Management of acute coronary syndrome

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Acute coronary syndrome encompasses a collection of three acute processes related to myocardial ischemia. These include: unstable angina, non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI). Myocardial ischemia is caused by inadequate perfusion within the myocardial tissue due to oxygen demand exceeding oxygen supply.

In a healthy person the amount of oxygen required by the myocardium (O2 demand) is determined by heart rate, myocardial contractility, myocardial wall stress, and afterload. As explained by Antman, et al (2012), " oxygen supply to the myocardium requires a satisfactory level of oxygen-carrying capacity of the blood (determined by the inspired level of oxygen, pulmonary function, and hemoglobin concentration and function) and an adequate level of coronary blood flow". The coronary vessels have the ability to adjust their level of resistance to adapt to the increased oxygen demand required by the myocardium during certain times (such as during physical exertion).

Ischemic heart disease is typically caused by atherosclerosis, which is a buildup of plaque inside the lumen of the coronary vessels. The emergence of atherosclerosis in the vessels does not occur overnight. Antman, et al. (2012) found that " atherogenesis in humans typically occurs over a period of many years, usually many decades" and that " growth of atherosclerotic plaques probably does not occur in a smooth, linear fashion but discontinuously, with periods of relative quiescence punctuated by periods of rapid evolution".

The process of atherosclerosis begins with an abundance of lipoproteins in the blood stream. These lipoproteins bind to the walls of vessels and are eventually deposited within the intima of the arteries. To counteract this process, phagocytes are sent into the vessel to attack these " foreign" particles (Antman et al., 2012). Once the phagocytes are within the intima, they mature into macrophages and become lipid-laden foam cells (Antman et al., 2012). As these plaques advance calcification occurs. This process is thought to be a key step in the formation of atherosclerotic plaques (Antman et al., 2012).

Normally this narrowing of the vessel lumen does not cause chest pain or discomfort. Eventually, however, these plaques may rupture. At this point platelet activation occurs, which eventually leads to clot formation at the sight of the plaque. This clot, or thrombus, may break off and lodge in a coronary vessel. These two processes are a common pathogenic finding with acute coronary syndrome (Lincoff, Califf, Anderson, Weisman, Aguirre, Kleiman, Harrington & Topol, 1997). A partial occlusion of the coronary vessels due to a ruptured plaque/platelet complex causes unstable angina or a NSTEMI. In this case, the oxygen demands of the heart cannot be met. A complete occlusion causes a STEMI (Anderson, Adams, Antman, Bridges, Califf, Casey Jr, Chavey II & Wright, 2011), which eventually leads to myocardial cell death.

Discussion/Analysis

The emergency department providers are often the first line of defense in the management of patients with chest pain. The ability to quickly evaluate whether or not the cause of chest pain is potentially fatal is of great

importance. Critical chest pain can be broken down in to non-cardiac and cardiac causes. Non-cardiac causes include: pneumothorax, pulmonary embolism, and Boerhaave's syndrome. Acute coronary syndrome is among several cardiac causes of emergent chest pain.

An accurate diagnosis of the cause of chest pain requires several key components. These include: patient history (including risk factors), physical examination, diagnostics, and labs.

History

History is instrumental during the evaluation of a patient with chest pain. Ischemic chest pain is often described as a severe " pressure" or " squeezing" and is classically described as the feeling of " an elephant sitting on my chest". Typically this pain is described as substernal chest pain which radiates to the neck, jaw, or down the left arm. Additional details regarding the onset of chest pain can also serve as important clues. For example, pain on exertion that resolves with rest suggests stable angina, whereas new onset chest pain or chest pain at rest suggests unstable angina. A good method to differentiate cardiac from non-cardiac chest pain is whether the pain improves after administration of nitroglycerin (NTG). If the pain is relieved by NTG it is considered to be likely due to cardiac causes. Additional details suggesting cardiac origin are shortness of breath, nausea +/- vomiting, diaphoresis, and the presence of syncopal/near-syncopal episodes.

It is important to note that a patient with chest pain often have a silent or atypical presentation. This is especially true in elderly men (Woon & Lim, 2003) and diabetics (Tabibiazar & Edelman, 2003). A patient with an atypical

presentation may present with shortness of breath but lack the classical symptom of angina pectoris which radiates to the jaw or left arm. Commonly these patients complain of a feeling of indigestion or epigastric discomfort. Thus it is very important to consider ACS in these patients.

The presence of risk factors plays an important role in the evaluation of chest pain, especially in a patient with known disease. The landmark Framingham Heart Study showed that cardiac risk can be influenced by diet, lifestyle, and familial risk factors (Oppenheimer, 2005). The more risk factors that a person carries, the greater their risk of developing ischemic heart disease. These risk factors are generally grouped into two categories: those that are modifiable and those that are not. Risk factors amendable are as follows:

Tobacco smoke (American Heart Association, 2012)

High blood cholesterol (AHA, 2012)

High blood pressure (AHA, 2012)

Physical inactivity (AHA, 2012)

Obesity and overweight (AHA, 2012)

Diabetes mellitus (AHA, 2012)

Risk factors that cannot be changed include:

Age- 82% of people who die of coronary heart disease are > 65 (AHA, 2012)

Male sex (AHA, 2012)

Heredity- this includes both family history and race (AHA, 2012)

Risk is higher among Mexican Americans, American Indians, native Hawaiians and some Asian Americans (AHA, 2012)

Patients presenting with unstable angina or NSTEMI have variable levels of risk of cardiac death and ischemic cardiac events (Antman, Cohen, Bernink, McCabe, Horacek, Papuchis, Mautner & Braunwald, 2000). The trial conducted by Antman et al. (2000) set out to " develop a simple risk score that has broad applicability, is easily calculated at patient presentation, does not require a computer, and identifies patients with different responses to treatments for UA/NSTEMI". In doing so, the TIMI risk score was created. The scores are calculated using a score of 1 for each risk factor (7 total categories) assigned to a given patient. According to Antman, et al (2000) the score determines the patient's risk of death, myocardial infarction, or severe ischemia. Antman, et al. (2000) found 7 prognostic variables that increase a patients risk. These are:

Age 65 years or older

At least 3 risk factors for coronary artery disease (male, dyslipidemia, smoking, hypertension, diabetes mellitus, obesity & family history)

Prior coronary stenosis of 50% or more

ST-segment deviation on ECG at presentation

At least 2 anginal events in prior 24 hours

Use of aspirin in prior 7 days

Elevated serum cardiac markers

In TIMI 11B/ESSENCE, event rates increase significantly as the TIMI-score increases (Antman et al., 2000). A score of 0/1 showed a 4. 7% event rate; 8. 3% for 2; 13. 2% for 3; 19. 9% for 4; 26. 2% for 5; and 40. 9% for 6/7. This landmark pair of trials allows practitioners a quick assessment of a patient's risk of suffering a serious cardiac event.

Physical Exam

Physical exam is also a key component in the evaluation of a patient with chest pain, as many clues can suggest acute coronary syndrome. Unstable vital signs can be an important hint that the patient has suffered an MI. A general examination may reveal a patient who is diaphoretic and/or using accessory respiratory muscles. The cardiovascular exam could reveal a new murmur, S3/S4 gallop, or JVD. Finally, during the pulmonary exam rales may be heard upon auscultation.

Diagnostics

Diagnostic testing is an essential part of the evaluation of a patient presenting with chest pain. Several important diagnostic tools were introduced to the emergency department in the latter half of the 20th century that greatly improved the diagnosis and care of acute coronary syndrome.

Electrocardiogram

The introduction of coronary care units in the 1960's allows physicians to utilize the electrocardiogram (ECG) to monitor potential fatal arrhythmias in

patients with acute myocardial infarction (Julian, 1987). Shortly thereafter the portable electrocardiogram became commonplace within the emergency department to assist in diagnosing complications of acute coronary syndrome (Drew, et al, 2004). A patient presenting with myocardial ischemia will typically have symmetrically-inverted T waves in leads V2-V6 (Dubin, 2000). As the name suggests, a STEMI is an ST-segment elevation myocardial infarction, though ST-segment elevation can occur with Prinzmetal's angina in absence of an infarction (Dubin, 2000). Additionally, the ECG allows us to evaluate necrosis of the heart in the form of the presence of " Q-waves". Q-waves are the first downward deflection of the QRS complex (Dubin, 2000). As Dubin (2000) explains, a positive Q-wave MI must:

Lack a preceding spike in the QRS complex

Be at least 1 mm wide

or

Have an amplitude of 1/3 the QRS complex

An additional benefit of the ECG is that it allows the practitioner to identify the location of an acute event. Each lead corresponds to a particular location of the heart. For example, leads II, III, and AvF are the inferior leads and reflect the inferior portion of the heart.

Due to the relatively high specificity but low sensitivity of the 12 lead ECG in diagnosis of acute coronary syndrome, a group of researchers in Canada recently set out to enhance ischemia detection by conducted a trial which

added a new criteria using a three vessel specific leads derived from the traditional 12 lead ECG (Horacek, Mirmoghisi, Warren, Wagner & Wang, 2008). This trial showed a statistically significant improvement in the ability of the vessel specific lead protocol to detect ischemia (Horacek et al., 2008). Horacek et al. (2008) found the following sensitivity and specificity for conventional STEMI criteria versus that of the vessel specific leads (VSL):

Vessel

Sensitivity

Specificity

Left Anterior Descending

74% conventional, 91% VSL

97% conventional, 97% VSL

Right Coronary Artery

60% conventional, 70% VSL

94% conventional, 94% VSL

Left Circumflex Artery

36% conventional, 71% VSL

100% conventional, 100% VSL

Totals Set

60% conventional, 76% VSL

96% conventional, 96% VSL

Based on these results, Horacek et al. (2008) concluded that using vessel specific leads " can identify acute ischemia better than existing STEMI criteria". While a STEMI criteria using vessel specific leads has yet to become a mainstay within the standard emergency room protocol, this study provides exciting new improvements in the detection and management of patients with ACS.

Serum Biomarkers

The use of biochemical markers to detect cardiac cell death significantly evolved in the 1980's and 1990's. Initially, nonspecific markers such as aspartate transaminase and total creatinine kinase were used to detect myocardial necrosis (Lewandrowski, Chen & Januzzi, 2002). During the mid-1990's the more cardiac specific enzymes CK-MB became the gold standard for detection of myocardial injury (Lewandrowski et al., 2002). CK-MB, which commonly rises 4-9 hours after the onset of angina, was not without its shortcomings. CK-MB may be falsely elevated due to several different causes, including recent strenuous exercise or skeletal muscle damage, or renal failure (Vivekanandan & Swaminathan, 2010). In the late 1990's a more predictable biomarker, troponin I, was introduced for more accurate detection of acute coronary syndrome (Heeschen, Goldmann, Moeller & Hamm, 1998). According to Heeschen et al. (1998), Troponin I can be evaluated at the bedside in the emergency room and " has a higher diagnostic sensitivity for the detection of acute myocardial infarction (60% vs 48%)" when compared to CK-MB. The reason for this improvement in accuracy is that troponin I is not found in skeletal muscle tissue or renal failure (Heeschen et al., 1998). As Heeschen et al. (1998) demonstrated in a

head to head study that " cTnI test systems produced no positive results in patients with end-stage renal failure and acute or chronic skeletal muscle injury, whereas 30% and 71% of the patients, respectively, had increased CK-MB mass concentrations". One disadvantage of troponin I, however, is that it has a lower sensitivity for the detection of acute myocardial infarction compared to that of CK-MB (Heeschen et al., 1998). This is due to an increased level of cTnI in patients with unstable angina (Heeschen et al., 1998). For this reason, a typical workup for a patient with chest pain in the emergency room includes both cTnI and CK-MB assays, which are drawn at presentation and every 3-6 hours thereafter (Ross, Bever, Uddin & Hockman, 2000).

Imaging

A common component of a chest pain protocol is a chest x-ray. This is normally either a standard AP/lateral series or a portable chest x-ray if the patient is unable to get out of bed. The chest x-ray is useful to eliminate other possible causes of chest pain, such as an aortic aneurism or a pneumothorax.

Contrast-enhanced computed tomographic angiography, or CTA, has become an integral part of the management of acute coronary syndrome due to its high sensitivity and specificity (Hoffman, Truong, Schoenfeld, Chou, Woodard, Nagurney, Pope & Udelson, 2012). According to the ROMICAT-I study performed by Hoffman et al., (2012), CTA is an effective way to rule out myocardial infarction or ischemia as well as major cardiovascular events over the next 2 years from presentation. The data presented in ROMICAT-I

showed that patients undergoing CTA decreased their hospital stay by 7. 6 hours compared to standard therapy (Hoffman et al., 2012). Additionally, 50% of CTA patients were discharged from the hospital within 8. 6 hours of presentation versus only 10% of patients undergoing standard therapy (Hoffman et al., 2012). Finally, the mean time to diagnosis was significantly decreased with the CT group versus the standard group (Hoffman et al., 2012). Overall, CTA was shown to reduce time spent in the hospital and time to diagnosis when compared to standard therapy for acute coronary syndrome. This is important to note considering the importance of quick coronary reperfusion of STEMI patients (Trost &Lange, 2011). An additional observation was that these benefits were achieved without an increase in the cost of care (Hoffman et al., 2012). There was no overall difference between the groups in incidence of myocardial infarction 30 days after initial presentation (Hoffman et al., 2012). It is important to note that a patient undergoing a CTA is exposed to increased radiation. Additionally, patients undergoing CTA were more likely to undergo invasive coronary procedures when compared to standard evaluation.

Based on this data, a question arises as to whether every patient presenting with possible acute coronary syndrome should undergo a CTA. The population studied in ROMICAT-I consisted of low to intermediate risk patients. Overall, CTA was shown to decrease the time to diagnosis and hospital stay for patients with possible ACS. In contrast, CTA increases a patient's exposure to radiation and increases the likelihood that these patients will undergo an increase in invasive coronary procedures. These

factors should all be considered when evaluating a patient presenting with chest pain.

Treatment

Pharmacologic

Aspirin: Early aggressive aspirin (ASA) therapy (162-325mg followed by 81-162mg daily) is currently recommended for all patients with acute coronary syndrome, unless contraindicated (Kirk, Kontos & Diercks, 2011).

Plavix (Clopidogrel): According to the CURE trial Clopidogrel has been shown to provide " a 20% reduction in cardiovascular death, MI, or stroke" for NSTEMI patients with positive biomarkers or ischemic ECG changes (Kirk et al., 2011). It is important to note that the significant anti-platelet benefits of Clopidogrel administration should also be weighed against the increased risk of bleeding events if the patient may be a candidate for coronary artery bypass surgery.

Antianginal Agents:

Nitroglycerin (NTG): NTG is commonly administered by EMS respondents but can also be ordered once the patient arrives in the emergency department, typically sublingually or in the form of Nitropaste. Nitroglycerin dilates the coronary arteries, which reduces myocardial oxygen demand (Trost & Lange, 2011). For this reason, it is important to evaluate the patient's baseline blood pressure. If SBP is less than 100, caution should be used.

Morphine: Intravenous morphine may be given in the event that chest pain is not relieved by NTG administration. Morphine reduces ventricular preload, thereby decreasing myocardial O2 demand (Trost & Lange, 2011).

Beta-Andrenergic Blockers: Beta-blockers decrease demand on the heart by decreasing heart rate, blood pressure, and myocardial contractility (Trost & Lange, 2011). In a patient presenting with ACS, IV Lopressor is typically the agent of choice. These are especially effective agents in patients with elevated blood pressure or tachycardia. It is important to evaluate relevant contraindications to beta-blocker therapy, such as: HR <45bpm, 2° or 3° AV block, uncompensated heart failure, SBP <100, cardiogenic shock, sick sinus syndrome without pacemaker, pheocromocytoma, or peripheral vascular disease (Epocrates, 2012).

Calcium-Channel Blockers: Diltiazem and Verapamil improve cardiac O2 supply by vasodilation of the coronary vessels, reduce O2 demand by reducing afterload, and reduce heart rate and contractility (Trost & Lange, 2011). Calcium-channel blockers are 2nd line treatments for ACS and are typically reserved for patients who are unable to take a beta-blocker (Trost & Lange, 2011). Contraindications include: sick sinus syndrome, 2° or 3° AV heart block, hypotension, acute MI with pulmonary congestion, atrial fibrillation or flutter with accessory bypass tract, and ventricular tachycardia, severe left ventricular dysfunction, and cardiogenic shock (Epocrates, 2012).

Antithrombotic therapy: Antithrombotic therapy is recommended in a patient with suspected ACS, unless contraindicated (Trost & Lange, 2011).

Unfractionated heparin is easy to administer (IV) and is rapidly reversible with protamine in the event of bleeding. (Trost & Lange, 2011). As with any antithrombotic, there is a risk of bleeding so these patients require close monitoring.

Low molecular weight heparin is more predictable, has a lower incidence of thrombocytopenia, and does not require monitoring (Trost & Lange, 2011). LMWH is the preferred agent for a more conservative, ischemia-guided strategy to prevent in hospital death or myocardial infarction (Trost & Lange, 2011).

Bivalirudin is an antithrombotic agent that does not cause thrombocytopenia (Trost & Lange, 2011). It has been shown to be equally as effective as unfractionated heparin or LMWH but with a significantly lower rate of bleeding (Trost & Lange, 2011).

Oxygen administration should be administered for patients who are short of breath, showing signs of shock, or O2 saturation <94% (O'Connor, Brady, Brooks, Diercks, Egan, Ghaemmaghami, Menon & Yannopoulos, 2010).

Next Step for NSTEMI or Unstable Angina Patients

If a patient is considered to be high risk, such as a patient is at risk of future ischemia or infarction, an early invasive strategy is recommended (Trost & Lange, 2011). For these patients, cardiac catheterization should be performed within 24-48 hours of admission (Trost & Lange, 2011). In a low risk patient, a more conservative treatment is typically recommended. For these patients, catheterization is only recommended if recurrent or

provocable ischemia occurs (Trost & Lange, 2011). TIMI scores are a valuable tool to assess the patients risk and to guide the practitioner on the appropriate next step.

Next Step for STEMI Patients

Prompt coronary reperfusion is paramount in patients presenting with STEMI (Trost & Lange, 2011). A " door-to-balloon" time of less than 90 minutes is considered to be the goal (Trost & Lange, 2011). If the patient presents to a facility without a percutaneous coronary intervention facility the patient should be either:

Treated with fibrinolytic therapy if not contraindicated (Trost & Lange, 2011)

Or

Transferred to a nearby PCI facility (Trost & Lange, 2011).

Conclusion

Acute coronary syndrome is spectrum of diseases typically caused by atherosclerotic disease. Emergency department practitioners must be able to rapidly diagnose and manage ACS patients in order to potentially preserve precious heart muscle. While treatments for ACS have improved dramatically over the past 30 years, several recent innovations have brought upon exciting new possibilities for the care of these patients. These include new vessel specific ECG leads, cardiac specific biomarkers, and the use of computed-tomographic angiography to assess patients with possible ACS.

One component of the management algorithm that has not changed is the need for a strong history and physical examination to aid in diagnosis. Urgency in obtaining diagnosis cannot be stressed enough, and patients presenting with STEMI should be rapidly sent for PCI or transferred to a facility with PCI capabilities.