A Review Based Study on Acute Coronary Syndrome

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Abstract:

Advances in treatment and early revascularization have led to improved outcomes for patients with acute coronary syndrome (ACS). However, elderly ACS patients are less likely to receive evidence-based treatment, including revascularization therapy, due to uncertainty of the associated benefits and risks in this population. Patients presenting with acute coronary syndromes (ACS) remain amongst the highest-risk of all acute medical admissions. Despite significant reductions in morbidity and mortality via refinements in treatment methods in recent years, such individuals remain at a high risk of recurrent ischemic events and death. Whilst 2012 has brought a wealth of novel data in the field of ACS regarding diagnosis and both medical and invasive management strategies, continued focus on this high-risk patient subset is necessary to further our understanding and improve patient outcomes.

This article addresses key issues regarding medical and revascularization therapy in elderly ACS patients based on a review of the medical literature and in concordance with clinical practice guidelines from the American.Heart Association (AHA) and the American College of Cardiology (ACC).

Keywords: *acute coronary syndrome, revascularziaton, medical therapy.*

INTRODUCTION:

Acute Coronary Syndrome (ACS) is a clinical syndrome comprising ST Segment Elevation Myocardial Infarction (STEMI), Non-ST Segment Elevation Myocardial Infarction (NSTEMI), and Unstable Angina (UA). ACS is a common and important diagnosis that is often made in the emergency department by front-line physicians and rapid recognition and diagnosis of ACS, risk stratification, and appropriate treatment have been shown to decrease morbidity and mortality

In the context of ACS treatment, dual antiplatelet therapy with ASA and clopidogrel (a P2Y12 receptor inhibitor) reduces rates of harmful cardiac events such as cardiovascular causes of death, myocardial infarction, and stroke .

However, with new agents undergoing evaluation in large clinical trials, acute care providers need to know if the new P2Y12 receptor inhibitor antiplatelet agents ticagrelor and prasugrel are clinically superior to the current standard clopidogrel. It has been established that a defined percentage of the population exhibits high platelet activity despite the use of clopidogrel. This phenomenon occurs anywhere from 5% to 44% of patients studied depending on the clopidogrel dose and patient population . It is uncertain what level of platelet activity during ACS is related to harmful cardiovascular outcomes such as cardiovascular death, myocardial infarction, and stroke.
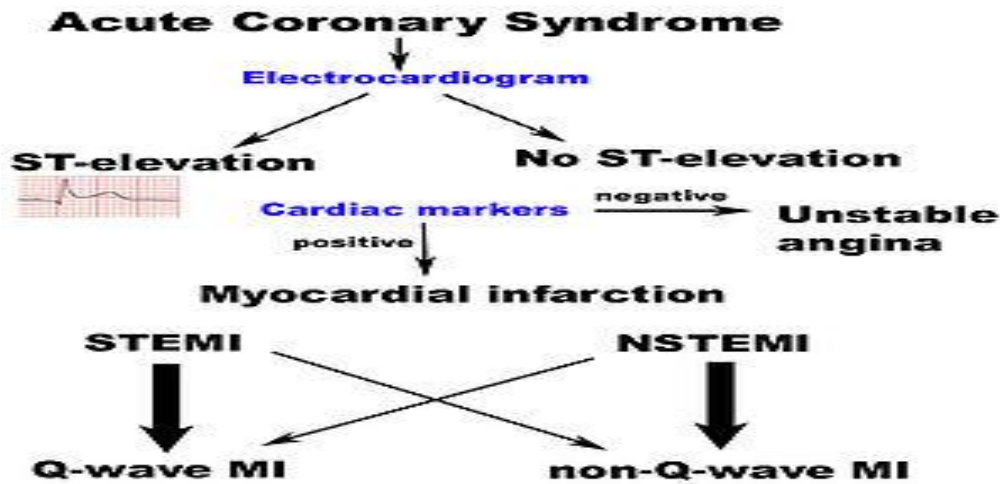
Ticagrelor and prasugrel have been demonstrated to reduce levels of platelet activation when compared to clopidogrel which could lead to reduced risk of thrombosis and improved artery or stent patency. However, there is debate as to which patients will gain the most clinical benefit from these costly and potentially harmful agents.
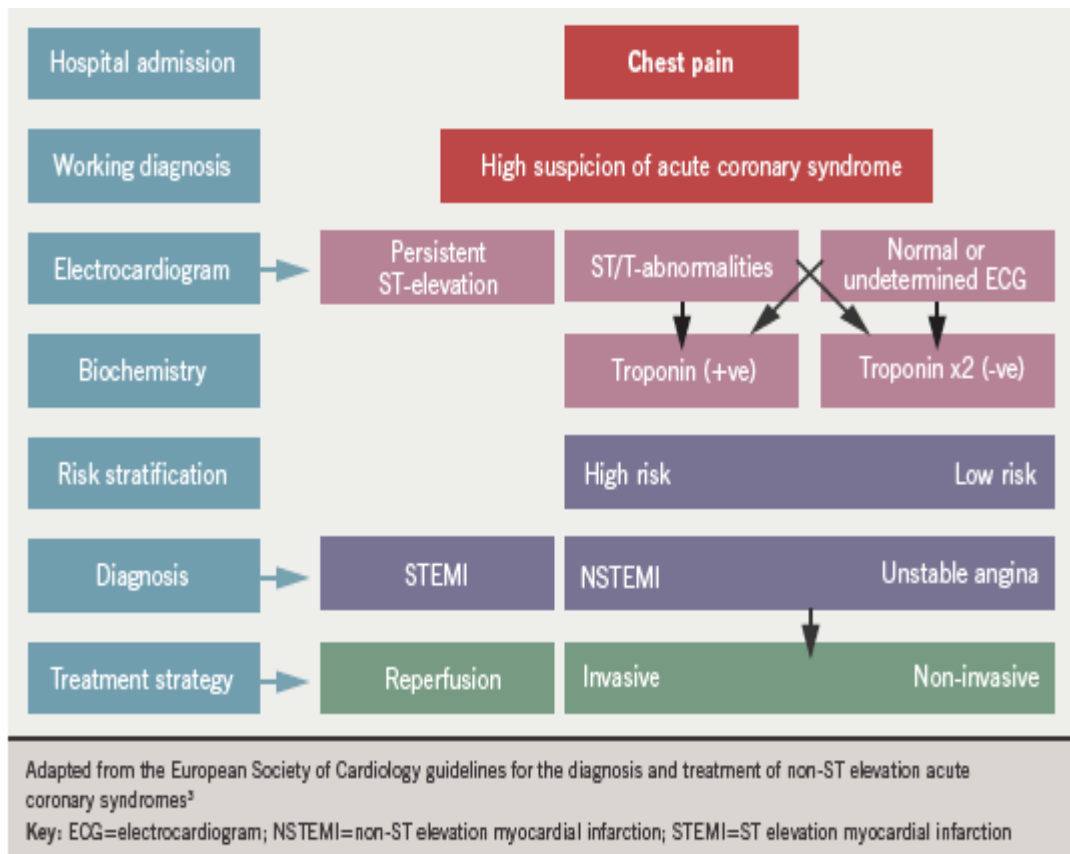
In this paper There have been few recent years where the management of acute coronary syndromes (ACS) has not been significantly advanced in terms of novel therapies and treatment strategies. In the last 12 months, new societal guidance has been published from Europe and North America, and there have also been important ACS studies concerning non-invasive diagnostics, stent type/choice, and adjunctive therapies designed to reduce infarct size in percutaneous coronary intervention (PCI) for ACS.

In similar fashion to recent years, the area most published in and most likely to alter practice concerns the choice and utilization of antiplatelet/anticoagulant strategies for ACS patients managed either medically or with an invasive/interventional strategy. This review will seek to summarize the most important advances in these areas over the last year.

Development of ACS:

Guidelines For Diagnosis & Treatment of ACS:

Adapted from the European Society of Cardiology guidelines for the diagnosis and treatment of non-ST elevation acute coronary syndromes[3]

Key: ECG=electrocardiogram; NSTEMI=non-ST elevation myocardial infarction; STEMI=ST elevation myocardial infarction

PATHOPHYSIOLOGY:

Morbidities related to atherosclerosis, such as acute coronary syndromes (ACS) including unstable angina and myocardial infarction, remain leading causes of mortality. Unstable plaques are inflamed and infiltrated with macrophages and T

lymphocytes. Activated dendritic cells interact with T cells, yielding predominantly Th1 responses involving interferon-gamma (IFN-γ) and tumour necrosis factor-alpha (TNF-α), while the role of interleukin 17 (IL-17) is questionable. The expansion of CD28nullCD4 or CD8 T cells as well as pattern recognition receptors activation (especially Toll-like receptors; TLR2 and TLR4) is characteristic for unstable plaque. Inflammation modifies platelet and fibrin clot characteristics, which are critical for ACS.

Understanding of the inflammatory mechanisms of atherothrombosis, bridging inflammation, oxidative stress and immune regulation, will allow for the detection of subjects at risk, through the use of novel biomarkers and imaging techniques including intravascular ultrasound, molecular targeting, magnetic resonance imaging (MRI) and 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET). Moreover, understanding the specific inflammatory pathways of plaque rupture and atherothrombosis may allow for immunomodulation of ACS. Statins and anti-platelet drugs are anti-inflammatory, but importance of immune events in ACS warrants the introduction of novel, specific treatments directed either on cytokines, TLRs or inflammasomes (Matusik P, 2012)
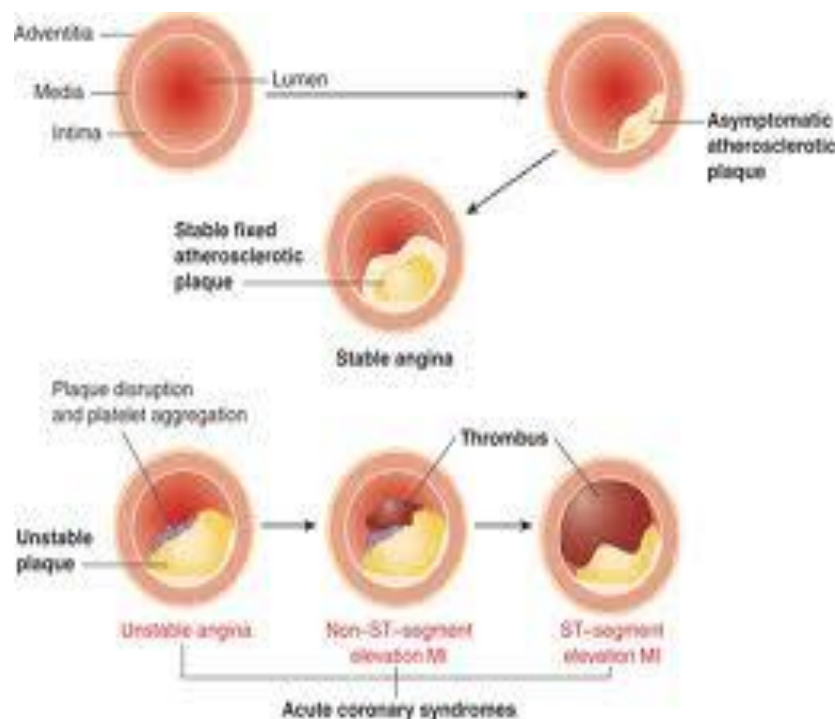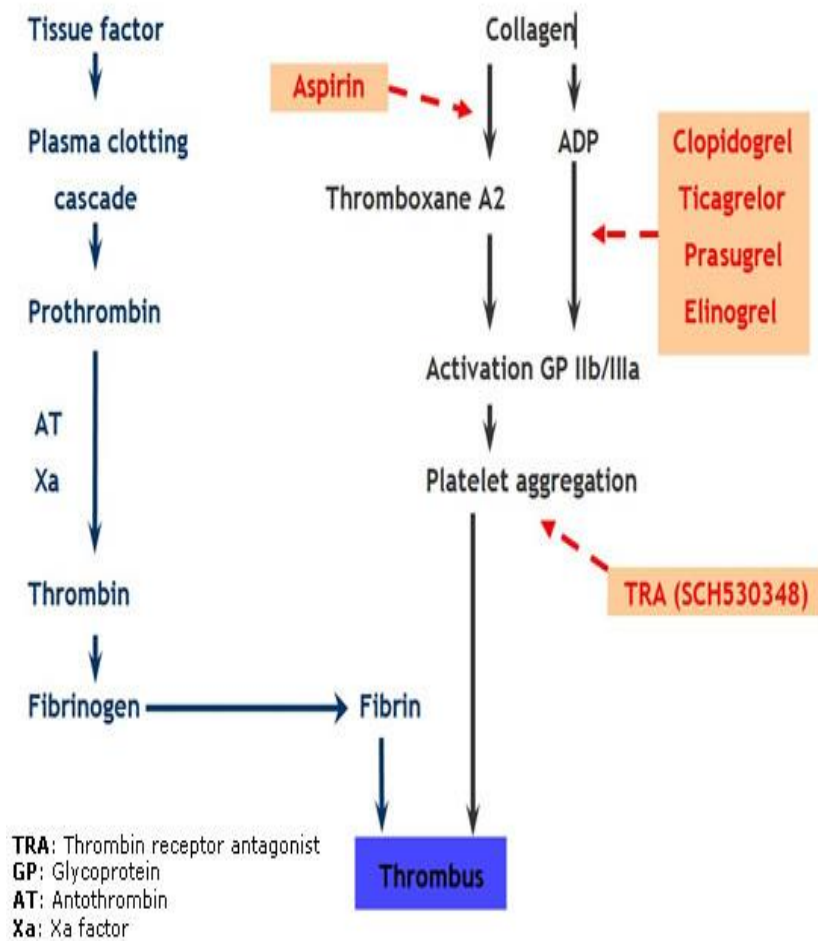

EPIDEMIOLOGY:

Each year more than 1.5 million Americans will experience an ACS, and 220,000 will die of an MI. In the United States, more than 7.6 million living persons have survived an MI. CHD is the leading cause of premature chronic disability in the United States. The cost of CHD is high, with direct and indirect costs estimated at$151.6 billion for 2007.(American Heart Association website).Chest discomfort is the second most

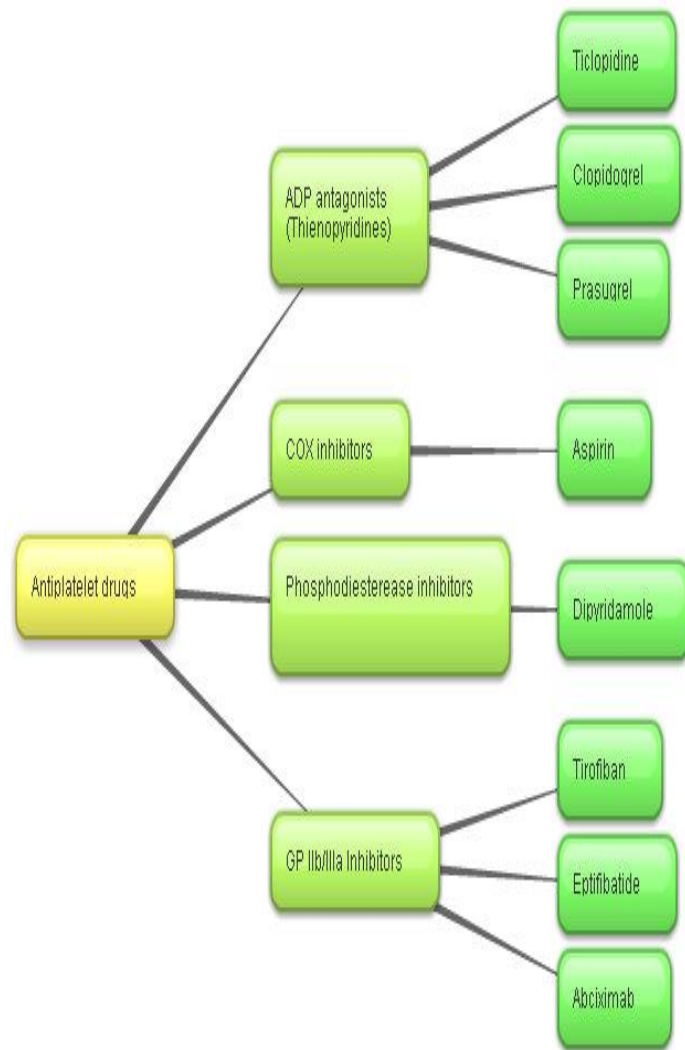frequent reason for patient presentation to emergency departments. Up to 5.6 million (~5.1%) emergency department visits are linked to chest discomfort and possible ACS (Anderson JL,

Antiplatelet Therapy:

2007). The median length of hospital stay for MI in 1999 was 4.3 days but decreased to a median of 3.3 days in 2006

TRA: Thrombin receptor antagonist
GP: Glycoprotein
AT: Antothrombin
Xa: Xa factor

Various Mechanism of Antiplatlet Agents:

Antiplatelets Overview

Drug	Indications	Possible Side effects	Some Potential Interactions	Precautions and Contraindications
Aspirin **Clopidogrel** **Prasugrel** **Ticagrelor**	• Acute coronary syndrome • Prophylaxis TIA/Stroke • Peripheral artery disease **Additional** **Aspirin** • Pain / fever • Inflammation • Rheumatic fever	• Hemorrhage • Rash • Nausea • Abdominal discomfort • Thrombocytopenia • Ulceration **Additional** **Prasugrel** • Neutropenia **Ticagrelor** • Dyspnea / cough • Epistaxis • Headache • Hyperuricemia • Muscle weakness • Tingling sensation	• Anticoagulants • Antiplatelet agents • Thrombolytic agents • Glucosamine • Ethanol • Antimetabolite • SSRIs • PPIs **Additional** **Clopidogrel** • Antifungals **Ticagrelor** • Rifampin • Digoxin	**Precautions:** • Risk of bleeding • Peptic ulcer disease • Hepatic / renal dysfunction • Pregnancy / lactation • Intracranial mass lesions • Planned surgeries **Additional** **Aspirin** • GERD **Ticagrelor** • Patients at risk for bradycardia **Contraindications:** • Hypersensitivity • Bleeding disorders • Active pathological bleeding • Severe hepatic impairment **Additional** **Ticagrelor** • Concomitant with strong CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin, ritonavir)
GPIIb/IIIa inhibitors				
Abciximab **Eptifibatide** **Tirofiban**	• Acute coronary syndrome • Percutaneous coronary intervention (adjunct)	• Hypotension • Chest pain • Nausea / vomiting • Minor bleeding • Back pain • Bradycardia • Rash	• Antiplatelet agents • Thrombolytic agents • Glucosamine • NSAIDs	**Precautions:** • Hypovolemia • Platelet count <150,000/mm^3 • Renal impairment • Pregnancy / lactation **Contraindications:** • Hypersensitivity • Active bleeding • CVA within 2 years • Intracranial neoplasm / AVM • Thrombocytopenia • Use of IV dextran prior to or during PCI

AVM: Arteriovenous malformation; **CVA:** Cerebrovascular accident; **GERD:** Gastroesophageal reflux disease; **PCI:** Percutaneous coronary intervention; **PPI:** Proton pump inhibitors; **NSAIDs:** Nonsteroidal anti-inflammatory drugs; **SSRIs:** Selective serotonin reuptake inhibitors; **TIA:** Transient ischemic stroke

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Guideline:

The former document updates previous guidance from the ESC and contains important new recommendations in key areas the importance of early diagnosis is stressed, with first ECG in patients with suspected STEMI recommended within 10 min of first medical contact (FMC) and primary percutaneous coronary intervention (PPCI) for STEMI ideally within 90 min (rated 'acceptable' out to a maximum of 120 min).

Such strict criteria may have an impact on more rural geographies where transit time to PPCI centres is an issue, and with this in mind, the guidance highlights the importance of collaborative networks to facilitate achievementof such targets.

The guideline also emphasizes the importance of prompt assessment and management of atypical presentations not always considered under the umbrella of STEMI, including left bundle branch

block (LBBB), paced rhythms, and isolated ST-segment elevation in lead aVR, especially when accompanied by symptoms consistent with myocardial ischaemia.

Therapeutic hypothermia is now recommended for all resuscitated patients with STEMI complicated by cardiac arrest cases, with immediate coronary angiography with a view to follow-on PPCI when the ECG demonstrates persistent ST-segment elevation. Additionally, in the light of recently published studies and meta-analyses, including that of Kalesan et al., drug-eluting stents (DES) are now routinely preferred to bare metal stents (BMS) in view of the reduced need for repeat revascularization and the lack of previously perceived hazard for stent thrombosis.

 The more potent antiplatelet agents prasugrel and ticagrelor are also preferred to clopidogrel for all STEMI cases, with duration of dual antiplatelet therapy (DAPT) ideally for 1 year, but reduced to a strict minimum of 6 months for patients receiving DES. Accompanying and integral to such guidance was the Third Universal Definition of Myocardial Infarction, published simultaneously with the STEMI guidance.

This guideline endorses cardiac troponin as the biomarker of choice to detect myocardial necrosis, with spontaneously occurring myocardial infarction (MI) defined as an elevation above the 99th percentile upper reference value for the specific assay used. There is further development and clarification of MI in different settings to allow standardization across trials and registries,

in particular after revascularization procedures: after CABG with normal baseline troponin,

MI is defined as a rise to a value 10 times greater than baseline in the first 48 h, and a rise to 5 times greater than 99th percentile upper reference after PCI in patients with a normal baseline level (or a 20% rise when troponin is elevated and stable or falling pre-procedure).

The ACCF/AHA also produced updated guidance on the management of unstable angina/non-STEMI angiography with a view to revascularization is now recommended within 12–24 h of presentation, with DAPT pre-loading prior to PCI procedures also now advocated.

Ticagrelor and prasugrel are cited as acceptable alternatives to clopidogrel, and the maintenance dose of aspirin recommended for the majority of cases has finally fallen to 81 mg daily. Although there remain some differences in nuance between North American and European practices, this guideline broadly brings about transatlantic agreement in most areas for the first time.

Risk stratification

Identification and appropriate triage of patients presenting to emergency departments with acute chest pain remains a difficult dilemma: many are low-risk and have a non-cardiac origin, but a significant minority with coronary artery disease may not be picked up on clinical grounds even when accompanied by appropriate tests, including ECG and biomarker estimation used in conjunction with a clinical risk score (e.g. GRACE, TIMI).

As endorsed in ESC guidance, there has been increasing interest in non-typical ECG patterns for the diagnosis of STEMI; although LBBB is an accepted surrogate, Widimsky et al.retrospectively analysed 6742 patients admitted to hospital with acute MI and found that

in patients presenting with right bundle branch block, a blocked epicardial vessel was more common demonstrated the importance of ST-elevation in lead aVR, often viewed as indicative of left main stem occlusion, betokening increased mortality in patients presenting with both inferior and anterior infarction.

Perhaps the most important data regarding the ECG in 2012 were also the most simple: Antoni et al. Highlighted a powerful and very simple method of risk stratification; they found that

heart rate measured on a 12-lead ECG at discharge after PPCI is a strong and independent predictor of mortality at 1 and 4 years of follow-up Patients with a discharge heart rate of

≥70 b.p.m. had a two-fold higher mortality at both follow-up time points, with every increase of 5 b.p.m. in heart rate equating to a 29% increase in mortality at 1 year and 24% at 5 years.

These findings have important implications for the optimization of patient therapies after MI (including the use of rate-limiting agents such as beta-blockers, calcium channel-blockers, and ivabradine), although large randomized trials are needed to confirm that interventions to reduce heart rate will replicate the benefits observed in this study.

Two important studies concerning the use of coronary computed tomographic angiography as a triage tool for suspected ACS were published this year the findings are discussed fully in another review in this series, but in essence, while improving the efficiency of the emergency department, the studies suggest no cost improvement and an additional hazard for radiation exposure without clear clinical outcome benefit, suggesting that such a

strategy has little data to support it at the present time.

Estimation of level of risk

Several risk assessment tools have been used to predict outcomes in ACS. The most commonly used tools are the TIMI risk score for UA/NSTEMI42 and the Global Registry of Acute Coronary Events (GRACE) predictive score for ACS Worthy of emphasis is the contribution of advanced age to increased risk status in all scores.

The TIMI risk score for UA/NSTEMI predicts the risk of death or cardiovascular events within 14 days42 and is determined by the sum of the presence of 7 variables on admission. These variables are coronary risk factors, known coronary stenosis of ST segment depression on ECG, anginal events within 24 hours, aspirin use, and abnormal levels of cardiac biomarkers. The more the sum of these variables, the greater the risk of death or ischemic events within 14 days after UA/NSTEMI.

The GRACE predictive score is also commonly used to predict the risk of death within 6 months

after ACS.The GRACE score uses a point system encompassing the variables of age, heart failure, previous MI, heart rate, systolic blood pressure, ST segment depression on ECG, serum

creatinine, abnormal cardiac biomarkers, and the availability of in-hospital PCI. Higher scores predict higher risks of death within 6 months of ACS. These risk assessment tools are useful in the management of UA/NSTEMI as higher risk patients would be more likely to benefit from CCU admission, glycoprotein IIb/IIIa inhibitors, and an early invasive strategy

ANCILLARY ACS TREATMENT:

Aspirin:

In the absence of contraindications, all ACS patients should receive 162 to 325 mg of chewable aspirin immediately, if ACS is suspected. Nonenteric-coated aspirin is preferable due to quicker antiplatelet inhibition.45 With the exception of patients treated with primary PCI, the recommended daily aspirin dose after the first 24 hours is 75 to 162 mg/day thereafter.

For ACS patients treated with PCI, aspirin should be prescribed as follows Bare-metal stent: aspirin 162 to 325 mg daily for at least 1 month and then 75 to 162 mg thereafter. Sirolimus-eluting stent: aspirin 162 to 325 mg daily for at least 3 months and then 75 to 162 mg indefinitely thereafter. Paclitaxel-eluting stent: aspirin 162 to 325 mg daily for at least 6 months and then 75 to 162 mg thereafter.In clinical practice, zotarolimus- or everolimus-eluting stents are treated like

sirolimus-eluting stents, but this has not yet been addressed in the guidelines.

Clopidogrel:

In elderly STEMI patients who receive thrombolytics, a loading dose of clopidogrel is not recommended due to increased risk of intracerebral hemorrhage A loading dose of clopidogrel is recommended in elderly STEMI patients only if primary PCI is performed. The recommended dose is 600 mg orally, before or at the time of PCI, which produces rapid antiplatelet activity.

For UA/NSTEMI, an oral loading dose of 300 mg is recommended at the time of presentation.

If PCI is not performed, a daily dose of clopidogrel 75 mg should be continued, in addition to indefinite aspirin, for at least 14 days in STEMI,2,3 and for 9 to 12 months in UA/NSTEMI.

If PCI with bare-metal stent is performed, a daily dose of clopidogrel 75 mg should be continued for at least 1 month and preferably up to 12 months. For PCI with a drug-eluting stent, clopidogrel 75 mg should be continued daily for at least 12 months. Prolonged dual antiplatelet therapy is required for drug-eluting stents due to delayed stent endothelialization associated with the antiproliferative effects of the eluted drugs (sirolimus, paclitaxel, zotarolimus, or everolimus). Dual antiplatelet therapy is continued until the stent has time for complete endothelialization, to prevent stent thrombosis. Aspirin should be continued indefinitely, and without interruption,

due to the persistent risk of stent thrombosis. For both, bare-metal and drug-eluting stents, the risk of stent thrombosis within the first year is very low as long as dual antiplatelet therapy is continued.

However, the risk of stent thrombosis after the first year appears to be higher in drug-eluting stents compared to bare-metal stents. This has been an area of controversy and received much publicity in the press. On balance, it is important to consider that the risk of stent thrombosis associated with drug-eluting stents after the first year is between 0.6% to 0.9% (cumulative risk), which is increased by 0.3% to 0.6% when compared to bare-metal stents.50,51 This should be balanced against the higher risk of early restenosis in patients who receive baremetal stents.

More important, no difference in mortality has been demonstrated between bare-metal and drug-eluting stents Glycoprotein IIb/IIIa inhibitors.The ACC/AHA guidelines recommend the use of glycoprotein IIb/IIIa inhibitors in high-risk NSTEMI patients, if PCI is planned, without modification based on age.

Appropriate dose adjustment based on renal function is emphasized. In STEMI, the use of glycoprotein IIb/IIIa inhibitors is reasonable prior to PCI. However, glycoprotein IIb/IIIa inhibitors play a secondary role in STEMI where early revascularization is the primary objective.

Antithrombin therapy In the absence of contraindications, the ACC/AHA guidelines recommend the use of either unfractionated heparin or low molecular weight heparin in patients with ACS without modification based on age.

Appropriate dose adjustment to weight and renal function is emphasized to reduce bleeding complications. Newer agents such as fondaparinux and bivalarudin may provide theoretical advantages, but data regarding their use in elderly ACS patients are limited. Morphine Morphine is a potent analgesic, anxiolytic, and venodilator, which may help reduce heart rate and myocardial oxygen demand in the setting of ACS. Despite the absence of clinical trial evidence, morphine use has long been a Class I recommendation in the treatment of ACS.

However,recent registry data indicate a possible increase in adverse outcomes associated with morphine use. For UA/NSTEMI, morphine use was downgraded to a Class IIa recommendation, but remains a class I recommendation for STEMI. Clinical trials are needed to establish the role of morphine in ACS patients in general and in elderly ACS patients inparticular.

Beta-blockers Oral beta-blockers reduce infarct progression and improve both long-term and short-term outcomes. Except in hemodynamically unstable patients, the magnitude of benefit from early beta-blocker use appears to be greater in the elderly, compared to younger ACS patients. Intravenous beta-blocker use is discouraged (Class III in 2007 ACC/AHA guideline), although their early use was advocated in previous ACC/AHA guideline statements (Class IIa in 2004).

This is due to the higher risk of hemodynamic compromise and bradycardia associated with intravenous beta-blocker use, which may be more profound in elderly patients. The initial use of a short-acting oral beta blocker is currently preferred. Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) Long-term treatment with ACE inhibitors after myocardial infarction is associated with improved outcomes, especially in patients with left ventricular systolic ejection fraction less than 40%. Elderly ACS patients appear to derive greater benefit from ACE inhibitors than their younger counterparts.

ARBs should be used as an alternative in ACE inhibitor intolerant patients.

ACE inhibitors and ARBs are not part of the initial management of ACS patients and should not be started until the patient is stabilized and is ready for hospital discharge. Renal function and electrolytes should be monitored closely, especially in elderly patients.

Aldosterone blockade Aldosterone blockade with eplerenone in addition to standard therapy after myocardial infarction improves outcomes in a broad range of ACS patients with left ventricular dysfunction. However, a high incidence of renal failure and hyperkalemia has been observed in patients above the age of 65 years.

The use of spironolactone has not been studied in the setting of ACS in the elderly. Therefore, caution should be used when prescribing spironolactone or eplerenone in elderly ACS patients. The patient's electrolytes and renal function should be monitored closely in follow-up. Aldosterone blockade is not part of the initial management and should not be started until the patient is stabilized and in preparation for hospital discharge.

Nitrates are recommended by the ACC/AHA guidelines as part of the initial management of both STEMI and UA/NSTEMI. Nitrates can provide symptomatic relief in ACS but are not associated with a survival benefit in younger ACS patients. However, nitrate use in the elderly ACS patients is associated with a reduction in mortality, heart failure, and left ventricular dysfunction at 6 months follow-up.

FDA APPROVAL OF TICAGRELOR:

FDA approves blood-thinning drug Brilinta to treat acute coronary syndromes

Boxed warning says daily aspirin doses above 100 milligrams decrease effectiveness

The U.S. Food and Drug Administration today approved the blood-thinning drug Brilinta (ticagrelor) to reduce cardiovascular death and heart attack in patients with acute coronary syndromes (ACS).

ACS includes a group of symptoms for any condition, such as unstable angina or heart attack, that could result from reduced blood flow to the heart. Brilinta works by preventing the formation of new blood clots, thus maintaining blood flow in the body to help reduce the risk of another cardiovascular event.

Brilinta has been studied in combination with aspirin. A boxed warning to health care

professionals and patients warns that aspirin doses above 100 milligrams per day decrease the effectiveness of the medication.

"In clinical trials, Brilinta was more effective than Plavix in preventing heart attacks and death, but that advantage was seen with aspirin maintenance doses of 75 to 100 milligrams once daily," said Norman Stockbridge, M.D., Ph.D., director of the Division of Cardiovascular and Renal Products in the FDA's Center for Drug Evaluation and Research.

The boxed warning also says that, like other blood-thinning agents, Brilinta increases the rate of bleeding and can cause significant, sometimes fatal, bleeding. The most common adverse reactions reported by people taking Brilinta in clinical trials were bleeding and difficulty breathing (dyspnea).

Brilinta was approved with a Risk Evaluation and Mitigation Strategy, a plan to help ensure that the drug's benefits outweigh its risks. As part of that plan, the company must conduct educational outreach to physicians to alert them about the risk of using higher doses of aspirin. In addition, Brilinta will be dispensed with a Medication Guide that informs patients of the most important information about the medication. The guide will be distributed each time a patient fills their prescription.

Brilinta is made by AstraZeneca of Wilmington, Del.

Prevention:

The ACC/AHA guidelines recommend that all ACS patients enroll in cardiac rehabilitation/secondary prevention programs, when available.Cardiac rehabilitation allows for monitored, supervised, and graduated exercise under medical supervision and has been shown to reduce the risk of sudden death and recurrent MI. Cardiac rehabilitation also provides

psychological benefits to the ACS patient.

Longterm survival may also be improved in cardiac rehabilitation participants. Secondary prevention refers to preventing recurrence of ACS, which can be reduced by treating all modifiable risk factors, including smoking cessation, weight reduction, treatment of diabetes mellitus, and precise blood pressure and lipid control. Fish oil supplementation (omega-3 fatty acids) is also recommended as this has been shown to reduce the risk of sudden death in patients with a history of myocardial infarction.

Coronary artery bypass graft surgery Advanced age is associated with higher morbidity and

mortality in patients undergoing coronary artery bypass graft CABG. Earlier studies reported prohibitive CABG-related mortality rates in patients over the age of 70 years. This led some to believe that advanced age was a contraindication to CABG.

More recent reports show improved outcomes after CABG in the elderly despite the increased severity of coronary artery disease and increased frequency of comorbid medical conditions in this

population. Therefore, patients over the age of 70 years should not be denied CABG solely

on the basis of age, as satisfactory recovery is possible in the majority of elderly patients undergoing CABG.

Indeed, select elderly patients have been shown to benefit from emergent CABG even in the setting of cardiogenic shock. Caution is advised before reaching the decision to recommend

CABG in the elderly, with particular attention warranted to baseline functional capacity, comorbid medical conditions, and patient preference. CABG is reasonable if the long-term benefits outweigh the procedural risk of CABG.

In elderly patients with indications for CABG, some evidence suggests that off-pump surgery, when available, may be preferable to on-pump surgery; in patients over the age of 70 years, off-pump bypass grafting is associated with a lower incidence of stroke, atrial fibrillation, as well as shorter mechanical ventilation times when compared to on-pump bypass grafting. No mortality benefit has been demonstrated for off-pump bypass grafting versus traditional CABG.

The Novel Antiplatelet Agents

Clopidogrel, prasugrel, and ticagrelor are all examples of P2Y12 receptor inhibitor antiplatelet medications that can be used in the treatment of ACS. Clopidogrel and prasugrel both are irreversible inhibitors of the P2Y12 receptors on the platelet surface. Platelets inhibited by these two agents are affected for the remainder of their lifespan, and therefore platelet aggregation returns

to baseline within 5–10 days of discontinuation of either drug. Clopidogrel is a prodrug that is activated in the liver by cytochrome P450 enzymes and genetic variability in enzyme function is known to cause the medication to be less effective in individuals who cannot

convert the drug to its active form. Prasugrel is a prodrug as well but appears to be effective in most individuals.

In contrast ticagrelor is a reversible noncompetitive antagonist of the P2Y12 receptor; its action and the recovery of platelet function likely depend on the serum concentration of the drug. Ticagrelor is not a prodrug. Of the three agents, clopidogrel has the longest onset of action at 2 hours after administration of the initial loading dose. Both ticagrelor and prasugrel cause inhibitionof platelet activity (IPA) within 30 minutes of the initial loading dose, and their time to achieve maximal IPA is 4–8 hours .

Clopidogrel has the shortest half-life elimination of its active metabolite at 30 minutes.The half-life of ticagrelor and prasugrel is 9 and 7 hours on average, respectively. Both ticagrelor and prasugrel show increased risk of bleeding. Additionally ticagrelor can cause dyspnea as an

adverse effect in 10–14% of patients. Dyspnea usually occurs early in the course of treatment and is self-limited. Ticagrelor is contraindicated for use in patients who are taking medications

that are strong CYP3A4 inhibitors; it is also contraindicated in those patients who have a history of intracranial hemorrhage. Prasugrel is contraindicated in patients with a

history of transient ischemic attack (TIA) or stroke.

Challenges and ethical concerns

Caring for the critically ill elderly patient can pose a unique set of practical challenges and ethical dilemmas. Cognitive impairment, communication difficulties, frailty, comorbid medical illnesses, and the patient's family dynamics are but a few factors that must be taken into account when caring for the elderly ACS patient. As with all physician-patient interactions, one must

always apply the four main ethical principles of autonomy, beneficence, nonmal eficence, and justice, when caring for the elderly ACS patient.

Autonomy is to respect the patient's right to self determination. Understanding the patient's wishes can be challenging in the presence of cognitive impairment.

Beneficence is doing good for the patient and acting in their best interest, which may not always be clear due to the potential.

3) Nonmaleficence is the principle of avoiding harm to the patient and is embodied by the phrase "do no harm". This principle is not absolute and must be balanced against the principle of beneficence.

4) Justice is the principle of equitable allocation of medical resources and providing similar care for all. Potentially beneficial treatments are often withheld from elderly patients solely on the basis of advanced age. The principle of justice must be balanced against the need to control

healthcare costs and the limited availability of resources. These principles should not be regarded as inflexible rules but as a framework to aid in the decision-making process in complex medical and ethical situations. The physician must have a clear understanding of ACS management, specifically regarding the associated benefits and risks of ACS treatments.Treatment decisions should be made after discussion with the patient (or surrogate) regarding the plan of care and one

must be cognizant of the influence of the physician's personal bias on the patient's decisions.

CONCLUSION:

This review summarizes the Advances in treatment and early revascularization has led to improved outcomes for patients with acute coronary syndrome (ACS). However, elderly ACS patients are less likely to receive evidence-based treatment, including revascularization therapy, due to uncertainty of the associated benefits and risks in this population. It also covers a wide range of parameters.

Ticagrelor achieved more rapid and greater platelet inhibition than high-loading-dose clopidogrel in patients with stable CAD. In patients with an acute coronary syndrome who were referred for an invasive strategy, there was no significant difference between a 7-day, double-dose clopidogrel regimen and the standard-dose regimen, or between higher-dose aspirin and lower-dose aspirin, with respect to the primary

outcome of cardiovascular death, myocardial infarction, or stroke.

In ACS patients who have an acute coronary syndrome with or without ST-segment elevation, treatment with ticagrelor as compared with clopidogrel significantly reduced the rate of death from vascular causes, myocardial infarction, or stroke without an increase in the rate of overall major bleeding but with an increase in the rate of non–procedure-related bleeding.

In patients with acute coronary syndromes, cardiac troponin I levels provide useful prognostic information and permit the early identification of patients with an increased risk of death.

Ticagrelor, when compared with clopidogrel, reduced ischaemic events in ACS patients irrespective of diabetic status and glycaemic control, without an increase in major bleeding events.