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www.reachmd.com
info@reachmd.com
(866) 423-7849

Updating Guidelines for ST-Elevation MI

LATEST GUIDELINES FOR MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION

You are listening to ReachMD, The Channel for Medical Professionals. Welcome to heart matters, where leading cariology experts explore the latest trends, technologies, and clinical development in cardiology practice.

Your host for heart matters is Dr. Janet Wright, Vice President for Science and Quality for the American College of Cardiology.

About half a million people suffer ST-segment elevation myocardial infarction each year in US. Guidelines for acute MIs are going to be discussed today with Dr. Elliott Antman. Dr. Antman is a Professor of Medicine at the Harvard Medical School and Director of the Samuel A. Levine Cardiac Unit at Brigham and Women's Hospital in Boston.

DR. JANET WRIGHT:

Welcome Dr. Antman.

DR. ELLIOTT ANTMAN:

Thank you very much.

DR. JANET WRIGHT:

May be you can tell us why this update was felt to be necessary at this time?

DR. ELLIOTT ANTMAN:

It is a very good question. We know that the evidence base that forms of foundation for these guidelines is rapidly changing. There are many, many clinical trials were actually quite fortunate in cardiovascular medicine that we have a number of clinical trials that can actually answer important questions that we have as clinicians caring for patients with cardiovascular disease. The test for some factors

guidelines decided that we needed to be much more nimble and have almost a turbocharged effort to change the recommendations if the evidence suggested that there was a need for change. So, the process now of the focused update technology is to have the writing committee review new evidence based upon reports that have come out, each of them 3 major meetings that occur during the year at the American College of Cardiology scientific sessions, the American Heart Association scientific sessions and the European Society of Cardiology scientific sessions. We also keep our eye on scientific statements or consents as documents that may have come out during the course of the year and as for a full guideline, the evidence must be published, you know pre-reviewed publication in order for it to be considered for possible updating of a recommendation, so we did that with respect to ST-elevation myocardial infarction and felt that there were a number of issues that had come up based upon several trials and therefore put together the focused update that we will be discussing today.

DR. JANET WRIGHT:

This process reminds me painting the golden gate bridge that it is really a continuous process, so you all are reviewing the evidence and then identifying when you have sufficient new data to share with practitioners.

DR. ELLIOTT ANTMAN:

Absolutely.

DR. JANET WRIGHT:

Or may be you can tell us a couple of the pieces of learning that have contributed to this new focused update.

DR. ELLIOTT ANTMAN:

Well, yes. Let me put this in perspective, I did mention that there were many trials that were being conducted now and cardiovascular disease and some of them are conducted in patients who are in North America and that is helpful to us because the guidelines that were discussed in today are written to a North American audience, but many of the trials that provide new information enroll patients from outside of North America and we had to discuss as a writing committee, how we would way evidence from studies outside of North America. We decided that we would include those studies for several reasons. The trials that we were looking at did employ a broad ray of management strategies for ST-elevation myocardial infarction. There were patients who had received reperfusion with a fibrinolytic. There were patients who had received reperfusion with percutaneous coronary intervention and about 30% of patients around the worlds still do not get reperfusion for ST-elevation MI. We also felt that these trials represented contemporary therapy the way we would practice it in the United States, for example, because of the concomitant treatments that have shown to have efficacy in reducing mortality such as the use of ACE inhibitors, statins, aspirin, these medications were used in a goodly proportion of patients in the trials that we were looking at and frankly we also felt that it was just impractical to expect that the tens of thousands of patients who would need to be enrolled to provide the adequate sample size to really test the questions could all come from North America. It is just not practical and we would not move the field forward if we insisted that all these important clinical questions were strictly tested in North America. So, with that background, we decided that we would move ahead and look at trials that were conducted outside of North America as well.

DR. JANET WRIGHT:

It reflects that this is a global disease and we will benefit from science that is being developed around the world.

DR. ELLIOTT ANTMAN:

Absolutely.

DR. JANET WRIGHT:

If you are just joining us, you are listening to Heart Matters on ReachMD, The Channel for Medical Professionals. I am your host, Dr. Janet Wright. Today our guest is Dr. Elliott Antman, Professor of Medicine at Harvard Medical School and Director of the Samuel A. Levine Cardiac Unit at Brigham and Women's Hospital in Boston. We were reviewing the latest guidelines for management of acute myocardial infarction.

What does the update have to say about beta-blockers, let's start there.

DR. ELLIOTT ANTMAN:

One of our most challenging recommendations that we have to update, when we put the STEMI guideline together in 2004, we made a recommendation that intravenous beta-blockers should be administered to patients with ST-elevation MI who had tachycardia or hypertension because of the protective effects of beta blockade both from animal models and from many, many clinical trials and we recognize that those clinical trials that form that evidence base were from in many cases 10 or even 20 years ago, we might call that the pre-reperfusion era. We knew that in 2004, we also knew that those trials generally did not enroll patients who had heart failure or impending cardiogenic shock. So in 2004, we made the recommendation that the acute administration of intravenous beta-blockers should not be undertaken in patients who have heart failure or shock, at the very least one needed to think extremely carefully about those patients. We then had a very interesting trial called the commit trial which had 45,852 patients enrolled. They were from China and the commit trial was a factorial design and will come back in a little while to the second aspect of what they were studying which had to do with clopidogrel, but this part of the trial had to do with intravenous metoprolol, followed by oral metoprolol. And the investigators in commit did a very interesting thing, they kind of pushed the envelope a little bit because 25% of the individuals in the commit trial had Killip Class II or III hemodynamic status at the time of presentation with STEMI. They did not have Killip Class IV because that is cardiogenic shock and they were not enrolled, but they did have Killip Class II and III. Now, interestingly, they found that the use of metoprolol compared with placebo had no impact on mortality and we were surprised to see that, but looking into it little bit further, it was quite clear that there was an increase in the early development of cardiogenic shock in patients who did receive metoprolol, particularly if they had risk factors for cardiogenic shock and that offset the protective effects of metoprolol in patients who didn't have those risk factors for shock that includes heart failure presentation, age greater than 70, a systolic blood pressure less than 120, sinus tachycardia greater than 110, heart rate less than 60, or increasing time since the onset of symptoms of STEMI. So, individuals who had more of those risk factors, the more you had of those risk factors, the more you were at risk for shock. So, if you actually have that profile and you have got an intravenous beta-blocker like metoprolol, unfortunately what happened is that there was an increased risk of shock and that upset the benefit. So, the commit investigators then did a very interesting thing. They looked at all the preceding evidence and they merged it with the data from the commit trial, but only looking at the low risk patients, those who did not have those risk factors for shock that I just went through and when you look at all that information, now you are up to about 52,000 patients, there indeed is a statistically significant reduction in death, recurrent infarction, and ventricular fibrillation. So, we ended up concluding this trial actually endorsed what we had said in 2004 and we strengthened our wording, so that it was quite clear that oral beta-blocker therapy should be initiated in the first 24 hours if you do not have any of these signs of heart failure or impending shock. We felt that it was reasonable to administer an intravenous beta-blocker in patients who are hypertensive and don't have any other risk factors that I outlined and that became a class IIa level of evidence B recommendation which is about where we were in 2004 as well. So, the real benefit of the commit trial was to reinforce and focus down on who would be an acceptable candidate for an intravenous beta-blocker. It is quite important because, for example, an emergency department of the front line physicians seeing patients with STEMI, we wanted to send a very clear message that any evidence of heart failure or impending shock or the stop sign which would mean that you should

not give an intravenous beta-blocker in the early phase of STEMI.

DR. JANET WRIGHT:

Now that you were reviewing the refinements in treatment or advice about treatment with intravenous and oral beta-blockade therapy, talk to us about facilitated and rescue PCI, perhaps you could start by defining those words.

DR. ELLIOTT ANTMAN:

Yes. Facilitated PCI refers to a management strategy where some preparatory pharmacologic regimen is given to a patient with STEMI with the intent of when taking that patient quickly to have PCI as soon as you can get that patient to a center where PCI can be performed. Now that preparatory pharmacologic regimen can vary. It can be full dose fibrinolytic alone, followed by immediate PCI. It could be an intravenous glycoprotein 2b/3a inhibitor alone, followed by immediate PCI or it could be a combination where one gives a reduced dose of a fibrinolytic, let's say half dose of fibrinolytic in combination with an intravenous glycoprotein 2b/3a inhibitor and then take the patient promptly for PCI. We looked at a metaanalysis that was published in Lancet in 2006 and that compiled the information from 4500 patients from a series of trials that had looked at this and I have to comment here Janet that compared to the kind of evidence that we have for other things that define our recommendations and ultimately our performance measures and quality indicators, this is a very small sample size. It pales in comparison to what we know about aspirin, ACE inhibitors, statins for example. Nevertheless, we found some very consistent information in this meta-analysis that there was no evidence that there was a reduction in mortality when one performed reperfusion using this facilitated PCI approach versus primary PCI. We just simply take the patient to the cath lab having given aspirin and typically an anticoagulant. There is no evidence for reduction in mortality, no evidence of reduction in reinfarction compared to primary PCI and there was distinct increase in the risk of major bleeding, so despite the scientific promise that facilitated PCI seems to hold, it just did not workout at the present, so we actually made a class III recommendation that a planned reperfusion strategy using full dose fibrinolytic therapy, followed by immediate PCI is not recommended and may be harmful.

DR. JANET WRIGHT:

We have been taking with Dr. Elliott Antman about the latest guidelines for acute myocardial infarction. Dr. Antman, thank you so much for being our guest today.

DR. ELLIOTT ANTMAN:

My pleasure.

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