaching 50%. The incidence of acute STEMI has decreased over the last decades, mostly in developed higher-income countries. In contrast to developing lower-income countries, the incidence of acute myocardial infarction has increased (3,4,5).

STEMI outcomes has improved significantly in the past few decades due to the faster reperfusion especially with primary percutaneous coronary intervention (PCI), and improved pharmacological therapy and coronary care units (6). Therefore, we aim in this review to discuss the advancement of the management of STEMI.

METHODOLOGY:

Sample

We performed comprehensive search using biomedical databases; Medline, and PubMed, for studies concerned with Myocardial Infarction management and diagnosis published in English language. Keywords used in our search through the databases were as {Myocardial Infarction, Management, Diagnosis and Outcomes}. More relevant articles were recruited from references lists scanning of each included study.

Analysis

No software was used, the data were extracted based on specific form that contain (Title of the study, name of the author, Objective, Summary, Results, and Outcomes). Double revision of each author outcomes was applied to ensure the validity and minimize the errors.

DISCUSSION:

Chest pain currently represents the second most common chief complaint of patients presenting to emergency departments in the United States, representing approximately 8 million visits. Only 10% to 20% of patients are ultimately diagnosed with acute coronary syndrome, with only one-third with acute myocardial infarction (7). Older age, diabetes mellitus, ongoing angina, heart failure, low systolic blood pressure, tachycardia and left bundle branch block are the risk factors for cardiogenic shock associated with STEMI (8). Age appears to be most predictive of these risk factors. A nearly 50% higher probability of developing cardiogenic shock is associated with 10 years increase in age. (3,9).

(Johansson et al.)(10) Compared with the general population, MI survivors remain at higher risk, particularly older individuals and also patients with comorbid hypertension, diabetes, peripheral artery disease, or history of stroke during the first year after the index MI was 18.3%.

STEMI reflects acute myocardial infarction resulting from the rupture or erosion of an atherosclerotic plaque with thrombotic occlusion of an epicardial coronary artery and transmural ischemia. The size of the resulting infarction depends on the size of the ischemic area at risk, the duration and intermittency of coronary occlusion and the magnitude of residual collateral blood flow and the extent of coronary microvascular dysfunction (11).

Morphologically, the infarcted myocardium is characterized by myofibrillar contraction bands, swollen and possibly ruptured mitochondria (12). It can be also associated with sarcolemmal rupture, microvascular destruction, hemorrhage, and infiltrating leukocytes. These histological signs reflect myocardial cell necrosis (13). At least 2–4 hours or longer are required to achieve complete necrosis of myocardial cells. This depends on the presence of collateral circulation to the ischemic zone, persistent or intermittent coronary arterial occlusion, the sensitivity of the myocytes to ischemia and individual demand for oxygen and nutrients. The entire process leading to a healed infarction usually takes at least 5–6 weeks. Reperfusion may alter the macroscopic and microscopic appearance (14). Ischemic dysfunction of cardiac myocytes during STEMI can impair systolic and diastolic function of the right, left or both ventricles. When ischemic injury is extensive, ventricular function can be impaired to such a degree that cardiogenic shock occurs, whereby cardiac output falls and elevated ventricular filling pressures lead to heart failure. Then, the decreased cardiac output will lead to progressively worsening coronary perfusion, myocyte dysfunction, and ultimately end-organ hypo-perfusion. Left ventricular dysfunction is implicated in the majority of cases of cardiogenic shock associated with STEMI (15). In addition to the acute infarction, patients in cardiogenic shock often have suffered prior infarcts and tend to have severe three-vessel coronary disease, all of which leaves them

prone to extensive ischemic injury and subsequent ventricular dysfunction (3,16).

Clinical Evaluation:

STEMI and cardiogenic shock patients often present with signs and symptoms of hypo-perfusion and heart failure. The common symptoms are chest pain and dyspnea. On physical examination, patients are hypotensive. Hypotension may lead to a systemic hypo-perfusion which can cause altered mental status or poor urine output (17).

Laboratory studies may show an elevated lactate level and a rising creatinine, which may be due to both decreased renal perfusion and venous congestion. Classically, cardiogenic shock has been associated with cool extremities due to low cardiac output and compensatory systemic vasoconstriction. In practice, however, systemic vascular resistance is often not elevated and may even be low. This may be due to concomitant septic shock, particularly as the hypo-perfusion from cardiogenic shock places patients at high risk for ischemic bowel and subsequent translocation of gut microbes. In addition, myocardial infarction alone can lead to a systemic inflammatory response. Patients may also demonstrate signs of volume overload. Decreased oxygen saturation and lung crackles on auscultation due to pulmonary oedema may be present in patients with predominantly left ventricular dysfunction. These patients may need intubation, but up to one-third of such patients present without pulmonary congestion and chest X-ray may be clear. Patients with mainly right-sided involvement tend to have clear lungs but may have distended neck veins and peripheral edema or ascites (17,18).

Current guidelines recommend ECG interpretation within 10 minutes of the patient's arrival. The ECG is the most important initial diagnostic test. If suspicion is high, the ECG should be repeated every 15 to 30 minutes during the first hour. A normal ECG does not exclude a cardiac event and it is silent in in 1% to 6% of such patients. ECG manifestations of acute myocardial ischemia (in absence of LVH and LBBB) are ST elevation, ST depression and T wave changes. New ST elevation at the J point in two contiguous leads with the cut-points of more than 0.1 mV in all leads other than leads V2 and V3 where the following cut points apply more than 0.2 mV. New horizontal or down-sloping ST depression more than 0.05 mV in two contiguous leads and/or T inversion more than 0.1 mV in two contiguous leads with prominent R wave or R/S ratio >1 (17,18).

Given that the clinical assessment of acute coronary syndrome is insufficient, the addition of blood tests to measure the concentration of cardiac troponin T or I is necessary to aid in the early diagnosis of acute myocardial infarction. The guidelines recommend that cardiac troponin is useful in the detection of myocardial necrosis. In addition, the detection of any increase or decrease is essential to the diagnosis of acute myocardial infarction. These assays quantify the amount of cardiomyocyte necrosis, and thus the higher the level the more cell death has occurred. An increased cardiac troponin concentration is defined as a value exceeding the 99th percentile of a normal reference population. These assays allow the earlier detection of acute myocardial infarction as well as the detection of smaller acute myocardial infarctions. However, physicians need to put in mind that not all increases in troponin level represent acute myocardial infarction. Any increase in troponin indicates increased morbidity and mortality risk, no matter the condition or chronicity, and thus emergency physicians should never disregard an increase and call it a troponin leak. Any detectable troponin is always worse than no troponin and higher levels of troponin always portend a worse prognosis than lower levels of troponin. Current guidelines recommend troponin testing should be measured at presentation and 3 to 6 hours after symptoms onset and additional levels obtained beyond 6 hours after symptom onset for an intermediate or high index of suspicion. In addition, if symptom onset is ambiguous, the time of presentation should be considered to be the onset time (17,18).

Echocardiography should be performed to assess ventricular function and to exclude mechanical complications of STEMI. Echocardiography findings in cardiogenic shock include severe impairment of ventricular function, which may be predominantly right or left-sided or both and may be either systolic or diastolic or both (18).

- **Calcium score and scintigraphy:**

Literature review shows that both calcium score and scintigraphy play an important role in the diagnostic evaluation of atherosclerotic heart disease. The possibility of removing extensive coronary disease by means of a calcium score zero, or indicating the presence of an extensive disease when it is severely increased, justifies the use of this method in the initial or joint evaluation, in asymptomatic patients with suspected CAD and in cardiovascular risk stratification. The evaluation of symptomatic low-risk patients, despite suggestive evidence, should be re-evaluated in upcoming guidelines. Confirmation of the disease with the application of more specific methods and positive predictive value as myocardial

perfusion scintigraphy is still fundamental in certain patients. Thus, although literature suggests that sequential or joint use of both methods is advantageous, more data are needed to establish a cost-effective strategy for diagnostic evaluation (19).

- **Pulmonary artery catheter (PAC):**

Placement of a PAC can both provide a definitive diagnosis of cardiogenic shock and guide resuscitative efforts. PAC hemodynamic measurements confirm the diagnosis of cardiogenic shock by showing a low cardiac index <2.2 L/min/m2 and elevated ventricular filling pressures. Mixed venous oxygen saturation is typically low, reflecting the decreased cardiac output and increased oxygen extraction from peripheral tissues (17,18).

- **Risk stratification scoring systems:**

Risk stratification scores help clinical prediction and decision aids. They have helped clinicians incorporate clinical and biomarker findings to risk stratify patients. These rules and aids are helpful in estimating pretest probability, and may help facilitate patient safety. Common risk assessment rules used in the ED include the Thrombolysis in Myocardial Infarction (TIMI). (Hess et al.)(20) conducted a meta-analysis to assess its prognostic accuracy in patients in the emergency department with potential acute coronary syndromes. It included 10 prospective cohort studies with a total of 17,265 patients. Their results indicated a strong linear relation between TIMI risk score and the short-term incidence of cardiac events. The incidence of cardiac events in the lowest risk stratum (TIMI score of zero) was 1.8%. Although the TIMI risk score is an effective risk stratification tool for patients in the emergency department with potential acute coronary syndromes, it should not be used as the sole means of determining patient disposition (20).

Classification

The universal definition of myocardial infarction proposes that we classify patients with myocardial infarction based on etiology (21).

Type 1: Spontaneous myocardial infarction, which is related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more of the coronary arteries leading to decreased myocardial blood flow or distal platelet emboli with ensuing myocyte necrosis. The patient may have underlying severe CAD but on occasion non-obstructive or no CAD.
Type 2: Myocardial infarction secondary to an ischemic imbalance:

In instances of myocardial injury with necrosis where a condition other than CAD contributes to an imbalance between myocardial oxygen supply and/or demand, e.g. coronary endothelial dysfunction, coronary artery spasm, coronary embolism, tachy-/brady-arrhythmias, anemia, respiratory failure, hypotension, and hypertension with or without LVH.
Type 3: Myocardial infarction resulting in death when biomarker values are unavailable:
ECG changes or new LBBB with symptoms suggestive of myocardial ischemia but death occurring before blood samples could be obtained, before cardiac biomarker could rise, or in rare cases cardiac biomarkers were not collected.
Type 4a: Myocardial infarction related to PCI:
Type 4b: Myocardial infarction related to stent thrombosis:
Type 5: Myocardial infarction related to coronary artery bypass grafting (CABG):

Management:

- **Hemodynamic compromise and cardiac arrest**

Resuscitation may be required for ventricular fibrillation or for ventricular tachycardia with diminished cardiac output, and guidelines for such resuscitation are provided within the framework of Basic and Advanced Life Support. For the patient with extensive myocardial ischemia and/or heart failure, additional circulatory support may be necessary, including the insertion of an intra-aortic balloon pump, as a bridge to revascularization.

- **Reperfusion therapy**

Prompt and effective reperfusion therapy is the cornerstone of treatment for acute STEMI and is the only widely applicable acute treatment to diminish infarct size and major cardiac complications. One of the most important components of STEMI management is getting the patients in a time efficient manner to a hospital that is capable of administering reperfusion therapies such as fibrinolytic therapy and primary percutaneous coronary intervention. Fibrinolytic therapy (FT) and Primary PCI are the two currently available modalities of reperfusion therapies (4).

Primary PCI is therefore the preferred strategy for patients with acute ST elevation MI if, with appropriate facilities, a skilled team can provide PCI within 60 minutes of hospital arrival. A series of studies have demonstrated more effective restoration of patency with PCI compared to fibrinolysis, less re-occlusion, improved left ventricular function, and

better clinical outcome (22).

When primary PCI is not available and when there is delay from first medical contact to primary PCI is more than 120 min, FT is indicated if the time of onset of symptoms is less than 12 h. It reduced mortality and morbidity when carefully administered within 12 h of symptom onset. The usefulness of FT in patients presenting greater than 12 h from the onset of symptoms is not well established (23).

Thrombolytic agents can be classified according to their generation or according to their mechanism in relation to fibrin. Fibrin specific agents include recombinant tissue plasminogen activator (t-PA), Alteplase, Tenecteplase (TNK-tPA), and Reteplase. Non-fibrin specific include Urokinase and Streptokinase (24). Tenecteplase offers a more favorable safety profile with similar survival benefits compared with other fibrin specific agents. Streptokinase, a less expensive option compared to fibrin-specific agents, offers a similar risk of major bleeding with slight increase of less than 1% in mortality within 30–35 days, compared with tenecteplase. Tenecteplase ranks the lowest in terms of bleeding risk and has a similar mortality benefit across all other fibrinolytics. (Jinatongthai et al.)(25) analysis suggested that fibrin-specific agents in combination with parenteral anticoagulants offer the highest level of efficacy in terms of short-term mortality reduction in patients with STEMI (24,25).
Delays in door-to-balloon times (D2B) are associated with increased mortality. Adherence to D2B goal of less than 90 min lowers mortality. Although primary PCI is superior to FT, emphasis should be placed on timely administration of some form of reperfusion therapy rather than the mode of treatment (26,27). In patients who present within less than 1-2 h of onset of symptoms, immediate FT may be advantageous even if the transfer times are short. Multiple trials have shown the safety and efficacy of pre-hospital FT. This approach reduces the time to treatment by approximately 60 min and decreases mortality by 17% (28). Figure 1 is an algorithm presenting the preferred reperfusion method and target time to balloon inflation.

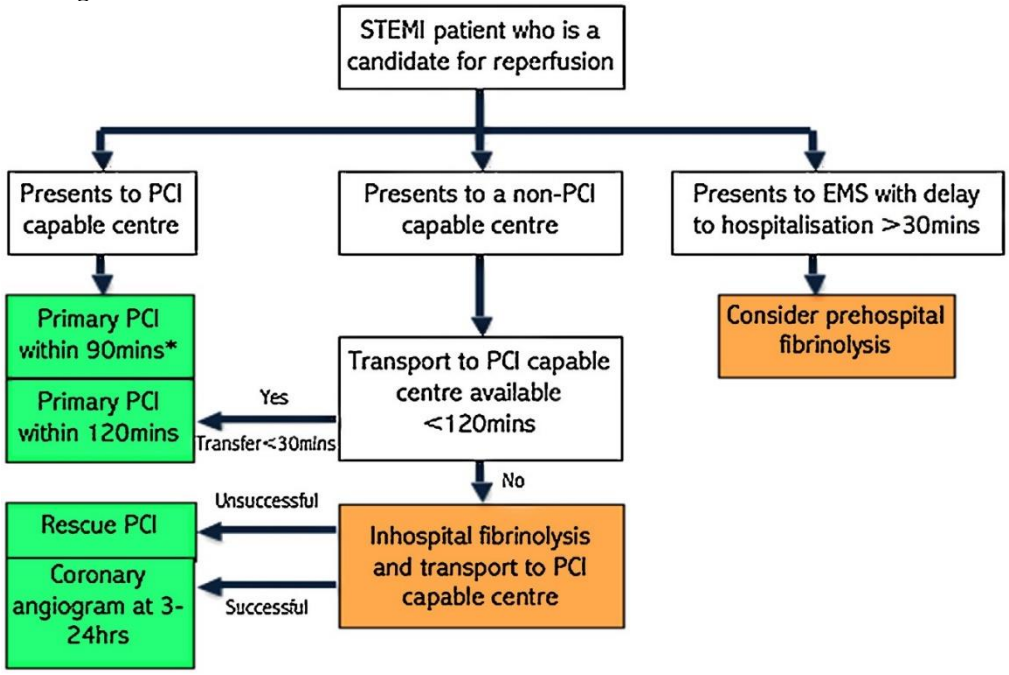

Figure 1: Australian algorithm for STEMI reperfusion: [2]

- **Antiplatelet Therapy**

Platelet adhesion and aggregation play an important role in the mechanism by which ruptured coronary artery plaques become a major cause of acute myocardial infarctions. The Subsequent Activation of the coagulation cascade and thrombus formation occurs as a consequence of initial platelet activation. Consequently, platelet inhibition is essential in the treatment of STEMIs. An initial single dose of 325 mg of Aspirin should be administered as early as possible. This should be followed by a maintenance dose of 81 mg once daily. Higher doses of Aspirin for

maintenance therapy have shown to increase the risk of bleeding (29).
Clopidogrel is an alternative antiplatelet agent that inhibits adenosine diphosphate (ADP)-induced platelet aggregation through irreversible inhibition of P2 nucleotide receptors on the platelet surface. It is commonly used for secondary prevention of atherothrombotic disease in place of low-dose aspirin in patients who have experienced gastrointestinal intolerance to aspirin-related adverse events or with aspirin allergy (30).

Prasugrel is a novel, third-generation, P2Y12 inhibitor that is structurally similar to clopidogrel. Prasugrel exhibits a more rapid onset of action and greater dose response compared to clopidogrel. Prasugrel is recommended for patients presenting with acute coronary syndrome and planned for invasive management with PCI based on superior efficacy relative to clopidogrel (31). Major bleeding risk is increased overall compared to clopidogrel, reinforcing the need for appropriate patient selection (32).

The benefit of dual antiplatelet therapy following an acute coronary syndrome was established. It is a combination of aspirin and clopidogrel. This therapy reduced the 1-year incidence of cardiovascular events by approximately 20% compared with aspirin alone. Current European and North American guidelines advise continuing dual antiplatelet therapy for 1 year following an acute coronary syndrome (29,33).

- **Adjunctive Antiplatelet Therapy**

The role of GPIIb/IIIa receptor antagonists has needed to be continually re-evaluated as antiplatelet have evolved. Abciximab is a chimeric monoclonal antibody that blocks the GPIIb/IIIa receptor on activated platelets. (De Luca et al.)(34) conducted a meta-analysis included 722 patients with STEMI from seven randomized trials. They found that early administration of abciximab compared to late or peri-procedural administration was associated with reduction in mortality, improvement in pre-procedural TIMI, post-procedural TIMI and ST-segment resolution. There was no difference in the rates of major bleeding complications between early and late abciximab administration (34).

- **Oxygen therapy**

Oxygen is widely recommended in international guidelines for treatment of acute myocardial infarction, but there is uncertainty about its safety and benefits. Recent studies suggested that oxygen may do more harm than good and results in a greater infarct size and possibly increase the risk of mortality (35,36). A systematic review and meta-analysis were performed to determine whether inhaled oxygen in acute myocardial infarction improves pain or the risk of death. A total of only five studies were found, involving 1173 participants. None demonstrated that oxygen therapy in acute myocardial infarction does more good than harm. There was no evidence from the randomized controlled trials to support the routine use of inhaled oxygen in people with acute myocardial infarction and a harmful effect cannot be ruled out (37).

CONCLUSION:

Prompt and effective reperfusion therapy is the cornerstone of treatment for acute ST elevation MI and is the only widely applicable acute treatment to diminish infarct size and major cardiac complications. Primary PCI is therefore the preferred strategy for patients with acute ST elevation MI. Fibrin-specific agents in combination with parenteral anticoagulants offer the highest level of efficacy in terms of short-term mortality reduction in patients with STEMI. Dual antiplatelet therapy reduced the 1-year incidence of cardiovascular events by approximately 20% compared with aspirin alone. Recent studies suggested that oxygen might do more harm than good and results in a greater infarct size and possibly increase the risk of mortality.

REFERENCES:

1. Zeymer, U., L. Eckert, and I. Dubroca. "Differences in Incidence of Hospital Admissions for Acute Coronary Syndromes in Five Western Countries." European Heart Journal 34, no. Suppl 1 (2013). doi:10.1093/eurheartj/eht307.p412.
2. Dind, Ashleigh, Usaid Allahwala, Kaleab N. Asrress, Sanjit S. Jolly, and Ravinay Bhindi. "Contemporary Management of ST-Elevation Myocardial Infarction." Heart, Lung and Circulation 26, no. 2 (2017): 114-21. doi:10.1016/j.hlc.2016.07.009.
3. Chang, Lee, and Robert Yeh. "Evaluation and Management of ST-elevation Myocardial Infarction and Shock." European Cardiology Review 9, no. 2 (2014): 88. doi:10.15420/ecr.2014.9.2.88.
4. Fox, K. A A. "Management of Acute Coronary Syndromes: An Update." Heart 90, no. 6 (2004): 698-706. doi:10.1136/hrt.2003.020321.
5. Babaev, A., P.d. Frederick, D.j. Pasta, N. Every, T. Sichrovsky, and J.s. Hochman. "Trends in Management and Outcomes of Patients with Acute Myocardial Infarction Complicated by Cardiogenic Shock." ACC Current Journal Review 14, no. 11 (2005): 1-2.

doi:10.1016/j.accreview.2005.10.004.
6. Puymirat, Etienne. "Association of Changes in Clinical Characteristics and Management with Improvement in Survival Among Patients With ST-Elevation Myocardial Infarction." Jama 308, no. 10 (2012): 998. doi:10.1001/2012.jama.11348.
7. Bhuiya, Farida A., Stephen R. Pitts, Linda F. McCaig. "Emergency department visits for chest pain and abdominal pain: United States, 1999-2008." NCHS Data Brief. 2010 Sep; (43): 1–8.
8. Lindholm, M. "Cardiogenic Shock Complicating Acute Myocardial Infarction Prognostic Impact of Early and Late Shock Development." European Heart Journal 24, no. 3 (2003): 258-65. doi:10.1016/s0195-668x(02)00429-3.
9. Hasdai, David, Robert M. Califf, Trevor D. Thompson, Judith S. Hochman, E.magnus Ohman, Matthias Pfisterer, Eric R. Bates, Alec Vahanian, Paul W. Armstrong, Douglas A. Criger, Eric J. Topol, and David R. Holmes. "Predictors of Cardiogenic Shock after Thrombolytic Therapy for Acute Myocardial Infarction." Journal of the American College of Cardiology 35, no. 1 (2000): 136-43. doi:10.1016/s0735-1097(99)00508-2.
10. Johansson, Saga, Annika Rosengren, Kate Young, and Em Jennings. "Mortality and Morbidity Trends after the First Year in Survivors of Acute Myocardial Infarction: A Systematic Review." BMC Cardiovascular Disorders 17, no. 1 (2017). doi:10.1186/s12872-017-0482-9.
11. Dewood, Marcus A., Julie Spores, Robert Notske, Lowell T. Mouser, Robert Burroughs, Michael S. Golden, and Henry T. Lang. "Prevalence of Total Coronary Occlusion during the Early Hours of Transmural Myocardial Infarction." New England Journal of Medicine 303, no. 16 (1980): 897-902. doi:10.1056/nejm198010163031601.
12. Jennings, Robert B. "Historical Perspective on the Pathology of Myocardial Ischemia/Reperfusion Injury." Circulation Research 113, no. 4 (2013): 428-38. doi:10.1161/circresaha.113.300987.
13. Heusch, Gerd, and Bernard J. Gersh. "The Pathophysiology of Acute Myocardial Infarction and Strategies of Protection beyond Reperfusion: A Continual Challenge." European Heart Journal, 2016. doi:10.1093/eurheartj/ehw224.
14. Thygesen, Kristian, Joseph S. Alpert, and Harvey D. White. "Universal Definition of Myocardial Infarction." Journal of the American College of Cardiology 50, no. 22 (2007): 2173-195. doi:10.1016/j.jacc.2007.09.011.
15. Alonso, Daniel R., Stephen Scheidt, Martin Post, and Thomas Killip. "Pathophysiology of Cardiogenic Shock." Circulation 48, no. 3 (1973): 588-96. doi:10.1161/01.cir.48.3.588.
16. Reynolds, Harmony R., and Judith S. Hochman. "Cardiogenic Shock." Circulation 117, no. 5 (2008): 686-97. doi:10.1161/circulationaha.106.613596.
17. Anderson, Jeffrey L., Cynthia D. Adams, Elliott M. Antman, Charles R. Bridges, Robert M. Califf, Donald E. Casey, William E. Chavey, Francis M. Fesmire, Judith S. Hochman, Thomas N. Levin, A. Michael Lincoff, Eric D. Peterson, Pierre Theroux, Nanette Kass Wenger, and R. Scott Wright. "ACC/AHA 2007 Guidelines for the Management of Patients with Unstable Angina/Non–ST-Elevation Myocardial Infarction." Circulation 116, no. 7 (2007). doi:10.1161/circulationaha.107.181940.
18. Chapman, Andrew R., Philip D. Adamson, and Nicholas L. Mills. "Assessment and Classification of Patients with Myocardial Injury and Infarction in Clinical Practice." Heart 103, no. 1 (2016): 10-18. doi:10.1136/heartjnl-2016-309530.
19. Siqueira, Fabio Paiva Rossini, Claudio Tinoco Mesquita, Alair Augusto Sarmet M. Damas Dos Santos, and Marcelo Souto Nacif. "Relationship between Calcium Score and Myocardial Scintigraphy in the Diagnosis of Coronary Disease." Arquivos Brasileiros De Cardiologia, 2016. doi:10.5935/abc.20160104.
20. Hess, E. P., D. Agarwal, S. Chandra, M. H. Murad, P. J. Erwin, J. E. Hollander, V. M. Montori, and I. G. Stiell. "Diagnostic Accuracy of the TIMI Risk Score in Patients with Chest Pain in the Emergency Department: A Meta-analysis." Canadian Medical Association Journal 182, no. 10 (2010): 1039-044. doi:10.1503/cmaj.092119.
21. Thygesen, Kristian, Joseph S. Alpert, Allan S. Jaffe, Maarten L. Simoons, Bernard R. Chaitman, and Harvey D. White. "Third Universal Definition of Myocardial Infarction." Global Heart 7, no. 4 (2012): 275-95. doi:10.1016/j.gheart.2012.08.001.
22. Keeley, Ellen C., Judith A. Boura, and Cindy L. Grines. "Primary Angioplasty versus Intravenous Thrombolytic Therapy for Acute Myocardial Infarction: A Quantitative Review of 23 Randomised Trials." The Lancet 361, no. 9351 (2003): 13-20. doi:10.1016/s0140-6736(03)12113-7.
23. Reddy, Koushik. "Recent Advances in the Diagnosis and Treatment of Acute Myocardial Infarction." World Journal of Cardiology 7, no. 5

(2015): 243. doi:10.4330/wjc.v7.i5.243.
24. Ali, Md. Ramjan, Mohammad Salim Hossain, Md. Ariful Islam, Md. Saiful Islam Arman, Golam Sarwar Raju, Prianka Dasgupta, and Tasnim Fariha Noshin. "Aspect of Thrombolytic Therapy: A Review." The Scientific World Journal 2014 (2014): 1-8. doi:10.1155/2014/586510.
25. Jinatongthai, Peerawat, Junporn Kongwatcharapong, Chee Yoong Foo, Arintaya Phrommintikul, Surakit Nathisuwan, Ammarin Thakkinstian, Christopher M. Reid, and Nathorn Chaiyakunapruk. "Comparative Efficacy and Safety of Reperfusion Therapy with Fibrinolytic Agents in Patients with ST-segment Elevation Myocardial Infarction: A Systematic Review and Network Meta-analysis." The Lancet 390, no. 10096 (2017): 747-59. doi:10.1016/s0140-6736(17)31441-1.
26. Rathore, S. S., J. P. Curtis, J. Chen, Y. Wang, B. K. Nallamothu, A. J. Epstein, and H. M. Krumholz. "Association of Door-to-balloon Time and Mortality in Patients Admitted to Hospital with ST Elevation Myocardial Infarction: National Cohort Study." Bmj 338, no. May 19 1 (2009). doi:10.1136/bmj.b1807.
27. Bradley, Elizabeth H., Brahmajee K. Nallamothu, Amy F. Stern, Emily J. Cherlin, Yongfei Wang, Jason R. Byrd, Erika L. Linnander, Alexander G. Nazem, John E. Brush, Harlan M. Krumholz, and Harold H. Hines. "The Door-to-Balloon Alliance for Quality: Who Joins National Collaborative Efforts and Why?" The Joint Commission Journal on Quality and Patient Safety 35, no. 2 (2009): 93-99. doi:10.1016/s1553-7250(09)35012-6.
28. Morrison, Laurie J., P. Richard Verbeek, Andrew C. Mcdonald, Bruce V. Sawadsky, and Deborah J. Cook. "Mortality and Prehospital Thrombolysis for Acute Myocardial Infarction." Jama 283, no. 20 (2000): 2686. doi:10.1001/jama.283.20.2686.
29. Sabatine, M.s., C.p. Cannon, and C.m. Gibson. "Addition of Clopidogrel to Aspirin and Fibrinolytic Therapy for Myocardial Infarction with ST-Segment Elevation." ACC Current Journal Review 14, no. 6 (2005): 1. doi:10.1016/j.accreview.2005.05.016.
30. Mcquaid, K.r., and L. Laine. "Systematic Review and Meta-analysis of Adverse Events of Low-dose Aspirin and Clopidogrel in Randomized Controlled Trials." American Journal of Ophthalmology 143, no. 1 (2007): 194. doi:10.1016/j.ajo.2006.11.002.
31. Coons, James C., Nicholas Schwier, Justin Harris, and Amy L. Seybert. "Pharmacokinetic Evaluation of Prasugrel for the Treatment of Myocardial Infarction." Expert Opinion on Drug Metabolism & Toxicology 10, no. 4 (2014): 609-20. doi:10.1517/17425255.2014.890589.
32. Wiviott , Stephen D., Eugene Braunwald, Carolyn H. McCabe, Gilles Montalescot, Witold Ruzyllo, Shmuel Gottlieb, Franz-Joseph Neumann, Diego Ardissino, Stefano De Servi, Sabina A. Murphy, Jeffrey Riesmeyer, Govinda Weerakkody, C. Michael Gibson, Elliott M. Antman, TRITON-TIMI 38 Investigators. "Prasugrel versus clopidogrel in patients with acute coronary syndromes. " N Engl J Med. 2007 Nov 15; 357(20): 2001–2015. doi:10.1056/NEJMoa0706482.
33. Wilson, Simon John, David E. Newby, Dana Dawson, John Irving, and Colin Berry. "Duration of Dual Antiplatelet Therapy in Acute Coronary Syndrome." Heart 103, no. 8 (2017): 573-80. doi:10.1136/heartjnl-2016-309871.
34. Luca, G. De, F. Bellandi, K. Huber, M. Noc, A. S. Petronio, H. -R. Arntz, M. Maioli, H. M. Gabriel, S. Zorman, M. De Carlo, T. Rakowski, M. Gyongyosi, and D. Dudek. "Early Glycoprotein IIb-IIIa Inhibitors in Primary Angioplasty-abciximab Long-term Results (EGYPT-ALT) Cooperation: Individual Patient's Data Meta-analysis." Journal of Thrombosis and Haemostasis 9, no. 12 (2011): 2361-370. doi:10.1111/j.1538-7836.2011.04513.x.
35. Wijesinghe, M., K. Perrin, A. Ranchord, M. Simmonds, M. Weatherall, and R. Beasley. "Routine Use of Oxygen in the Treatment of Myocardial Infarction: Systematic Review." Heart 95, no. 3 (2008): 198-202. doi:10.1136/hrt.2008.148742.
36. Beasley, R., S. Aldington, M. Weatherall, G. Robinson, and D. Mchaffie. "Oxygen Therapy in Myocardial Infarction: An Historical Perspective." Journal of the Royal Society of Medicine 100, no. 3 (2007): 130-33. doi:10.1258/jrsm.100.3.130.
37. Cabello, Juan B., Amanda Burls, José I. Emparanza, Susan E. Bayliss, and Tom Quinn. "Oxygen Therapy for Acute Myocardial Infarction." Cochrane Database of Systematic Reviews, 2016. doi:10.1002/14651858.cd007160.pub4.