ISCHEMIC HEART DISEASE IN THE ABSENCE OF OVERT CORONARY ARTERY DISEASE ALLAN S. JAFFE pdf

1: Universal definition of myocardial infarction | European Heart Journal | Oxford Academic

Ischemic Heart Disease in the Absence of Overt Coronary Artery Disease. / Jaffe, Allan S. Markers in Cardiology: A Case-Oriented Approach. Blackwell Publishing Ltd, p.

Advanced Search Abstract Background WHO has played a leading role in the formulation and promulgation of standard criteria for the diagnosis of coronary heart disease and myocardial infarction since early s. Methods The revised definition takes into consideration the following: Category B definition of MI is to be applied whenever there is incomplete information on cardiac bio-markers together with symptoms of ischaemia and the development of unequivocal pathological Q waves. In these situations, the term probable MI should be used when there is either ECG changes suggestive of MI or incomplete information on cardiac biomarkers in a person with symptoms of ischaemia with no evidence of a non-coronary reason. In epidemiological studies, the incidence of MI in a population can be used as a proxy for estimating the coronary heart disease burden. The burden of cardiovascular disease is rising both in high-income countries and low- and middle-income countries LMICs because of ageing populations, but the burden is greater in LMICs because of much larger population sizes and widespread exposure to increasing levels of risk factors such as unhealthy diet, physical inactivity, obesity, tobacco use, diabetes, raised blood pressure and abnormal blood lipids. Often in LMICs there is a lack of information on the role of risk factors. It has been shown that risk factors for cardiovascular disease are largely similar in high-income countries as in LMICs. Case definitions for different presentations of coronary heart disease are required. They need to be scientifically valid, consistent when applied across countries, generally applicable and robust. The new definition of MI by the World Health Organization WHO should facilitate epidemiological monitoring, coding of the clinical diagnosis, validity of death certificates and disease classification. Such a standardized case definition of MI is of special importance since it is a means to obtain reliable and comparable data for evaluation of the effectiveness of prevention and curative strategies in countries with widely varying health systems. The definition has implications for epidemiology, disease monitoring, content of registries, clinical research studies, clinical trials, quality assurance, economic analysis, medico-legal disputes and estimation of health-care costs. At the individual level, the diagnosis of MI has a major impact on physical and psychological health and often on family, legal and insurance matters. Definition of MI MI is defined by the demonstration of myocardial cell necrosis due to significant and sustained ischaemia. It is usually, but not always, an acute manifestation of atherosclerosis-related coronary heart disease. MI results from either coronary heart disease, which implies obstruction to blood flow due to plaques in the coronary arteries or, much less frequently, to other obstructing mechanisms e. Plaques are always a consequence of atherosclerosis. Coronary heart disease may relate to stable or unstable underlying plaques. Unstable plaques are characterized by activated inflammation of the vascular wall at the site of plaques. There may be erosion, fissuring or even rupture of the plaques. Platelets can accumulate at the site of an active plaque, further obstructing blood flow and leading to unstable angina. Rupture of atherosclerotic plaques usually leads to acute coronary syndromes or overt MI. Atherosclerotic plaques may expand slowly but more often enlarge in steps. After platelets accumulate on the surface, the healing process adds a further layer to the plaque, which eventually can become fibrous, lipid laden and calcified. The clinical presentation of MI varies from a minor coronary event to life-threatening clinical situations or sudden death. Those who survive the initial event are vulnerable to repeat attacks of MI. As alluded to above, information on the distribution of MI in a population, if standardized, provides useful information regarding the burden of coronary artery disease in a population. If standardized data can be collected on sudden coronary death and incident and repeat episodes of MI, then the totality of this burden can be determined. WHO has played a leading role in the formulation and promulgation of standard criteria for the diagnosis of coronary heart disease and MI. MI was diagnosed in the presence of one of the following: Most importantly, all possible situations with incomplete information on the ECG, enzymes or

symptoms were covered. These advances called for a re-evaluation of the case definition of MI. New cardiac biomarker assays are more costly than older assays and are not accessible to large segments of the population in LMICs where the incidence of coronary heart disease is rising. Furthermore, events in patients reaching hospital, although suspect, may not have complete clinical information, including measurement of the new biomarkers. A major problem with the revised definition 14 is that although it is quite appropriate for high-resource settings, it falls short of the clinical and epidemiologic needs in low-resource settings. New or revised definitions need to embrace recent advances in medical science; however, there must be provision in any new definition for persons in LMICs and even resource-constrained settings in developed countries to be able to diagnose MI and monitor rates of MI. Such data are necessary in order to make epidemiological comparisons within and between populations in a standardized manner. Comparisons are important for two reasons. First, the largest increase in the cardiovascular disease burden over the next 10 years will occur in LMICs, where there are resource constraints. Second, there is a social gradient in relation to coronary heart disease in developed countries, with higher prevalence rates and fatality rates in people in lower social classes, who often have suboptimal access to healthcare. However, assays for the new biomarkers may be available, even in low-income countries, within the private medical sector at a price that is unaffordable for majority of people. The new definition accepts one measurement of troponin only if the value exceeds the decision level for MI. If this is not the case, demonstration of a rise and fall of such levels will require at least two measurements, which may be unaffordable to health systems and people in many low-resource settings. For these reasons, it was felt necessary to allow some flexibility in the definition of MI in order to broaden its applicability to settings with high resources as well as to settings with resource constraints. The process consisted in a consultation of experts held at WHO in Geneva, on 16â€”17 April followed in for an extensive peer review. The definition may change again in the future as science advances and blood tests of whatever nature become inexpensive and more widely available in countries with limited resources. Any one of the following criteria meets the diagnosis for MI. Category B definition and diagnostic criteria of MI if the requirements for diagnostic tests in Category A above have not been met. I 21 Whenever there is incomplete information on cardiac biomarkers preferably troponin and other diagnostic criteria needed to apply Category A, the term MI should be used if: Category C definition and diagnostic criteria of probable MI. When features of MI occur in the first 28 days after an incident event, the event is not counted as a new event for epidemiological purposes. If features of MI occur after 28 days of an incident event, it is considered to be a new infarct a recurrent event. I 21 The term reinfarction is used for an MI that occurs within 28 days of an incident or a recurrent MI. Fatal coronary heart disease is death with none of the above and no other cause of death with any one of the following: I 21 For percutaneous coronary interventions or coronary artery bypass grafting in patients with normal baseline troponin values, elevations of cardiac biomarkers above the 99th percentile of upper reference limit are indicative of peri-procedural myocardial necrosis. By convention, for percutaneous coronary interventions-related MI, cardiac biomarker values three times greater than the 99th-percentile upper reference limit are considered diagnostic. It is essential that the increases occur from a normal baseline. If values are rising, distinguishing between the rise due to the acute event whether appreciated or not or due to the procedure itself is difficult. By convention, for coronary artery bypass graftingâ€”related MI, cardiac biomarkers values five times greater than the 99th-percentile upper reference limit plus either new pathological Q waves or new LBBB or angiographically documented new graft or native coronary artery occlusion or imaging evidence of new loss of viable myocardium are considered diagnostic. MI associated with stent thrombosis as documented by angiography or autopsy. Unstable angina Unstable angina is diagnosed when there are new or worsening symptoms of ischaemia or changing symptom pattern and ischaemic ECG changes Minnesota codes 4. The distinction between new angina, worsening angina and unstable angina is notoriously difficult and based on a clinical assessment and a careful and full clinical history. Implications So that there is uniformity in the reporting of data, MIs should be reported as outlined above. In that way, the outcomes of clinical trials and the findings in registries across the globe can be applied

and compared more appropriately.

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2: Allan S Jaffe, MD â€“ Research Output â€” Mayo Clinic

Association of specific overt behavior pattern with blood and cardiovascular findings; blood cholesterol level, blood clotting time, incidence of arcus senilis, and clinical coronary artery disease. J Am Med Assoc. Mar 21; (12)

Evaluation of patients who present to the hospital with a complaint of chest pain or other signs or symptoms suggestive of acute coronary syndrome ACS is time-consuming, expensive, and problematic. Recent investigations have indicated that increases in biomarkers upstream from biomarkers of necrosis cardiac troponins I and T , such as inflammatory cytokines, cellular adhesion molecules, acute-phase reactants, plaque destabilization and rupture biomarkers, biomarkers of ischemia, and biomarkers of myocardial stretch may provide earlier assessment of overall patient risk and aid in identifying patients with higher risk of an adverse event. The purpose of this review is to provide an overview of the pathophysiology and clinical and analytical characteristics of several biomarkers that may have potential clinical utility to identify ACS patients. These biomarkers myeloperoxidase, metalloproteinase-9, soluble CD40 ligand, pregnancy-associated plasma protein A, choline, ischemia-modified albumin, unbound free fatty acids, glycogen phosphorylase isoenzyme BB, and placental growth factor have demonstrated promise and need to be more thoroughly evaluated for commercial development for implementation into routine clinical and laboratory practice. Specifications that have been addressed for cardiac troponins and natriuretic peptides will need to be addressed with the same scrutiny for the biomarkers discussed in this review. They include validating analytical imprecision and detection limits, calibrator characterization, assay specificity and standardization, preanalytical issues, and appropriate reference interval studies. Crossing boundaries from research to clinical application will require replication in multiple settings and experimental evidence supporting a pathophysiologic role and, ideally, interventional trials demonstrating that monitoring single or multiple biomarkers improves outcomes. Clinical Importance Millions of patients with chest pain present annually to hospitals, and many more present with other symptoms potentially indicative of ischemia 1 2 3 4. A considerable proportion have suspected acute coronary syndromes ACS. Accordingly, there are still unnecessary admissions to expensive coronary care units, step-down units, and non-intensive care beds when discharge might be equally appropriate. A low threshold for consideration of a myocardial etiology of chest pain or related symptoms is necessary, because the presentation of an ACS is often atypical and because a missed diagnosis of ACS carries considerable risk to patients. If we had markers that would further define risk, it would not only reduce the number of patients kept in the emergency department ED , in a chest pain center, or admitted to the hospital, but would also allow for prevention of substantial numbers of new events. Recent investigations have indicated that increases in biomarkers upstream from markers of necrosis, such as inflammatory cytokines, cellular adhesion molecules, acute-phase reactants, plaque destabilization and rupture biomarkers, biomarkers of ischemia, and biomarkers of myocardial stretch may provide an earlier assessment of overall patient risk and aid in identifying patients with higher risk of having an adverse event. This review was developed to address a need that the committee perceived to clarify the state of the art in this important area. Its purpose is to provide an overview of the pathophysiology and clinical and analytical characteristics of several biomarkers Fig. These biomarkers have demonstrated promise and need to be more thoroughly evaluated before implementation into routine clinical and laboratory practice. However, it should be appreciated that initial studies, as impressive as they may appear, are preliminary at best. We point out the following issues to keep in mind when evaluating these preliminary studies reviewed here: Often the analytical characteristics of the assays are not adequately described. We need to know the stability of the samples over time; this is key to the analysis of so many sample sets, which are often many years old. We need established reference intervals in general and in key subsets of patients. A recent editorial has called attention to the critical nature of this issue 8. Populations studied are often convenience populations for initial studies. As such, they may overrepresent those with disease and thus make evaluation of true sensitivity and specificity problematic. In addition, if the samples are older, they may provide data that are not

relevant given contemporary changes in the treatment of patients. There is a publishing bias in favor of positive rather than negative reports. A negative evaluation is unlikely to be the first one published, and once a highly positive report is published, negative reports often have difficulty finding their way into print because they are invariably compared with the original positive report. Open in new tab Figure 1. Biochemical profile in ACS patients: Evaluations have to start somewhere, but often these critical caveats are not reflected on when the results are discussed by authors who are invested in the development of the new analyte. Myeloperoxidase Myeloperoxidase is a hemoprotein molecular mass of kDa consisting of a pair of heavy and light chains. It is stored in azurophilic granules of polymorphonuclear neutrophils and macrophages and functions to catalyze the conversion of chloride and hydrogen peroxide to hypochlorite. Myeloperoxidase is released into the extracellular fluid and general circulation during inflammatory conditions. This enzyme has been implicated in the oxidation of lipids contained within LDL 9. Myeloperoxidase activity can be measured in blood and tissues by assays using hydrogen peroxide and o-dianisidine dihydrochloride as substrates Recently, mass assays based on an enzyme-linked immunoassay have been developed for research use only Oxis Research and Assay Design. In addition, myeloperoxidase content can be measured in neutrophils as an index of degranulation with the Coulter counter and flow cytometry. Oxidative stress and inflammation play important roles in the pathogenesis of the destabilization of coronary artery disease CAD leading to ACS. Infiltrating macrophages and neutrophils participate in the transformation of stable coronary artery plaques to unstable lesions with a thin fibrous cap. These cells are found more frequently and in higher concentrations in the culprit lesions of patients with acute MI and unstable angina UA than in patients with stable coronary disease Macrophages secrete matrix metalloproteinases MMPs and metal-independent myeloperoxidase, which degrade the collagen layer that protects atheromas from erosion or abrupt rupture As a result, plaques that have been highly infiltrated with macrophages have a thin fibrous cap and are vulnerable to erosion or rupture, precipitating events to ACS. This is particularly true in the shoulder regions of coronary artery lesions, where the shear stresses of arterial blood are highest. Neutrophilic infiltration has also been implicated as the cause of myocardial reperfusion injury after successful recanalization of previously occluded coronary arteries Therapeutic trials of drugs designed to minimize reperfusion injury rely in part on demonstrating a reduction in neutrophil infiltration, as documented by tissue myeloperoxidase concentrations There have been a few clinical studies examining the role of myeloperoxidase as a marker of risk for ACS. Using an enzyme assay, Zhang et al. There was no tabulation of the subsequent rate of adverse events in that report. A key study by Buffon et al. The myeloperoxidase content of the leukocytes collected from the arterial circulation and the coronary sinus effluent were compared. Myeloperoxidase content was determined on the Coulter counter, which measures the neutrophil count by flow cytometry and subsequently calculates the mean myeloperoxidase content in that population. Not only was there a gradient for myeloperoxidase across the coronary sinus in patients with ACS, but that gradient was present even when the culprit lesion involved with the ACS was in the distribution of the right coronary artery, a situation in which the venous effluent from the right coronary artery does not drain into the coronary sinus. Increases in myeloperoxidase correlated with values of high-sensitivity C-reactive protein CRP. This finding in the 33 patients with ACS but not those with variant or stable angina strongly suggests that neutrophil adhesion and inflammation are not unique to the presumed culprit coronary lesion identified by angiography, but more likely identify a systemic predilection. Such data are in keeping with the recent concept that, in addition to vulnerable plaques, the vascular milieu, i. The potential usefulness for risk stratification of blood concentrations of myeloperoxidase was examined in 2 recent studies. The death and MI rates were determined at 6 months of follow-up. However, only the admission cTnT was used to define this group. In a study of sequential patients presenting to the ED with chest pain, Brennan et al. Differences in the designs of the two studies may account for this. The study by Brennan et al. All 4 studies described above used different assays and reporting units that cannot be converted to each other. A standardization effort will be needed if this marker is to be used beyond research purposes. In summary, although myeloperoxidase participates in the inflammatory process of ACS, neutrophil activation is

apparently not induced by ischemia Thus, myeloperoxidase is more of a marker of plaque instability and unlike a marker of oxidative stress and damage. Increased myeloperoxidase is not likely to be specific to cardiac diseases, as activation of neutrophils and macrophages can occur in any infectious, inflammatory, or infiltrative disease process. MMP-9 MMPs are a class of 24 endopeptidases that are physiologic regulators of the extracellular matrix They are found in most tissues. These compounds are regulated by transcription, by certain precursors, and by interaction with ground substance and have specific endogenous inhibitors known as tissue inhibitors of metalloproteinases TIMPs. In the heart, these substances participate in vascular remodeling, plaque instability, and ventricular remodeling after cardiac injury. MMP-9 is zinc-dependent and is known as gelatinase B. Gelatinases have 3 repeats of the fibronectin-binding domain that allow them to bind to gelatin, collagen, and laminin. Activation of proMMP-9 to the active moiety can occur as a result of exposure to NO or via proteolytic activation. TIMPs also can have a variety of independent biological effects on inflammation and angiogenesis, which may have important consequences for cardiac structure and function That area, which is thinner, is thought to be the area prone to rupture. Experimentally, monocytes are a rich source of MMPs and can be stimulated by specific T-cell populations via CD40 ligand signaling In heart tissue, MMP-9 is partially responsible for the degradation of ground substance after cardiac injury. Transgenic animals susceptible to ventricular rupture are protected by deletion of MMP-9 In other models, that inhibition of MMPs, including MMP-9, inhibits ventricular remodeling after acute MI, and there is therapeutic interest in testing such a strategy clinically. It is clear that some degree of MMP production is likely essential as part of the reparative process after acute cardiac injury For all of these reasons, there has been interest in developing an assay for measurement of MMP-9 in peripheral blood in patients with ACS. The first report was published in by Kai et al. They collected blood and prepared both serum and EDTA-plasma samples for analysis by a sandwich enzyme immunoassay marketed by Fuji Chemical Industries Ltd. Thirty-three ACS patients were studied. The criterion for MI was based on total CK activity. MMP-9 concentrations then gradually decreased in those patients. In the patients with acute MI, those with high concentrations had decreasing concentrations between day 1 and day 7. Those without increased concentrations initially developed increased concentrations that peaked at day 3 and then began to return to baseline. Treadmill-induced ischemia did not lead to further increases. The authors hypothesized that the MMP-9 measured was from the myocardium and not the vessel wall. Although aortic concentrations initially were similar to those in patients with stable angina and healthy people, there was a substantial gradient across the heart with secretion of both MMP-9 and TIMP They found a distribution of reference values similar to that reported by the Japanese group with a mean SD value of Those with single- or double-vessel disease had a mean value of There were no differences between those with and those without previous MI. The authors hypothesized that the increased concentrations were related to inflammation in the plaques, which in aggregate might be related to the extent of the CAD. They used the Fuji assay originally reported by the Japanese to stratify the patients into quartiles. Those in the highest quartile had a significantly increased risk of cardiac death whether in the stable or unstable group. These data again suggest the potential importance of MMP-9 in predicting eventual coronary events. For this reason, there have been several studies evaluating the effects of therapies on MMP

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3: - NLM Catalog Result

Tracy Y. Wang, John M. Castor, L. Kristin Newby. 4 Ischemic heart disease in the absence of overt coronary. artery disease. Allan S. Jaffe (Mayo Clinic). 5 So you think you have a "false positive" troponin?.

The development and implementation of sensitive and high-sensitivity cardiac troponin assays has not only expedited the early ruling in and ruling out of acute myocardial infarction, but has also contributed to the identification of patients at risk for myocardial injury with necrosis, as confirmed by the presence of cardiac troponin concentrations above the 99th percentile. Myocardial injury with necrosis may occur either in the presence of overt ischemia from myocardial infarction, or in the absence of overt ischemia from myocardial injury accompanying other conditions. Much debate has surrounded T2MI and its interrelationship with myocardial injury. We provide a detailed overview of the current concepts and challenges regarding the definition, diagnosis, management, and outcomes of T2MI, as well as the interrelationship to myocardial injury, and emphasize several critical clinical concepts for both clinicians and researchers moving forward. T2MI and myocardial injury are frequently encountered in clinical practice and are associated with poor outcomes in both the short term and long term. Diagnostic strategies to facilitate the clinical distinction between ischemic myocardial injury with or without an acute atheroma-thrombotic event vs nonâ€”ischemic-mediated myocardial injury conditions are urgently needed, as well as evidence-based therapies tailored toward improving outcomes for patients with T2MI. In the late 19th century, postmortem examinations demonstrated a possible relationship between thrombotic occlusion of a coronary artery and myocardial infarction MI 1. However, it was not until the beginning of the 20th century that the first clinical descriptions appeared expressing a connection between the formation of a thrombus in a coronary artery and its associated clinical features 2 â€” 3. Nonetheless, acute MI ends up as the preferred designation, rather than coronary thrombosis, but even so, there was still a need for a unified definition of MI. That occurred during â€”, when working groups of the WHO established a primarily electrocardiographic ECG -based definition of MI intended for epidemiological use 5. Open in new tab Fig. Changing criteria for the definition of myocardial infarction. In recent years, this approach was not felt to be sufficient for a definitive clinical diagnosis. Biomarkers were identified as the way forward to support clinical examination and ECG test results. In this document we review the current concepts and challenges regarding the definition, diagnosis, management, and outcomes of T2MI, as well as the interrelationship to myocardial injury, and emphasize several critical clinical concepts for both clinicians and researchers moving forward. Frequency of T2MI in selected studies. Selected studies have shown variable frequencies of T2MI ranging from 1. Specific vs Broad Criteria for T2MI Surveys have differed in whether the diagnosis of T2MI is established by using specific predetermined oxygen mismatch criteria or whether applying a more wide-ranging approach to support this term 12 â€” Specific criteria were employed in a prospective study of unselected patients who had cardiac troponin I cTnI measured on clinical indication, in which consecutive patients were enrolled through 1 year with the purpose of elucidating the incidence and features of T2MI using standards developed partly on the basis of data from literature The main advantage of using strict, specific criteria is the reduction in the ambiguity and subjectivity in diagnosing T2MI, which may facilitate the replication of findings by other researchers. Others have categorized such cases as myocardial injury, even despite the presence of concomitant myocardial ischemia 18 , Improved guidance in the future Universal Definition of MI documents is urgently needed in this regard owing to the discrepant perspectives and prevailing uncertainty on whether patients with coexisting conditions e. According to the presence or absence of concomitant significant coronary artery disease CAD , Spatz et al. However in contrast, Matsue et al. Although the variability in reported rates of ST elevation may reflect various underlying causes of T2MI, lingering suspicion for unstable CAD should lead to coronary angiography CAG or other ischemia tests to establish an appropriate treatment. However, the Universal MI Task Force has refrained from recommending CAG realizing that the access to this procedure is limited in

various regions of the world. Prevalence of coronary artery disease among patients with T2MI undergoing coronary angiography A and proportion of patients with T2MI undergoing coronary angiography B. It should be noted that these studies are observational and retrospective in nature, and therefore unable to control for selection bias. Furthermore, even if CAG is available, patients with angiographically normal coronary arteries particularly women may have underlying plaque rupture and ulceration as detected by other methods, such as intravascular ultrasound, resulting in misclassification Interrelationship between T2MI and Myocardial Injury Myocardial injury is a prerequisite for the diagnosis of MI in the setting of acute myocardial ischemia. However, myocardial injury is also an entity in itself. For patients with increased cardiac troponin concentrations above the 99th percentile upper reference limit URL , clinicians must distinguish whether patients have myocardial injury or MI Fig. Myocardial injury, whether ischemic or nonischemic, defined as any cardiac troponin concentration above the 99th percentile URL 9 is frequently encountered and associated with a poor prognosis 20 , 28 â€” Chronic myocardial injury is often met in patients with comorbidities, such as advanced chronic kidney disease and heart failure Conceptual models for myocardial injury and myocardial infarction. Few studies have compared the incidence and clinical features of T2MI vs myocardial injury. By using a high-sensitivity hs -cTnI assay, in a cohort study examining all-comer consecutive patients presenting to the emergency department, Similarly, Sarkisian et al. However, in a study by Shah et al. The key distinction between myocardial injury and T2MI is made on a clinical basis, with MI being diagnosed when there is clinical evidence of overt myocardial ischemia, as supported by the presence of at least one of the following: Prognosis Several studies have reported both short- and long-term outcomes for patients with T2MI 12 , 13 , 20 , 22 , 28 , 29 , A similar poor long-term survival has been observed in patients with myocardial injury 20 , 28 â€” Studies have focused on all-cause mortality, rather than cardiac mortality; however; future studies are needed to clarify whether T2MI patients die from cardiac or noncardiac causes. Management of T2MI While the term T2MI has been endorsed since , no clinical practice guidelines address how to manage this entity. This approach was associated with an increase in healthcare resource utilization and improved prognosis for T1MI patients. Conversely, for patients with T2MI, lowering the cTnI diagnostic threshold led to an increase in cardiology referrals, echocardiograms, and angiography, without leading to changes in the treatment and with no impact on the prognosis. However, these patients did not receive additional therapies, potentially representing a missed opportunity to improve outcomes Despite the dearth of scientific information that can help to make management decisions it appears expedient in the acute setting to treat the underlying ischemic imbalance of oxygen supply and demand. This treatment may include: However, if CAD is absent, the benefit of cardiovascular risk reduction strategies with T2MI remains uncertain 10 , 11 , Cardiac Troponin The preferred biomarker for myocardial injury and MI is cardiac troponin, which has both high myocardial tissue specificity and clinical sensitivity, although not decisive for a disease 9. Hence, clinicians and researchers are challenged with distinguishing whether cardiac troponin increases are due to myocardial injury in the absence of other supportive ischemic features or an acute MI. From a biomarker perspective, patients with T1MI have an overall trend towards higher maximum cardiac troponin concentrations than those with T2MI 12 , 15 , 18 â€” 20 , The development of a plaque-rupture specific biomarker to aid in the distinction of myocardial injury due to plaque rupture T1MI vs myocardial injury from other pathologies would represent a unique clinical breakthrough Advanced cardiac imaging, such as cardiac magnetic resonance, may be particularly useful in distinguishing whether myocardial injury occurs due to an acute MI vs due to other nonischemic conditions such as myocarditis. For investigators and clinicians doing cardiac troponin diagnostic performance studies, a conundrum often faced is whether analyses should be based on patients with any MI including both types 1 and 2 or T1MI alone. Recent studies demonstrate heterogeneous designs in this regard, with some studies basing their analysis on all MIs including both T1MI and T2MI , others focusing exclusively on T1MI, and others not clearly describing the adjudication of MI types despite reporting adherence to the Universal Definition of MI recommendations 34 â€” The choice to focus studies on T1MI alone is supported by the following arguments: Moving forward, a practical approach

may be to focus on ruling out myocardial injury, which encompasses both T1MI and T2MI, while continuing to rule in MI and its subtypes. Clinicians and researchers should describe whether there is presence or absence of concomitant significant CAD. Future studies are needed, ideally in all-comers with T2MI rather than only those selected to undergo CAG that are subject to selection bias , to determine the frequency and implications of concomitant CAD in patients with T2MI. In equivocal, difficult cases with acute myocardial injury, in which the clinical distinction between myocardial injury, T1MI, and T2MI is challenging, further diagnostic efforts may be considered in an appropriate clinical context to discern the underlying mechanism, primarily due to the potential therapeutic implications if deemed related to atherosclerotic plaque rupture. Myocardial injury, ischemic or nonischemic, defined as any cardiac troponin concentration above the 99th percentile URL is frequently encountered and associated with a poor prognosis. In cases of myocardial necrosis occurring primarily as a consequence of sepsis, renal failure, heart failure, cardioversion, electrophysiological ablation, myocarditis, toxic agents, or infiltrative diseases, the term myocardial injury condition applies rather than MI. Studies addressing outcomes, including cardiac morbidity and mortality as well as management strategies, including therapeutic investigations, are urgently needed to better define the risk and management of both T2MI and myocardial injury. Conclusions The increasing analytical sensitivity of cardiac troponin assays, as well as their wide-ranging use in various clinical circumstances has contributed to the increased detection of T2MI and myocardial injury. These clinical entities are frequently encountered in clinical practice and associated with poor outcomes in both the short term and long term. Further guidance is required in regards to how clinicians and researchers define these conditions. Diagnostic strategies to facilitate the clinical distinction between ischemic myocardial injury with or without an acute atheroma-thrombotic event vs nonâ€”ischemic-mediated injury are urgently needed, as well as evidence-based therapies tailored towards improving outcomes for patients with T2MI.

4: Myocardial Infarction Type 2 and Myocardial Injury | Clinical Chemistry

Markers in Cardiology: A Case-Oriented Approach Ischemic Heart Disease in the Absence of Overt Coronary Artery Disease (pages) Allan S. Jaffe. Summary.

5: Markers in Cardiology : Allan S. Jaffe :

An epidemic of coronary heart disease (CHD) began during the 20th century in most industrialized countries, where CHD is a leading cause of mortality among adults.1 Developing countries show the beginnings of the same epidemic.

6: Ischemic Heart Disease in the Absence of Overt Coronary Artery Disease â€” Mayo Clinic

Ischemic heart disease, hypertensive heart disease, cerebrovascular disease, and atherosclerosis in the arteries of the lower limbs constitute major public health problems. Coronary and cerebral atherosclerotic vascular diseases are the major causes of morbidity and mortality in the industrialized world.

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