Acute Coronary Syndrome
Institutional Protocols

Moderated by Christopher B. Granger, MD
Discussants: Deborah Diercks, MD; Peter B. Berger, MD; Timothy D. Henry, MD

DR. GRANGER: This is Dr. Christopher Granger. I’m a Professor of Medicine, Professor in the School of Nursing, and Member in the Duke Clinical Research Institute at Duke University School of Medicine. With me today are Dr. Deborah Diercks, Professor and Chairman of Emergency Medicine at UT Southwestern Medical Center, Dr. Peter Berger, Senior Vice President of Clinical Research and an Interventional Cardiologist at Northwell Health, and Dr. Timothy Henry, Director of Cardiology at the Cedars-Sinai Heart Institute.

Let me introduce the topic of acute coronary syndrome (ACS) institutional protocols by stating that there are a wide variety of evidence-based options for the management of patients presenting with ACS. We have good evidence that these treatments are applied in an inconsistent way, and that there is substantial opportunity for better application of treatments that are proven to improve outcomes.

Part of the reason for the gap between effective applications of these treatments is the lack of a systematic approach that includes, I would suggest, several different areas that we can touch on. Those include the interface between emergency medical services (EMS), emergency departments (ED), catheterization labs, and the hospital wards. Another major opportunity is to improve the transition to outpatient care at the time of hospital discharge. Between different institutions, often times even in the same health system, there is lack of coordination of care.

Then there are distinct issues in the different categories of patients, including patients with ST-segment elevation myocardial infarction (STEMI), with non-STEMI, and with cardiogenic shock. There are patients presenting with ACS who will need bypass surgery, and there are issues in what to do in the gap between presentation and undergoing bypass surgery.

Deb, as our emergency medicine representative, please provide some perspective on what you see as the
challenges that can be addressed through a more systematic approach, including algorithms and standard orders for patients presenting with the spectrum of ACS.

**DR. DIERCKS:** Currently practice is patient-dependent and it is institution-dependent. The biggest challenge is getting that consistent strategy across all the providers that are going to eventually touch the patient. Specifically, I think the challenges are around the use of clopidogrel, prasugrel, or ticagrelor, who you give it to, when you give it, and when you don’t.

STEMI patients are a little easier because they go up so quick, and in centers that do a lot of cardiac catheterization where a lot of the ED time is spent on early identification, rapid notification, and getting the patient ready to go. In my mind, it is really the patients with the non-ST segment elevation of ACS that are the biggest challenge, because that downstream coronary anatomy may or may not be known at the time.

When to initiate therapy and with whom to initiate therapy is always a big issue for us. I think standard orders make that easy. There are some places that use the History, Electrocardiogram (ECG), Age, Risk Factors, and Troponin (HEART) score\(^1,2\) or the Thrombolysis in Myocardial Infarction (TIMI) score\(^3\) to help guide therapy. However, there is inconsistency amongst practitioners.

**DR. GRANGER:** Peter, you’ve done a lot of thinking about systems of care and you have worked in Geisinger, and now in Long Island in a huge healthcare system. Would you comment on what your experience has been? Maybe also comment about whether or not there is an optimal approach, or is the optimal approach really still somewhat subjective?

**DR. BERGER:** I do think that despite all of the studies, there remain a lot of unanswered questions. That contributes to the fact that there is such wide variation in practice patterns. Like Deborah said, I do tend to be a splitter, and think of how I would want to treat patients with different kinds of ACS differently. I think that makes sense. Patients with ST elevation, patients with clear-cut non-ST elevation infarction, people with unstable angina, and patients whom you are unsure have an ischemic basis for their pain—I think you could make very sound arguments based on the limited knowledge we have that there are different optimal treatment patterns for all of them.

I also share Deborah’s view that eliminating the unjustified variation in the way these patients are cared for is good for patients and for our health system. If a patient with a particular type of presentation finds themselves in the ED, and the way they are treated depends on who is on-call or who will ultimately be assuming responsibility, I think that generally represents a weak system of care.

Now, you asked about Geisinger versus Northwell Health, which is not only on Long Island, but the five boroughs of New York City and Westchester and now crossing the Hudson River. The practice patterns there were somewhat different. Geisinger is a 100+-year-old health system, very mature, fantastic informatics, very well-connected electronically, and it has a very mature STEMI network. Patients received pretty much the same standard treatment anywhere they presented at the roughly 18 hospitals that referred patients for primary percutaneous coronary intervention (PCI) to Geisinger’s tertiary care centers.

Northwell has tripled in size in less than 7 years; it has 21 hospitals, and is still growing rapidly. It is not yet as well aligned, and there are still important differences in the treatment that patients will receive depending on where they present in the system. I hope and expect that this will change, and that we will be successful in the near future at eliminating unjustified variation and, instead, base treatment patterns on the best available data.

**DR. GRANGER:** Peter, what we would like to do, I think, is make recommendations to our readers about what should be done, and where there are options. Maybe one of the principles...
is to try to be relatively simple and streamlined, at least in terms of some of the most basic decisions.

Let me ask you, from the point of view of the EMS, what is your current recommendation for EMS for, let’s say, a patient who is diagnosed with a high likelihood of ACS? Maybe in this case the best example would be a STEMI. Do you think there is a role for doing anything with antithrombotic therapy other than giving 325 mg of aspirin in the United States?

DR. BERGER: Great question. If I was having a STEMI and a prehospital ECG was clear-cut, and I was being taken for primary PCI, I’ll tell you what I would like, even though it is not strongly supported by the data, I would like my aspirin and P2Y12 inhibitor administered as early as possible, ie, at the time of diagnosis.

I know that hasn’t yet been proven to be beneficial in randomized trials. It cannot, however, be that a P2Y12 inhibitor beats placebo in STEMI, and yet pretreatment can’t be better than post-procedural treatment. It is just that it is hard to demonstrate, and has not yet been demonstrated to be beneficial in the trials that have examined it. Nonetheless, without firm evidence, that is what I would want to receive: a P2Y12 inhibitor administered at the time of diagnosis, or as early as possible after diagnosis, if the diagnosis of STEMI was clear-cut and I was heading to primary PCI.

DR. GRANGER: I think that is a key issue. We do know when paramedics activate, there is about a 25% over-activation or false activation rate. That may be high enough that being somewhat more restrained in the more potent treatments is prudent unless, as Peter points out, those are the cases that are perfectly clear-cut. Tim Henry has done good work reporting on this issue of “false activation” of the catheterization lab for STEMI.

DR. BERGER: Chris, let me just say one additional thing. As you know, not only do paramedics vary in their skill of reading ECGs, but also different systems use different approaches to ECG analysis for patients with a possible STEMI. For example, at Geisinger, a paramedic would transmit the ECG to an emergency room physician at the tertiary care center that the patient was being taken to. When it was thought to be a case of clear-cut symptoms, the “false positive” rate was much, much smaller than what you just quoted. When very skilled paramedics interpret ECGs, or when they are over-read by physicians who are good at reading ECGs, and a patient has clear-cut symptoms consistent with a STEMI, the false positive rate is not very high.

DR. GRANGER: I’ll just say, Peter, I think your point is also important not only for EMS, but for the first hospital that a patient arrives at with an ACS to have as a priority to give a P2Y12 antagonist for at least patients with the clear-cut diagnosis. I’m going to ask Tim, because there is controversy here too, right? I think there are probably reasonable arguments to be made for varying approaches.

Perhaps at the end what we’re going to come back to is to have an approach that is agreed to for one’s institution for the categories of patients, rather than depending on the need to decide what to do at the time for each patient. For example, a relatively low-risk patient going straight to the catheterization lab, or even a patient, let’s say, with ST elevation in lead aVR and diffuse ST depression where one might be more concerned about the need to go to coronary artery bypass graft, is it reasonable to hold off on acute P2Y12 administration? If the patient is going to the catheterization lab within an hour or two, is it OK to just wait until the angiography is performed? This is another important question.

Tim, let’s get back to the issue of first treatment and how to address choosing antithrombotic therapy at first presentation. In Minneapolis, you got a standard protocol to every one of your referring hospitals for STEMI, and this established a standardized approach in your system for use of antithrombotic therapy.

DR. HENRY: No question. Let me comment on several things that we’ve talked about so far! The P2Y12 inhibitor can be given by the paramedics. We had several pilot trials where we did it...
very successfully and we were able to decrease treatment time by probably 30 minutes. Peter was correct that the pretreatment data are conflicting. I think, certainly from a pharmacodynamic point, the earlier you get the P2Y12 inhibitor on board, the better.

The completed trials all have nuances. I still think overall evidence supports having the P2Y12 inhibitor on as soon as possible, but being able to do it accurately is important. The only risk is an increase in bleeding if you have to go to surgery. For STEMI, from my perspective this is an extremely uncommon problem, less than 2% for sure. In non-STEMI it is less rare, more like 8% to 12%. You need to consider those things in your standard protocol.

What I would like to do, Chris, is jump back even more generally and consider this whole concept of institutional protocols. I think it is critical that every institution actually takes the time to do this. For ACS we had what we called Level One, which was STEMI. We had Level Two, which was non-STEMI, including urgent Level Two, for patients who had ongoing chest pain, or had dynamic ECG changes, rising enzymes, or heart failure or arrhythmia. In other words, a non-STEMI patient that was high-risk. We had a plan for that patient, and a standardized protocol for non-emergent STEMI. Level Three was unstable angina, and Level Four included patients with non-cardiac chest pain (Figure).

Figure. Minneapolis Heart Institute® Chest Pain Program.

Adapted from the Minneapolis Heart Institute.
When they presented in the emergency room, we had a standardized approach to all those patients so that everybody knew the plan and it was done very efficiently. That protocol needs to include the pre hospital component, the ED component, the catheterization lab or diagnostic component all the way through discharge and, in my perspective, even after discharge. For example which STEMI patient needs a follow-up echocardiogram? When do you obtain follow-up lipid labs? The more you can standardize the process from prehospital to 1 year post-discharge, the better the outcomes you’re going to get for your system.

For each of these areas, it requires a small group of interested parties—interventional cardiologists, non-interventional cardiologists, administrative, nursing, ED representatives—depending on the problem you’re trying to solve. Get them in a room and empower them to design a protocol. Then, implement the protocol in your institution and, just as important as implementing it, keep track of how it works.

Some protocols will be perfect from the beginning. Great! Some won’t be and will need revisions. When you put a protocol in place, you’ll quickly see what works or what doesn’t work, and then you’ll be able to adapt that protocol. Also, as we gain new medical knowledge, we are able to utilize new medical knowledge to adapt the protocol.

I’ve seen the absolute benefits of having these protocols in place to decrease variability, and to improve outcome. I really want to emphasize, it is not just in the prehospital or in the ED phase, it is all the way through discharge. Those things make a big difference.

We’re talking about ACS today, so certainly that includes STEMI, non-STEMI, unstable angina, out-of-hospital cardiac arrest, but I really do believe that this concept applies to all acute cardiovascular emergencies. We should have the exact same approach—in fact, we did—for aortic dissection, for abdominal aortic aneurysm, for critical ischemia, for pulmonary embolism, and for stroke. The better that we’re able to standardized care, the better the outcomes we’re going to have.

DR. GRANGER: Thanks, that is a great summary, Tim. I’m going to make the presumption that, because you said it so clearly and so well, we all agree that one of our strong recommendations from this particular discussion is going to be that every institution should have a protocol for the basic framework of applying these treatments for ACS.

"We’re in an era where providing more efficient care and shorter length of stay when safe is something that we all want to be doing. That increases both the need and the value for having institutional standardized approaches for how we manage these patients. We’ve talked about everything from EMS through hospital discharge, and out to a year later where the transitions provide important challenges and opportunities to improve how we provide care."

– Christopher B. Granger, MD

STEMI would benefit if the surgery were delayed a little bit. When surgical disease—multivessel disease or left main disease—is found on a catheterization for STEMI, I nonetheless think it is almost always appropriate to still treat the infarct vessel, abort the infarct, and then, when the patient is less critically unstable, take care of left main or multivessel disease if indeed it is not percutaneously revascularizable.

The other thing I want to say relevant to pretreatment with a P2Y12 inhibitor in STEMI is that radial procedures are performed in the overall majority of STEMs at the place I last practiced, Geisinger, and in many of our hospitals where I now practice at Northwell. That reduces the potential downside of giving a potent P2Y12 inhibitor upstream.

DR. GRANGER: That is an important point, I think, and it addresses another one of these transition clinical interfaces of going from the ED to the catheterization lab. Deb, from an ED perspective, comment further on the whole issue of risk stratification. You mentioned a couple of tools—the HEART score, TIMI risk score—and we have the Global Registry of Acute Coronary Events (GRACE) risk score,45 for which we have some evidence might be useful to guide who would get particular benefit from an earlier catheterization strategy.

And then we have simple things like, I think Tim mentioned, are there elevated cardiac biomarkers at presentation? Dynamic ST changes? Heart failure? Could you speak a little bit more to what is helpful to you as an emergency physician for risk stratification?

DR. DIERCKS: I think the biggest challenge we have are management of those without a classic presentation. I fully agree, for the patient with typical symptoms, elevated markers, and an abnormal ECG, everyone tends to agree with the management strategy. In those patients without such
a clear management path are where algorithms, protocols, and order sets are invaluable to get everyone the right medications as soon as they need them. Where the risk stratification tools become very helpful are with those with more atypical symptoms, who have low elevation in their initial troponin, and then you’re stuck asking, “Alright, is the next one going to be higher or should I just wait? Is this really secondary to some other cause?” That is where the risk stratification tools are useful.

I think emergency physicians are much more comfortable using risk stratification tools to rule out a disease and to identify low risk. In these situations, the way we are really using them is to identify those at higher risk for adverse events. The TIMI score has been used for that, with high-risk being scores over four. The GRACE score, because it is so complex—although I think it has probably got the best data—hasn’t gotten used as much in the ED setting.

DR. GRANGER: Deb, we should probably at least mention the fourth-generation troponins that we anticipate may be available in the United States in the next several months. You may have more updates on that, and that will also be quite valuable in a more rapid ability to identify at least the very low-risk patients.

DR. DIERCKS: Exactly. I think that we’re going to be transitioning to more a rapid decision, including discharge to those low-risk patients, and probably changing how we use our observation units a lot for these patients with chest pain.

DR. GRANGER: Actually, Deb, comment on this, because I think this may be another key opportunity for us around this topic of institutional protocols. When we get the ultrahigh sensitivity troponin, if there isn’t a protocol in place, it is going to be a disaster for cardiology and for emergency medicine, I think, not knowing what to do with detectable troponins. And if one uses, for example, the Abbott troponin-I assay, something like 80% of normal people will have a detectable level. We really will be forced to have more guidance around what to do with these, and that might be an opportunity to make sure institutions have their ACS algorithms up to date.

DR. DIERCKS: I’ve been going through that process in developing a pathway at UT Southwestern. It is interesting the barriers that come up from an emergency medicine perspective, and that is fear of discharging someone inappropriately, and having the institution not support them if something happens. That is really where these multidisciplinary pathways and institutional protocols really help the emergency physician.

We have developed an institutional pathway, and that provides some reassurance that if you’re going to disposition somebody and they’re that less than 1% that come back with something different than expected, that you’ll have some institutional support for your decision making. It has been interesting really getting down to the bottom of what the barriers are to protocol development, and it really is physician fear of critique if something goes wrong.

DR. GRANGER: Peter, let’s say that you have an algorithm that features one of the newer P2Y12 antagonists, ticagrelor or prasugrel, because you believe that the trial results showing about a 15% to 20% additional reduction in major cardiac thromboembolic events is meaningful. You have that on your algorithm. Let’s say someone gets started in the ED on ticagrelor, and then they can’t afford it. What advice do you have to give to institutions around this problem where we start something, and then we either have to transition or they get sent home and their pharmacy benefits don’t cover it, and then they end up stopping the treatment. How do we deal with this?

DR. BERGER: I think that it is a very common issue, either because of price or other considerations. I will tell you—and again, I don’t have very strong data to support this belief and practice of mine—I believe that what is the best medication at the time of a presentation may change in the days, weeks, or months after an intervention.

Let me skip the price one for a moment, although that is an important consideration. For example, if I have a very noncompliant patient for whom a twice-a-day reversible P2Y12 inhibitor is going to be a challenge, I’m not going to recommend that. If that is what they were started on at the time of discharge, I may well change to a one-a-day irreversible P2Y12 inhibitor days, weeks, or months after the procedure. If the person develops a need, for example, for an anticoagulant, I’m not going to administer one of the more potent anticoagulants along with the anticoagulant.

Clinicians need to know how to switch antplatelet therapy most safely. Sometimes you need to re-bolus the patient, and sometimes you don’t. And I would recommend that everyone get comfortable with knowing how to go from one P2Y12 inhibitor to another. But again, I believe that in a given patient, the drug believed to be optimal for that patient may change over time.

DR. GRANGER: That is a great point, and that probably should be part of a comprehensive ACS algorithm, to include what your institution recommends in terms of switching. Peter, one thing I was really impressed by when you were at Geisinger is you had a policy to improve adherence, especially during the highest risk period of stent thrombosis. For patients who’d undergone stents, they did not leave their hospital room to be discharged
unless they had a supply in their hand of 30 days of a P2Y$_{12}$ antagonist. Is that something that we should promote as a standard around the country, and are you doing that at Northwell?

**DR. BERGER:** We are in the process of trying to implement that at Northwell; I do think it should be done. It wasn’t only that we gave patients a 30-day supply of their P2Y$_{12}$ inhibitor prior to discharge, but we gave a 30-day supply of other newly prescribed cardiac medications as well. But importantly, we also followed up at around 20 days and 25 days with phone calls and other sorts of reminders. Best available data suggest that we ended up with an unheard of 99% compliance rate at 3 months.

One of the motivators for us to launch this was we had an insurance company, and we were able to analyze billing data for the approximately 500,000 patients that we insured. We saw the frequency with which patients discharged after receiving a coronary stent filled their prescription on the day of discharge, the day after, 2 days after, 3 days after, and never. The results confirmed what we all know, that adherence to medication is very poor, that non-adherence turns out to be enormously expensive if the patients suffers stent thrombosis and is not in the 20% or 30% or so patients who die suddenly from the stent thrombosis, but rather, is in the remaining 60% or 70% of patients who typically suffer a large MI. We targeted P2Y$_{12}$ inhibitors first with this adherence initiative, and it couldn’t have gone better.

**DR. GRANGER:** Good. Tim, you brought this up as well; I wonder if you have any other comments. For example, it depends on which data source you look at, but let’s say for continuing non-STEMI are very challenging.

**DR. HENRY:** Yes.

**DR. GRANGER:** Two other issues with non-STEMI are very challenging. Right now there is considerable controversy about how quickly a patient

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**Clinical Implications**

- There are several evidence-based clinical options for the management of ACS patients. However, many institutions lack a standardized approach to ACS treatment.
- Every institution should have a protocol or a basic framework for applying ACS treatment that includes the use of algorithms and standard orders.
- The effective treatment of ACS in the hospital should be a systematic approach that includes an interface between the EMS, ED, catheterization labs or diagnostic component and the hospital wards.
- A P2Y$_{12}$ antagonist should be administered upon arrival at the hospital for those patients with a clear-cut ACS diagnosis.
- The clinical algorithm should also include information on how to switch antiplatelet therapy safely.
- Effective standardized ACS treatment should also include a systematic transition to outpatient care, follow-up and treatment up to 1-year post discharge.
- Patient education is also critical and should be implemented as part of a standardized protocol both in the hospital and at discharge.
- Follow-up treatment should emphasize the importance of dual platelet therapy.
with a non-STEMI should undergo cardiac catheterization, and it varies dramatically from across the country. The average time in some institutions is less than 10 hours. In other institutions, it is 2 days. Having a standardized plan of how fast you get these people to the lab, I think is very important. There was a trial just recently that showed that if you actually have a cardiac catheterization in less than three hours, those patients did better than if it was 24 hours.9,10

While the data are somewhat conflicting, I would also say the earlier you get these patients to the lab and get them revascularized, the better it is in terms of discharge efficiency. If you can get patients to the lab within 10 hours, likely most of those patients go home the next day. If you don’t catheterize somebody for two days or three days, well then you automatically have a longer hospital stay, so cost effectiveness and hospital flow play a role as well.

The second point that it is controversial now, is which P2Y₁₂ inhibitor to use, and should you pretreat? I think in STEMI, it is pretty clear you should get the P2Y₁₂ inhibitor on as quickly as possible. In non-STEMI, it is a little less clear because about 10% of those patients will have multivessel disease and may need surgery. The question is, should you give the P2Y₁₂ inhibitor before or at the time that you decide to do the PCI?

Then you also have a new intravenous P2Y₁₂ inhibitor, cangrelor, which is available. Where should we use cangrelor? When should we pretreat? Should we pretreat? I think it is a challenging area, and that illustrates even if you had a really good protocol 6 months ago, new data, new things come along that make you constantly look at your protocols and consider whether you adjust them.

**DR. GRANGER:** Great point, and of course your strategy for the timing of catheterization strongly influences that, right? If you’re going straight to the catheterization lab with a non-STEMI and the patient hasn’t yet gotten a P2Y₁₂ antagonist, then the trade-off is different than if you’re going to wait a day or so.

You bring up another key point, including for Deb and the ED, and that is that the length of stay now is becoming shorter and shorter. That really requires us to begin patient education earlier and earlier, because the last thing we want is somebody going home without understanding their treatment plan, because then they’re going to be much less likely to be adherent.

**DR. DIERCKS:** It is interesting. I think all of us would argue that the length of stay for people in the ED in particular is short for those going immediately to the catheterization lab. The overall length of stay in the ED is increasing because our hospitals are full a lot of times, which kind of adds another layer to your statement—I do think the ED can be used for education. The question is, who can do it? That is really where I think emergency physicians just don’t have the time unless there are pathways already created, and pamphlets available for the patients while they wait to go upstair. Again, there are, in my mind, a lot of opportunities and hours that are spent not being as productive for patients while they wait for inpatient beds.

**DR. GRANGER:** Great. This has been a great discussion. I think this discussion has been incredibly useful to highlight the fact that all of us are going to need to be re-looking at our care pathways, algorithms for managing the patient with ACS in our institutions and health systems, because things are really changing. Length of stay is shortening. Deb, as you pointed out, ED stay may be increasing, it certainly is a big issue for us here, and our tools are changing with new biomarkers that will be coming available.

We’re in an era where providing more efficient care and shorter length of stay when safe is something that we all want to be doing. That increases both the need and the value for having institutional standardized approaches for how we manage these patients. We’ve talked about everything from EMS through hospital discharge, and out to a year later where the transitions provide important challenges and opportunities to improve how we provide care.

I would like to thank you Deb, Peter, and Tim, for a great discussion, and conclude our medical roundtable.

**REFERENCES:**


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