

STEMI Interventions: Managing the Chaos

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Slide 1

Sameer Mehta, MD: Hello, I am Sameer Mehta, Co-Director of Lumen. It's my pleasure to welcome you to our program entitled: "STEMI Interventions: Managing the Chaos."

STEMI Intervention: Managing the Chaos

This program will discuss the appropriate treatment decisions for prehospital care, hospital-to-hospital transfer of patients with ACS, and methods to minimize adverse events for these individuals.



Slide 2

This program will discuss the appropriate treatment decisions for prehospital care, and hospital-to-hospital transport of patients with ACS [acute coronary syndrome] and methods to minimize adverse events for these individuals. I am joined today by Michael Mooney, MD, Director of Interventional Cardiology at the Minneapolis Heart Institute in Minneapolis, Minnesota; Dr. Michel Le May, University of Ottawa Heart Institute in Ottawa, Ontario, Canada; Dr. Tim Henry, Director of Research, Minneapolis Heart Institute Foundation in Minneapolis, Minnesota.

STEMI Intervention: Managing the Chaos

Because of the complex interaction between the different components of a STEMI team, there is inherent chaos in STEMI interventions.

Fortunately, there are deliberate exercises in deconstructing this chaos.

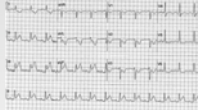
To improve D2B efficiencies and outcomes, it is essential to separate the STEMI intervention into the “process” and the “procedure” of STEMI interventions.



Slide 3

Because of the complex interaction between the different components of the STEMI [ST-elevated myocardial infarction] team, there is inherent chaos in STEMI interventions. Fortunately, there are deliberate exercises in deconstructing this chaos to improve total balloon angiographies and outcomes; it is essential to separate the STEMI intervention into the process and the procedure of STEMI interventions.

“Process” and “Procedure” of STEMI Interventions



Slide 4

Here is an illustration of what I have just explained. To better understand any STEMI intervention, break it into the process -- which is on the left. These 3 slides show you the process and, of course, the procedure of how the STEMI intervention is performed in the cardiovascular laboratory. In Miami, I have been working with the SINCERE [Primary PCI and the Single Individual Community Experience Registry for Primary PCI] database, which now has 387 short door-to-balloon interventions, all performed by a single individual, and I have tried to standardize these procedure improvements. I call them the 10 commandments of the SINCERE database. These include: a focus on the culprit lesion in the infarct-related vessel; achieved all 4 parameters of a successful pre-profusion; relief of chest pain; ST-segment resolution; restoration of TIMI [thrombolysis in myocardial infarction] grade 3 flow; and myocardial perfusion grade 3.

“Procedure” Improvements – Lessons From SINCERE Database

Focus on the culprit lesion in the infarct-related artery.

Achieve all 4 parameters of successful reperfusion – relief of chest pain, ST segment resolution, restoration of TIMI 3 flow, myocardial perfusion Grade 3-4.

STEMI lesions contain thrombus – consider thrombectomy or aspiration.

Establish an anticoagulation strategy: bivalirudin has numerous benefits for this application.

Early upstream antiplatelet strategy involving aspirin, clopidogrel, and possibly abciximab.

Guiding catheters of 6 French size are sufficient; venous sheaths may be avoided.

Hydrophilic wires appear to be very useful.

Intracoronary nitroprusside causes profound coronary microvasculature dilation and significantly improves myocardial blush grade.

Administer the quick 30-sec “Plavix Test” to determine feasibility of using long-term clopidogrel.

For uncomplicated, successful short DTB STEMI interventions, early hospital discharge may be feasible.



Slide 5

STEMI lesions inherently contain thrombus and they should be considered for treatment with thrombectomy, or aspiration. Establish an anticoagulant strategy; Bivalirudin clearly has numerous benefits for this application. The only upstream antiplatelet strategy involves aspirin, clopidogrel, and possibly abciximab. Guiding catheters of six French will suffice mostly, and venous sheaths are to be avoided in the majority of the cases. Hydrophilic wires appear to be useful for this indication, intracoronary nitroprusside causes profound coronary microvascular debilitation, and significantly improves myocardial blush rate.

Finally, a quick 30-second test was administered to determine the feasibility of using long-term clopidogrel, but with most uncomplicated, successful, short door-to-balloon interventions early discharged from the hospital can be expected.

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Temporal Trends From the SINCERE Database

	Median DTB (min)	DTB < 90 min (%)	Mean procedure time (min)	Procedure success (%)
Cases 1-50	120	21.6 %	30.3	91.1 %
Cases 51-100	109	42.6 %	21.1	95.8 %
Cases 101-150	89	56.0 %	19.4	100 %
Cases 151-200	80	93.5 %	17.0	98 %
301-387	76 min	91%	14 min	95%
Cases 301-350				



Slide 6

These are the data from the SINCERE database, 387 short door-to-balloon interventions. And the message here is very clear, that in the 4 years that it has taken to accumulate this experience, the median door-to-balloon time has come down from 120 to 76 minutes, with the number of procedures being performed in less than 90 minutes to be 91%, a mean procedure time of 14 minutes, and success rates of 95%. When one is talking about improving this complicated and chaotic STEMI process, there are various concepts which are important. One of them is particularly difficult for interventional cardiologists, and even for cardiologists because it means a threat to their autonomy where they have to let go of the decisions which are now going to be made by physicians who are the first and the early responders. As an example, this is the interventional cardiologist. He needs to relegate the decision making to the ED physician, who needs to even let the EMT and the folks with the EMS make this decision. I call this a backward integration, and I think this is one of the very effective ways of producing door-to-balloon times.

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Improving the STEMI Process (1)



EMT



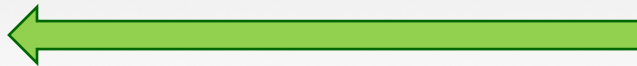
ED Physician



Interventional
Cardiologist

ED physician
allows EMT to
diagnose STEMI

Interventional
cardiologist allows ED
to call STEMI alert

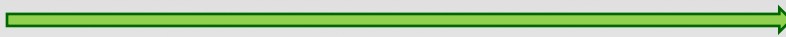


Backward integration to reducing D2B times

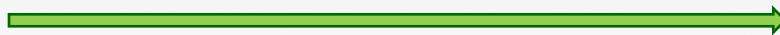


Slide 7

Improving the STEMI Process (2) Prehospital Management



Pathway 1 – IT penetration with STEMI alert



Pathway 2 – Advanced paramedics



Slide 8

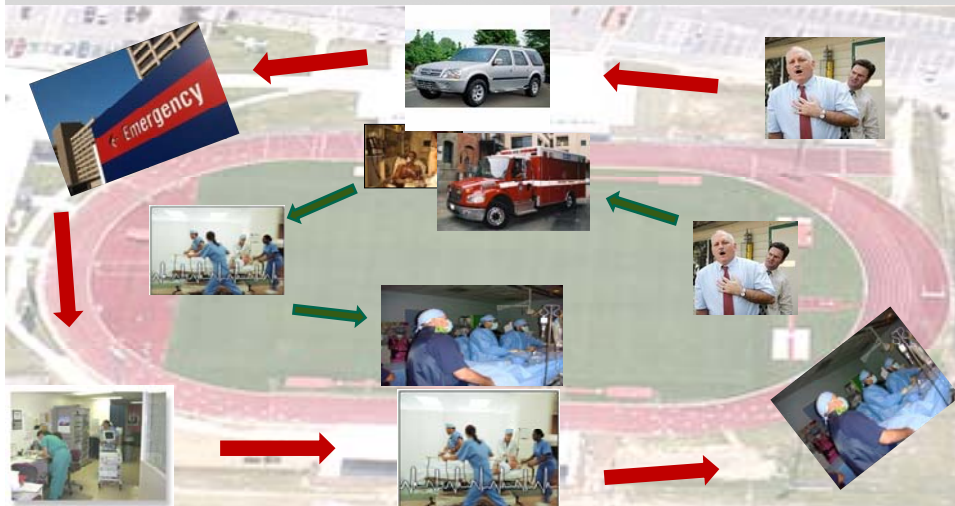
When you move on further to improving the STEMI process, it is critical that prehospital

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management occurs. Now there are 2 apparent ways how this can be done. There could be IT penetration with this early STEMI alert called in by the EMS. This is one of the pathways I present with. You have the capability within the ambulance of diagnosing and transmitting the ECGs. There are various methodologies which are being worked upon, and this appears to be one very effective pathway. As opposed to this -- as was done in certain programs, including notably in Ottawa -- you could have the creation of advanced paramedics and the pathway there is almost similar, except that the ECG is diagnosed on site and called into the hospital, so prehospital management is a critical part of improving the STEMI process.

Improving the STEMI Process (3)

Team Work!
Training & In Situ Simulation



Slide 9

I often compare a STEMI process to a relay race in which there are 4 players running, 4 x 100 or 4 x 400 relay. The baton is passed amongst these 4 people, the 4 constituents include: the patient, the EMS, the ED, and finally the interventional cardiologist. Unfortunately, it is the interventional cardiologist who is the last person handling the baton, and he has often to make up for the time lost in the process. This also captures the important ingredient of teamwork. Not everything is still right, this is one of the highlights. Here is a sample, an example of the baton handling. This is what is happening in various hospitals in the United States. A patient has a myocardial infarction [MI], he drives himself, or somebody drives him to the emergency room [ER], an ECG is called, acute MI is diagnosed, the cardiac cath lab is called, and hopefully a successful PCI is done.

On paper, this looks pretty good. But, in a moment, we will realize the big problems here. This is how I think it should be done, and this is how it is being done in advanced programs in Europe, in Canada, and happily, in some parts of the United States. Once again, this is a

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patient who has a MI. Fortunately, now he does not self transport, he calls EMS, the STEMI diagnosis is made in the ambulance, and he is rushed, bypassing the ER, straight into the cardiac cath lab, and a successful PCI [percutaneous coronary intervention] is done.

Improving the STEMI Process (3)

Team Work!
Training & In Situ Simulation



Slide 10

Now let's look into the area where we are doing wrong. There are various missteps, this is one of them, self transport. I think it is a very bad idea. You can miss early treatment, as well as not have management of any complications. You need to bypass the ER, you need to have a faster way to activate and, of course, this running around to the cardio cath lab can be avoided. These are the pragmatic methods of how improvements in the STEMI process can be done.

Discussion

Three major unanswered questions about STEMI interventions:

1. Are D2B times realistic for an entire nation – should we be reverting back to 120 minutes like the ESC?
2. Should STEMI interventions be performed only at tertiary centers or at smaller institutions without surgical back-up?
3. What is the best prehospital activation strategy – advanced paramedics or IT penetration into EMS?



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I think this leads us into 3 critical questions which need to be answered. Firstly, are door-to-balloon times realistic for an entire nation, or should we be reverting back to the 120 minutes, like the European Society of Cardiology has done recently? The second question is should STEMI interventions be performed only at tertiary centers, or at smaller institutions without surgical backup? And, finally, I think this is also important, what is the best prehospital activation strategy; to have advanced paramedics or penetrate the ambulance with information technology.

We are now going to review the triage, the transfer, and prehospital activation strategies, and I am going to request Dr. Mooney to reflect on this.

Triage, Transfer, and Prehospital Activation Strategies for STEMI Patients



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Michael Mooney, MD: Well, thank you, Dr. Mehta. The Lumen conference, I think, will do a lot to advance the understanding of the importance of reaching defined parameters in the prompt care of patients with acute MI.

It's been known in part of the guidelines now for several years that there are 6 important operating parameters defined by Bradley that allow for a success. These parameters, briefly, are that the ER needs to be able to directly activate the cardiovascular team, that there needs to be real-time feedback to the parties involved and the care of the patient as to the efficiency of their end of things, and then the patient outcome. Importantly, there needs to be a single call to activate the system, and that in-house cardiology at the PCI system hospital is helpful. The cardiovascular teams then need to be available within 20 minutes, and that the EMS pre-activation is going to be a very important part of how we move things forward.

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Triage

Critical detail: must diagnosis the STEMI to call it!

	Medicine	Zone 1	Zone 2
Demographics			
Total Patients	70	80	81
Age >= 65 Yr	17	13	15
Female	14	13	13
Male	56	13	15
Cardio. Arrest	13	117	61
Cardiogenic Shock (n=5)	9	9	8
Time Intervals (min)			
Medicine to PPCI to PPCI	5	6	6
Medicine to PPCI to PPCI	13	12	18
Medicine to PPCI to PPCI	48.3	49	52
Medicine to PPCI to PPCI	115.5	15	14
Medicine to PPCI to PPCI	15	14	14
Medicine to PPCI to PPCI	0	0	0
Medicine to PPCI to PPCI	210	210	210
Medicine to PPCI to PPCI	44	44	52
Percentages			
All Transfer	44	44	52
Cardiac Rehab Referral	76	76	76
Angiogram	100	100	100
Beta-Blocker Given	88	87	87
Anti-Thrombotic Given	97	96	99



Slide 13

Now when these were first defined in 2006, 40% of participating hospitals did none of these, and currently as a result of the combined effort that has truly been outstanding, including Get With The Guidelines, the HQA effort, and then the D2B, or Door-to-Balloon Alliance efforts, have in a very short time been nothing short of transformative in influencing a very important parameter, and that is door-to-balloon time. Currently now, when the program started, about 9% of patients were at the door-to-balloon time of less than 90 minutes. Currently, in 2 short years, 75% of the patients arrive accomplished, the door-to-balloon parameters, in less than 90 minutes.

Now this is an outstanding success, but it's only the beginning of a process; 81% of the MIs do not present to the transferring hospital and are called transfer patients, and the guidelines do not address those issues comprehensively. So we are taking baby steps. I think what we are trying to define now is a system of care that leads to an integration of outside hospitals to a tertiary center, enforcing and utilizing standardized protocols and communication requirements and ongoing research.

Prehospital Activation

Technology is not standardized for ECG transmission to serve multiple metro PCI centers.

Minneapolis/St. Paul hospitals agree to standardize preactivation standards by EMS interpretation in 2005.

Provide feedback to EMS with data.

Provide education and ECG training for medics.



Video Shoot
EMS training film



Slide 14

Now I wanted to just mention some of the problems that we've had, and I think you have alluded to, and that is that currently even in the city, approximately 40% of the patients do not use the EMS system. And when the EMS system is not activated, the diagnosis of acute MI cannot be made, and that represents delays in appropriate treatment of the patients. Particularly in the rural areas, this number now jumps to 70% of the patients not utilizing EMS. The most likely person not to use the EMS is a young male in his 50s. They typically will avoid doing that and jump in the truck and head to the ER, so that is an area that we need to spend time on. Prehospital activation is really critical, but it's a complex task to be accomplished in a statewide program because there are so many different EMS systems and the communication between any given technology with the central PCI center is difficult and would require redundancies that are complex. At the present time there is not a unified format to do that. That is our goal, it is a laudable goal, uniform standards need to be developed and are currently being considered.

Transfer

Preactivation outstate, same criteria as Metro

Ground EMS calls 1st ED for Helicopter to rural hospital



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"Hot Loading"

Helicopter Meets Ground EMS at Local Hospital



Avg time skids
down/skids up
= 12 min after



Slide 17

This is the technique that we use, it's called hot loading. The helicopter meets the ground EMS

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at the local site, the patient EMS contact initiates the acute MI protocol, and then the patient is quickly brought to a local ER, which has a helicopter base to transport the patients. In broadly applying these strategies, not only to your hospital but your referring network of hospitals and beyond, a simple cookie cutter approach often does not work and creativity is required.

Transfer

The more rural, the more creativity!

Intercept for BLS units to ACLS



When a Heart Attack Isn't Just a Heart Attack

Beyond pioneering the Level 1 Heart Attack protocol, MHI at Abbott Northwestern is poised to deliver excellent cardiac care for any heart-related emergency, including:

- Aortic dissection
- Critical limb ischemia
- Cardiac arrest
- Acute aortic aneurysm

Apply "SYSTEMS OF CARE"



Utilizing "SYSTEMS OF CARE"



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We have now branched beyond acute MI to include other acute cardiovascular catastrophes utilizing the same principles of connecting a tertiary hospital to a rural hospital. The programs that we have had some success with are acute aortic dissection, critical limb ischemia, cardiac arrest -- which has been particularly rewarding with our cool-it program -- and acute aortic aneurysm.

Dr. Mehta: So these are just additional benefits that are coming from you creating a very effective regionalized system.

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3 Divisions & 3 Focus Areas

ACCESS

DATA COLLECTION

Outstate Hospital

TRANSPORTATION

FEEDBACK

EMS Transport

STREAMLINE CARE

RESEARCH

Tertiary Center



Cardiac Arrest (Resuscitation Center)
Acute Abdominal Aneurysm

Ascending Aortic Dissection
Critical Limb Ischemia



Slide 20

Dr. Mooney: Right, it's all about systems of care. We are getting our training wheels by doing door-to-balloon initiatives, and then broadening it out to a transfer population, and then utilizing the same system of care to incorporate other clinical conditions, utilizing the same principles of standardized protocols, education, and data monitoring and research. Just to give you an idea, these are the 3 areas that we focus on; our out state hospital, which requires education, EMS transportation, and then tertiary care center, its access, transportation, and streamlining of care.

Type A Dissection Protocol Treatment Times 01/04/08

Note: Surgical case only	Type A Before protocol	Type A After protocol	Difference
Median time presentation to diagnosis confirmed	365 min (n=13)	175 min (n=22)	(190 min)
Median time diagnosis suspected to confirmed	45 min (n=13)	16 min (n=23)	(29 min)
Median time diagnosis confirmed to into OR	147 min (n=13)	95 min (n=23)	(52 min)
Median time arrive ANW to into OR (presented at ANW)	164 min (n=4)	181 min (n=5)	+17 min
Median time arrive ANW to into OR (presented at RH)	97 min (n=9)	44 min (n=20)	(53 min)
Median time RH to ANW OR	728 min (n=9)	282 min (n=20)	(446 min)
Inhospital mortality	31%	15%	(52%)



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These are the results of our acute aortic dissection. I was dumbfounded with the ease of implementing this, having gone through similar efforts with acute MI, it was then relatively easy for us to drop our inhospital mortality from 30% to 15% with acute aortic dissection and drop the time from 8 hours to 181 minutes, median time to arrival at the hospital. So we are particularly excited with this as an approach to advancing the standard of care across the country.

Dr. Mehta: You mentioned the Bradley paper. I think that is one of the bigger first steps to deconstruct systemic cares. Yet, you have been doing it this way before the paper was published. What have you found in your experience is that all the 6 parameters are something that you need, or is there going to be a local variation to that, that maybe you realize that at a certain hospital, just 4 of those programs are adequate and, as an example, you don't need a cardiologist to be in-house?

Dr. Mooney: Right. And a regional implementation that is somewhat flexible is key to success. It is important to get by in, to the tenants, of what you are trying to accomplish by the EMS nursing, regional hospitals, and the cardiologist. Once you do that and people are earnestly looking at achieving a goal, flexibility is important. I think the most important piece has been giving the ER physician the authority to initiate the protocol, and then there being a single call that activates the entire system.

The one issue that was very clear to us is that this system requires maintenance. You don't set up the protocol and then expect it to be self sustaining. It needs continuous effort for

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improvement and maintenance for it to be a successful program, and then for it to be all that it can be, broadening it out to other clinical issues.

Dr. Mehta: Mike, I'm also very aware of your deep experience with cooling hyperthermia protocols for these out of hospital cardiac arrests. What has been your experience, your success, in that you do have extensive experience in this?

Dr. Mooney: Well, the coolant protocol was implemented state wide. It was meant to treat the patients with cardiac arrest who remained unconscious. These are typically the worst cardiac arrests that we approach. We were simply astounded. We were able to show that patients presenting 120 miles away with a cardiac arrest in a comatose state were cooled and had the same clinical outcome as patients presenting to our primary hospital, with a survival rate of 55% in all comers and 70% survival in the STEMI group.

Dr. Mehta: Simply astounding, and I congratulate you on establishing such a wonderful system. Michel, I would like to discuss with you and get your thoughts on the appropriate timing and dosing of the pharmacologic interventions that you are using in STEMI interventions in your program.

Appropriate Timing and Dosing of Pharmacologics in STEMI Intervention

Michel Le May, MD: Well, to start off with, I think we should look at what has been done for several years. It's very simple. With aspirin, we know that antiplatelet therapy is the cornerstone of treatment in acute MI. It couples well with either thrombolytic therapy or primary PCI. We know from the ISIS-2 [second International Study of Infarct Survival] trial, that aspirin

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alone, a really cheap drug, reduces mortality by an absolute 2.5%. We know that aspirin is critical in angioplasty. We've known that for several years. It prevents abrupt closure. It is one of the vital things that we need to use during an acute MI. The medication aspirin is administered in the field by our paramedics. Either the primary care paramedics or the advanced care paramedics will give aspirin in the field.

In the ER, it is the ER physician that gives aspirin. But those that we've chosen are 160 mg chewable aspirin. You can give 160 to 325 but the dose that we've chosen is 160 chewable. As I mentioned the paramedics, we have 2 types of paramedics in Ontario. These paramedics are the primary care paramedics who receive 2 years of training in a college. The advanced care receives 3 years of training. The advanced care paramedics, in Ottawa, are trained to read the ECGs, so they can also make the diagnosis of STEMI. Now, we talked about antiplatelet therapy.

Dr. Mehta: How accurate are they? Did you look into that?

Dr. Le May: The advanced care paramedics, we've reported on this previously in the Canadian Journal of Emergency Medicine. We have developed a tool, in Ottawa, to measure their accuracy. We know that the sensitivity and specificity is in the high 90s, that their negative predictive value is 99%, which means that they hardly miss any STEMI. The positive predictive value is in the low 80s. This means that they will bring in some false positives. They'll bring in some patients, for example, with early repol or left bundle branch block.

Dr. Mehta: You have a mechanism in place for somebody to override them?

Dr. Le May: They come, when the paramedics call a code STEMI, this means that we are notified. The call comes in through a central area and there is a receptionist that receives the call on 1 single phone that is dedicated to the paramedics. In this situation, what happens is there is a code STEMI that is called. Everybody gathers, basically, in a STEMI room. The STEMI room in this situation is within the cath lab facility. We have a nurse coordinator. We have a cardiology fellow. An interventionist will be appointed to do the case. So, in this situation, when the paramedic arrives, immediately, we get a very quick exchange of information. We will confirm that the patient has a STEMI. Then, the patient goes into the cath lab. We look at the tracings that are obtained from our paramedics. We don't repeat the ECG. There's no need to repeat it. The quality of the tracing is sufficient to make that decision.

Dr. Mehta: Does the ECG become part of the medical record?

Dr. Le May: It does. It becomes part of the medical record. In the STEMI room we start off by talking about antiplatelet therapy. We will give clopidogrel in the STEMI room. We have decided to standardize our protocol as much as possible. We use 600 mg of clopidogrel. In some centers, particularly in Europe, they use clopidogrel in the ambulance. Now, I know that there are people who are shy to use clopidogrel. They are concerned that if they go into the cath lab there may be some cases which may be left main disease or the type of case where

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you would think that maybe a patient is more likely to go to surgery. I think that what we've seen in our experience, the likelihood of needing a surgical intervention is very--

Dr. Mehta:--Extremely low.

Dr. Le May: Extremely low. So I think we don't need to fear as to adding clopidogrel in the STEMI room. The questions as to what dose should we be using, I think we're learning from some of the trials. We translate the information from the ARMYDA-2 [Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty] trial that 600 mg is better than 300 mg. I think that we're learning from trials like HORIZONS-AMI [Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction] trial that 600 mg is better than 300 mg. So, we're seeing more and more trials now that are published. We had the TAPAS [Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction] trial that was published and used also 600 mg. I think that this is a dose that people are becoming more and more comfortable with. There is also some laboratory information that would suggest that this is the right thing to do.

There is probably going to be a new drug on the market in the same class as thienopyridine. That is prasugrel, which we've seen in TRITON [Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel] to be, perhaps superior to clopidogrel. It has a faster onset kinetics. But, we still have to learn about these drugs in the context of STEMI because STEMI patients are a bit different than the stable patient who comes in, because in STEMI patients, there is a bit of a spectrum. There are patients that have high sympathetic tone. Their liver may be a little bit in a state of shock. We know that these drugs need to be activated, the thienopyridines. So, perhaps in the future, there will be a role for other drugs. We are waiting for the results of the PLATO [Platelet Inhibition and Patient Outcomes] study and the CHAMPION [Cangrelor vs. Standard Therapy to Achieve Optimal Management of Platelet Inhibition] study that are looking at the new molecules. That may help us in the context of STEMI, but for now, we are using dual antiplatelet therapy. Aspirin and clopidogrel have been the standard of our care that we use in Ottawa.

Now, we have an inner circle where we do primary PCI and we reach out beyond the city now. We reach out to some of the community hospitals where we feel that we can offer primary PCI. Again, in these small communities, we choose 600 mg of clopidogrel. But, once you get beyond that inner circle, we enter the outer circle. And, a little bit like the other groups, like Tim Henry's group, we use a pharmaco-invasive approach. We believe that today, there is enough data from the GRACIA-2 [Grupo de Análisis de la Cardiopata Isquémica Aguda] trial, our own CAPITOL [Captopril Post Infarction Tolerance MI] study, the transfer protocol, the WEST [Which Early ST Elevation Myocardial Infarction Therapy] study, and the CARESS in AMI [Combined Abciximab Reteplase Stent Study in Acute Myocardial Infarction], that there is a role for coupling patients that receive thrombolytic therapy to the cath lab.

I think there is now good evidence that we should be marrying those 2 strategies together. In fact, the Europeans have recommended in their most recent guidelines that anybody who gets

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thrombolytic therapy, regardless of symptoms or evidence of reperfusion, that they should be in the cath lab within 3 to 24 hours. So, for those patients that are in our outer circle, we use 300 mg of clopidogrel coupled to thrombolytic therapy, as suggested in the CLARITY [Clopidogril as adjunctive reperfusion therapy] study. However, in patients over 75, we omit the clopidogrel.

Dr. Mehta: What about in the cath lab? What are you using as an anticoagulant? Are you staying with unfractionated heparin?

Dr. Le May: Yes.

Dr. Mehta: Or have you converted to Bivalirudin?

Dr. Le May: So that is another important question. In moving on to anticoagulants, we give unfractionated heparin in the ER or on arrival with the paramedics. We give 60 U/kg up to a maximum of 4000. Again, this is a question of standardizing dosages. It's easy to apply that to primary PCI as well as to thrombolytic therapy for our outer circle of care.

So, in the cath lab, we'll measure a quick ACT [activated clotting time]. In the past, we were very strong with glycoprotein IIb/IIIa inhibitors. We know historically that there have been a number of trials that have suggested that there is a big role for IIb/IIIa. In particular, remember, the ACE [Acarbose Cardiovascular Evaluation] trial. We showed a mortality benefit actually at 1 year. Then, there was the abciximab before ADMIRAL [Direct Angioplasty and Stenting in Myocardial Infarction Regarding Acute and Long-Term Follow-up] trial, with Gilles Montalescot. But, these trials did not use clopidogrel. There was not a lot of other antiplatelet therapy at the time. If we look at more recent trials, like the ON-TIME 2 [Ongoing Tirofiban In Myocardial infarction Evaluation], and we look at BRAVE-3 [Value of Abciximab in Patients With Acute MI Undergoing PCI After High Dose Clopidogrel Pretreatment], and our own ASSIST [A Prospective Randomized Trial Evaluating Early Eptifibatide Administration in Patients with Acute Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention After Thienopyridine Loading] trial, which used 600 mg of clopidogrel, we have now more than 2000 patients what would suggest that when you give 600 mg of clopidogrel, it is getting harder and harder to show clinical events.

In the ON-TIME 2 trial there was some ST-segment resolution. But this is a circuit endpoint. And we know that we just have to look at the FINESSE [Facilitated Intervention With Enhanced Reperfusion Speed to Stop Events] trial where we looked at the arm with the half-dose lytics in IIb/IIIa, there was improvement in the ST-segment resolution but there was no difference in clinical outcomes. So, I think that from our point of view we feel now that with 600 mg of clopidogrel we don't need to use routinely IIb/IIIa. This is not to say that in the case where we have a refractory case, where we have residual thrombus, where we don't achieve TIMI-3 flow, that on an individual case we still have to be physicians.

There are patients that perhaps have some resistance to clopidogrel or even to aspirin. In

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these cases a IIb/IIIa may have a role. We need to have larger studies looking at intracoronary IIb/IIIa. We've seen some data now that looks very promising. We need to see data in larger trials and these are ongoing. Now, as to the direct thrombin inhibitors, like bivalirudin -- and this becomes a bit of a dealer's choice, because now the patient is in a cath lab -- many of us are switching over to bivalirudin. Bivalirudin has shown some interesting results in that the net clinical benefit at 30 days was superior to unfractionated heparin combined with IIb/IIIa. It also showed what was a bit of a surprise, that there was a reduction in mortality. This reduction in mortality at 30 days grew to an absolute 1.7% by 1 year. This is very interesting. It is very promising. It may be related to the fact that there are not the bleeding complications associated with bivalirudin. There was 1 aspect of bivalirudin that was a bit scary. That as you know is the story with the abrupt vessel closure. It was scary because there was about a 3- to 4-fold increase in abrupt vessel closure using bivalirudin.

Dr. Mehta: In the very early stages?

Dr. Le May: In the very early stages, within 24 hours. A bit like the story we saw in the CADILLAC [Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications] trial.

Dr. Mehta: Do you think a 600 mg dose of clopidogrel or maybe prasugrel will overcome that?

Dr. Le May: That is a very good question. I think that there is a very good chance that 600 mg of clopidogrel will reduce that. And prasugrel which has a faster kinetics will be very interesting to see whether or not it can reduce that. –

Dr. Mehta: An hour or longer? Two hour or 4 hour duration of bivalirudin?

Dr. Le May: I'm glad you brought this up because this is exactly what we're doing in Ottawa. If you remember in HORIZON trial, the trial was designed such that the interventions could prolong the duration of bivalirudin by 2 hours. The dose of bivalirudin that was used in the cath lab, the infusion dose was 1.75 mg/kg per hour. We reduced this. You know the dose that we used is dialysis dose, basically .25 mg/kg per hour. We ran that for an additional 2 hours afterwards. Instead of pulling our sheets at 2 hours, we would pull them at 4 hours. So, I think that time will tell. With a combination of better antiplatelet therapy, with either a larger dose of clopidogrel or the newer molecule prasugrel combined with a longer infusion with bivalirudin, time will tell whether we can produce –

Dr. Mehta: The data with the HORIZONS trial is so robust. I do not know of another trial which had mortality reduction. One wonders if you're going to be using bivalirudin as almost a default strategy, can the use of Bivalirudin be extended either on to the ER and even for a patient that's being transferred from another institution? Because that's the patient who is truly at risk because they are going to be inherent dealings.

Dr. Le May: I think that's interesting. But I think that there are 2 aspects to look at there. The

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first aspect is there are not a lot of data. It has a level of complexity. You know, you talk about small hospitals. It is so easy to use unfractionated heparin. Everybody is familiar with it. In the HORIZON trial, patients, some patients did get unfractionated heparin before they go to the cath lab. It doesn't appear that it led to more complications. The second aspect is cost and whether these patients, you know, all these ERs need to start the bivalirudin. We think that maybe it's going to reduce; it may lengthen the time of transferring the patients. If you add another drug in the ER, maybe physicians say when you look at a large metropolitan area, and then you go out and look in many hospitals, there may be a problem with stocking this drug and being familiar with it. When you look at some of our rural hospitals that have maybe 10 or 15 STEMIs a year, you know this is adding a level of complexity.

Dr. Mehta: Well, in addition, somebody at one of the workshops at the Lumen Conference brought up the point that their EMS is not even allowed to have an intravenous drip. So you are right, there are many other practical issues. Let's move on to reviewing the new data and protocols for reducing door-to-balloon times. Tim, you have been a pioneer in this field, illuminate us on what you think are some of the most pertinent factors.

New Data and Protocols for Reducing Door-to-Door Balloon Time



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Timothy Henry, MD: Well, thank you Sameer. First of all I'm delighted to be here in Miami. It's really an exciting time for me because you watch now and you see that this concept of having systems of care is really spreading across the country. I think we've really made a tremendous headway. When we began our program 7 or 8 years ago and we had early evidence from European trials that actually showed that transfer for PCI had superior outcomes to fibrolytics just like it did in PCI hospitals. But, at the time it was really felt that it can't really be done in the

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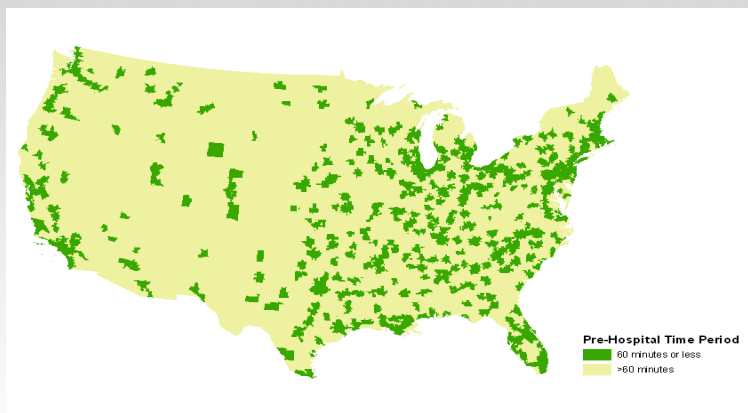
United States. You know it can be done in small European countries like Denmark with short transfer distances. I think it's been fun to see now that it not only can be done but it can be done as effectively.

What I'd like to do is really step back from the individual hospitals which have been covered, I think really nicely, by Mike and talk about it really from a national policy level. Several years ago, as part of the ACC Emergency Care Committee, and with Doug Weaver who was the chairman of the committee at the time, we wrote a paper that was published in *Journal of American College of Cardiology* that talked about is it time to have a national policy. It is sometimes frustrating, if you look at this, we have a national system of care for trauma, yet for STEMI where there are at least more than 3 times as many people who die from MI in this country than die from trauma, we don't have an organized system at all. Theoretically, that would be the nicest way, if we actually had an organized system. Unfortunately, or fortunately, we haven't waited for that from a policy level. Actually, you've seen people go forward.

Primary PCI: Access

42% PCI hospital is closest facility

79% within 60-minute prehospital time



Nallamotheu BK, et al. *Circulation*. 2006;113:1189-1195.



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What I'd like to do is talk a little bit about the initiatives from the ACC and the American Heart Association that have allowed us to do that. So what I'd like to start with is to really talk about this concept. I think all of us believe that PCI is the best strategy. So, really the focus is to increase timely access to PCI. There is a really important paper that was published in *Circulation* by Dr. Brahmajee Nallamotheu, who was here yesterday and gave a wonderful talk. The point is 80% of the population of the United States is actually within 60 minutes of a prehospital time. So this is clearly doable if we are dedicated to it and can focus on it. I think that if you look at it, the problems that we are facing is this lack of an integrated healthcare

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system in the United States, the lack of standardized care protocols, or even, maybe we can do it in a system but certainly across systems, the lack of a well-organized interhospital transport system.

Timely Access to PCI – Barriers in the United States:

- Lack of an integrated healthcare system in the US
- Lack of standardized care protocols
- Lack of well-organized interhospital transport system
- Reimbursement policies - negative impact on hospitals without cath labs
- Hospital bed capacity issues



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This is a major problem in the United States, is our support for EMS. It varies tremendously across the country from region to region, state to state, even counties. There are a lot of things that really hinder our bet, like for instance, there are places where the EMS system can't cross county lines. So there is a lot of work to be done in terms of organizing our EMS transport system. You know reimbursement policies, people are worried about how do we do these. If the best care is that we get patients to PCI centers in a rapid manner, what impact will that have on non-PCI centers? We have to be careful about that and develop policies that really deal with that. Then there are bed capacity issues. Many hospitals in the United States that are actually full and are on divert. A key component of having this system is you really can't be on divert. You really need to be 24 hours a day, 7 day a week access for PCI in your cath lab.

Mike talked specifically about the Elizabeth Bradley paper that was in the *New England Journal of Medicine*. I think it's very important because what she did is she looked at what the best hospitals were doing at the time and how much effect that actually had on it. I think this really formed the background for the ACC's D2B Alliance. I think it has made a tremendous input. I agree with Mike, it's amazing what has happened in a very short time. But you have to step back and remember, this is just a focus on PCI centers. So, that's great for PCIs, and door-to-balloon is a very critically important part of it. But if we are going to have a system of care for STEMI, it involves 75% of the hospitals in the United States are not PCI centers. We

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really need to expand that out. The key components of the D2B Alliance are here and one key is that the ED physician activates the cath lab. It is critically important. Cardiologists need to get over it. But I'll even go beyond that now. I think we're really into the era where paramedics need to activate the cath lab and the ED physicians need to get over it.

Dr. Mehta: Which would be something closer to what they are doing in Ottawa for example?

Dr. Henry: Yeah, in and across the country. Now large shares of our patients in Minneapolis are being pre-activated not only at our hospital but in most of them. It's really been an initiative from the EMS system itself.

Dr. Mehta: But then the question comes, do you train people to diagnose on site and transmit, or are you just putting in a system that is going to append the ECG and then transmit online?

Dr. Henry: That's a really key issue. It can be done differently in different places. I think the point is whether you use the ECG, the diagnosis on the ECG machine, or you use paramedics reading and interpreting the ECG themselves, or whether you use transmission. I think really that's more of a local issue on what's available. The point is any of those can be effective. Now, you'd need careful feedback and quality assurance to make sure that you're not having excessive false-positive activation. But clearly, there have been a number of examples where this can be done effectively. Not only is it being done in the cities, but a key focus for us has been to expand this pre-activation into the rural areas. That's why I think it depends, because in more rural areas in particular, transmission is not available in many places. Number 2, you are dealing with, in many times, with volunteer EMS. You don't have paramedics that have been trained in ECG. So, we've really relied on the ECG diagnosis itself to use and have set the bar, and it has been very effective.

Dr. Mehta: But even there you need to strike a balance because every ECG which you are missing is a patient missed. So where is the right balance? The ACC says that the false-positive rate should be less than 15%. Is that the range of criteria you're aiming for?

Strategies to Reduce D2B

ED physician activate the cath lab	8.2 mins
Single call to central page operator	13.8
ED activate cath lab while patient en route	15.4
Cath lab staff available within 20 minutes	19.3
Attending cardiologist always on site	14.6
Real-time data feedback to ED staff	8.6



Bradley EH, et al. *N Engl J Med*. 2006; 355:2308-2320.



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Dr. Henry: Well I don't know if there is a specific number that we know yet. More importantly even the issue of false-positives is of some debate. For instance, Dr. Dave Larson who works with me had a very nice paper in *JAMA* a year ago that looked at this. We found that 14% of our patients don't have a clear culprit artery, but of those patients, there are about 40% who have positive enzymes. So there are other things that cause acute STEMI that are not necessarily related in need PCI. For instance, you can have spasm, you can have thrombus that resolves, and you can have stress cardiomyopathy. There are a variety of things that can do it. So if your patient has true ST-elevation and positive enzymes it's hard to call that a false positive. So, I just think that what you do is a true false-positive rate, using it with ED and paramedic activating the cath lab is really between 6% to 8%, which we certainly think is acceptable.

D2B Alliance

<http://www.d2balliance.org/>

Evidence-based Strategies

1. ED physician activates the cath lab
2. One call activates the cath lab
3. Cath lab team ready in 20-30 minutes
4. Prompt data feedback
5. Senior management commitment
6. Team-based approach



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So the other key components for the D2B Alliance is to have a cath lab team ready in 20 to 30 minutes, prompt data feedback, and senior management involvement. I can't emphasize that enough. If we are really to be successful, your hospital administration needs to empower the physicians and the nurses, and to supply resources to make this effective. I think then the final component is really team work. So, these components from the D2B Alliance I think have been very effective having been applied, and PCI hospitals in the United States have done a great job.

Mission Lifeline

Improving the System of Care for STEMI Patients

A community-based national initiative to improve quality of care and outcomes in heart attack patients by improving the healthcare system readiness and response to ST-elevated myocardial infarction (STEMI) patients.



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But what about the next step? This is really important. I'm involved in the Mission Lifeline program and I think it's critical. A few years ago, when we started our program, we actually looked at all the hospitals in Minnesota. Even though we have known for 20 years that every hospital should have a standardized protocol, a standardized order or have a plan for how you deal with it, what we found was it just wasn't happening. It just wasn't happening at all.

EMS Components of a System

1. Prehospital
2. Triage
3. Transfer



Only 50% of STEMI use EMS in the US
10% Prehosp ECG

Non PCI
Capable

PCI
Capable

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The beauty of Mission Lifeline is with the help of the American Heart Association that theoretically the goal, or at least my goal for the program is that in several years from now every hospital in America has a plan, has a standardized plan of how they are dealing with ST-elevation which includes standardized orders, standardized protocol, and transfer policy. I think when you look at that, any system of care has to involve 3 things. It really does and all 3 are critical. You need a prehospital component; that prehospital is not only for identification but activation is also critical. The second component is triage; clearly it's better to triage from EMS to PCI hospitals if possible. So, to that extent, and particularly in urban and suburban areas, that's been quite effective. The third component is transport; it has to be a part of any system of care, because as Mike talked about earlier, is that more than half of the people don't use the EMS system. It's clearly important in more rural areas, but in urban and suburban areas as well, it's still important to have a plan for those patients who actually present to non-PCI hospitals.

Dr. Mehta: Tim, I'm going to start with you. Let's say if you have to give 1 single biggest factor which can reduce the STEMI related chaos, what would you say?

Dr. Henry: Number 1, have a standardized protocol in place. And work on that ahead of time. Have an MI committee. Sit down ahead of time and make a plan for what you are going to do so that you are prepared at 2 o'clock in the morning.

Dr. Mehta: Excellent. Michel?

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Dr. Le May: I could not agree more with what Tim was saying. I think standardization is actually critical to making the system work. Everybody has got to be on the same page. It's got to be simple. That's the way to get your times down.

Dr. Mehta: Mike, do you echo the same sentiment?

Dr. Mooney: I would just add that you need a field general, somebody who can spot weld the problems and get certain elements that fall out of line back into appropriate performance standards. So, in our system, having an organized leader who is able to make sure that all of the elements are working together, communicating well, and achieving has been important to our sustained effectiveness.

Dr. Mehta: I could not agree with all 3 of you more on that topic, with the additional caveat that so far, as the review of these systems is concerned, I think people will realize that achieving door-to-balloon times is still the low-hanging fruit. The much larger issues are going to be legislation and patient education, so that the patient who is having an acute MI does not wait at home for 6 hours before he comes and calls you. Now, it's 3:00 am, driving across the highway at 100 miles an hour trying to save somebody's life in 90 minutes whereas for 6 hours he was sitting at home. I thank you all for making this a very useful exercise. I thank the audience for joining in and I hope that you will take home important messages to deconstruct the STEMI care. Thank you.