(PLEASE NOTE: Transcribed automatically by Vimeo; mistakes are possible/likely. Our apologies.)

TRANSCRIPT - GR 12 13 24 ***"Contemporary Questions in the Management of ST-Elevation Myocardial Infarction"*** guest speaker Patrick Stafford MD, University of Virginia

Internal Medicine Grand Rounds

- Welcome to medicine grand rounds, everyone, Brian Newloud. I'll take us through some of our Cme. Slides as we await great learning from Dr. Patrick Stafford. Today Chief Resident Shaina San will introduce Patrick in a second. Again, for faculty recording. Cme, this is your key slide here with today's activity. Code 2, 2, 6, 3, 3, and let's welcome up, Patrick. Now, alright. So China treatment.
- Hi, good afternoon, everyone. It's my distinct pleasure to introduce Dr. Patrick Stafford. Admittedly. It feels strange to call you Dr. Stafford as calling you Patrick, all of your residency and fellowship. But Dr. Stafford is currently an assistant Professor of Cardiology at the University of Virginia. He attended Medical School at the University of Maryland, followed by Internal Medicine Residency, here at Uva and stayed on for fellowship in cardiovascular disease and interventional cardiology, for which he's made a very remarkable impression among the internal medicine residents, noting him as an excellent educator and mentor, and during his time here at Uva he's been active in research with multiple 1st author publications, abstract presentations, and a book chapter. He's won the Department of Medicine Fellow of the Year Award, and the Npgo Nursing Excellence, award for Exemplary Resident and Fellow Physician and the Department of Medicine Research and scholars week outstanding publication award. We're very glad that he stayed on as faculty here, and we're very pleased to have him speak with us today, so please join me in welcoming him perfect.
- Hopefully. You guys can hear me. Okay.
- awesome. So thank you for the very kind introduction. So today I'm going to be talking about contemporary questions in the management of stemicare
- disclosure slide, no financial disclosures. I am a sub investigator for the complete 2 trial which I will mention today.
- but nothing else there. A couple of learning objectives to keep in mind. So we're going to review the epidemiology and history of the treatment of Acs and stemicare
- demonstrate some multiple large landmark clinical trials, and how that forms an evidence base for what we do for our patients with Stemi review, some ongoing areas of investigation and debate in Stemi care that will make up the bulk of the talk and then highlight some future directions for the care of our Stemi patients.
- So we know that cardiovascular disease has been the leading cause of death in the United States since at least 1921 cardiovascular disease is a very broad category of diseases that includes ischemic heart disease, stroke, hypertensive heart disease, arrhythmias, valve, disease.
- heart failure, etc, etc. On and on this map from the Cdc. Shows the concentrations of States with the highest cardiovascular death prevalence with the top quintile being in the south and southeastern United States, comprising of States like Mississippi, Alabama, Arkansas, Tennessee, Kentucky, etc.
- Fortunately, over the past

- couple decades the cause of death rate or adjusted death rate for cardiovascular disease has been decreasing at about 5% over that period of time.
- About 20.1 million adults, age 20 and older, have coronary disease and coronary disease is the cause of death in some 400,000 patients in 2020,
- 20% of those in individuals less than the age of 65 so very prevalent.
- Looking county by county for this Virginia.
- as you would expect southwest of the State and the eastern shore of Virginia have some of the highest prevalence for cardiovascular disease. These are our more healthcare.
- empty regions, so to speak, with fewer major referral centers surrounding it, fewer cardiologists and then a little bit closer to home. Charlottesville itself has a total death rate for cardiovascular disease of 311 per 100,000 patients.
- So more data
- approximately every 40 seconds. Someone in the United States will have a myocardial infarction. There's about 600,000 new myocardial infarctions every year, and 200,000 people with recurrent mi, who have had one previously.
- 1.2 million individuals are hospitalized with acute coronary syndrome every year, the majority of those being and Stemi non-st elevation, myocardial infarction. The remainder are stemi patients, and this has tremendous healthcare cost to insurance companies Us. etc. The economic impact has been estimated as high as 150 billion dollars annually.
- I think it is important always to discuss where we've come from in the care of these patients. Just puts it into context a little bit.
- So over a century ago Herrick described the clinical features of patients with Mi. During postmortem examination. He was among the 1st to publish this on this topic, and found that the majority of the patients that he investigated with myocardial infarction had thrombosis of the coronary artery. What was still unclear, if the thrombosis was the cause of the mi, or the consequence or effect of it.
- Unfortunately, early in the care of Mi there were very limited medical treatment options. Things like morphine, oxygen, digitalis and diuretics were kind of the mainstay of treatment. We know most of these to be hazardous, or at least ineffective. In the current age of stommy care patients
- patients spent weeks in the hospital in their bed. They were only allowed to shower on the 10th day of hospitalization. Otherwise they were just laying around
- getting their medications, and physicians would often come in the next morning caring for their Stemi patients to find that they had passed away overnight from sudden cardiac death of some flavor.
- Whether it was arrhythmia or a mechanical complication of their mi.
- So from up until 1961. We really didn't have much to treat these folks, and we just convalesced them in bed.
- Subsequent to that era.
- the development of continuous Ecg. Monitoring and admission to patients into the coronary care unit, or some specialized cardiac Icu became more into favor. Physicians like Desmond Julian at the Edinburgh Royal Infirmary developed the Ccu with specialized nursing care. Most importantly, a defibrillator available at bedside to shock people out of life, threatening arrhythmias
- as well as training staff in acls and resuscitation of these patients with their Mi.
- The immediate defibrillation or the availability of that reduced in hospital mortality from 30% down to 15% with just that one intervention being available

- subsequent to that, we have our more modern coronary reperfusion era with medications initially, like streptokinase and Tpa, and that has since obviously progressed to
- more widespread things like
- facilitated and rescue Pci. And in the more modern areas we're all familiar with primary Pci taking folks to the Cath. Lab with St. Elevation. Myocardial infarction early.
- Looking back at things, though in 2,005, only about 25% of Stemi patients were treated by primary Pci, despite there being evidence for many years that this was beneficial to patients, this was due to lack of cath lab availability, lack of infrastructure to transport patients from the field to the Pci center or from outside hospital to a pci center
- so early on thrombolytics were the mainstay of therapy. There
- some economic analyses from original trials, like the Pami trial, showed that Pci was cost effective even compared to a relatively cheap therapy at the time, such as Streptokinase or Tpa.
- and it was cheaper, and not not only cheaper, but more beneficial to patients to take them to the Cath lab sooner.
- This ultimately led to the adoption of 24 h Cath labs, as we know today.
- So getting into some trial data as any good cardiology talk will have.
- There are many advancements since the original discussions of pathogenesis and pathophysiology of Mi by Herrick et Al. In 1912, and then jumping through some of the different trials and eras
- multiple advancements in treatment. Even over the past 2 decades, stents evolving from bare metal stents to drug eluding stents, refinements in pharmacologic therapy with more potent antiplatelet agents shifting away from certain drugs that are shown to be less beneficial, like Gp.
- 2 b. 3. A. Inhibitors that
- usually only cause bleeding complications and have less of a routine clinical benefit.
- The 1st randomized trial, comparing Pci with balloon Angioplasty versus Intracoronary, Thrombolysis was
- published in 86 by O'neill et Al. And New England Journal. Medicine, 56. Patient trial
- showed improvement in ejection, fraction, and less residual stenosis with Angioplasty as compared to Thrombolysis. 7 years later Pami was published. This was nearly 400 patients with acute mi randomized in the 1st 12 h to receive Thrombolysis or balloon Angioplasty. Primary Pci Pci demonstrated reduction in mortality at 6 months from
- to 8.5% from 17% compared to Thrombolysis. So pretty remarkable improvement there, and this these trials, among others, really ushered in the
- early era of Pci as a viable strategy for mi therapy.
- Many more trials here. Tammy, I had mentioned
- prior ones, such as the Gisi trial, which was really the 1st cardiology. Mega trial demonstrated reduction in mortality of Streptokinase infused intravenously. More recently trials like Cadillac, a large multi-center randomized control trial, enrolling 2,000 patients, showed lower composite outcome with those who received stents as composed to Poba alone.
- and then the most recently on this list, at least horizons. Ami, published in 2,009, took 3,000 patients with drug, eluding stent compared to bare metal Stent and

showed benefit and efficacy of drug, eluding, stent compared to bare metal stent. So lots of trials that lead us where we are today.

- Lots of pharmacology trials as well. Again, I haven't mentioned Gissi and some of these other ones.
- Along with all of the technologies and cath lab toys we have available. We have a lot of medications and pharmacologic therapy that has been evolving over the years, again shying away from medications like 2 b 3, a inhibitors still anticoagulation and antiplatelet agents are a mainstay of what we do in the Cath lab and what you folks see us caring for them up in the coronary care unit or on the acute Cardiology service.
- I found this
- couple of graphs interesting. So this was insights from the Sweetheart Trial, which is a Swedish national registry showing the uptake and the use of different medications and procedures for the treatment of mi over time.
- With things that we've had for a while like beta blockers, and some form of coronary perfusion
- being really key treatments and high percent of patients get treated with those later. The uptake of some of these newer therapies, as they gain more and more data, more and more availability, showing benefit to these patients on the right graph with decreased morbidity. Mortality, mi heart failure, rate, etc, etc, across the board over time.
- So the take it for the Europeans to have really good, clean, long-term data for countrywide patients. That's something we've lacked a little bit in the United States. Unfortunately.
- now, onto the bulk of the talk, looking at the areas, investigation and debate for stemicare itself.
- So what causes lots of questions? These slides are courtesy of Dr. Gimple, who has given the fellows for many years an excellent talk on Stemicare and a lot of these trials in great detail to us.
- But think about all the questions we have surrounding Stemicare, and there's a trial for it at some point.
- But there's a lot of questions with care of Stemi, whether what causes heart attacks, what medications should we or shouldn't we use? What combinations of therapies and procedures and medications, we should or should not use
- as many questions as there are. There are still many challenges, sometimes with the care of these patients, even though there may be a best test answer or best study answer. There unfortunately, can be access challenges, availability challenges, and somewhat
- paralysis of choice. Sometimes that can make it a little bit more difficult to care for these patients.
- 1st thing I wanted to bring up as an area of ongoing question or debate is the definition of Stemi itself. So over the years multiple different definitions have been used leading to controversy and confusion. In the 19 fifties, the Who World Health Organization came out with the
- 1st definition of Stemi through a more epidemiological approach. Primarily Ecb Ecg. Based definition of Mi with. And
- that's been the case, since with very minor modifications to specific criteria. But we still use an Ecg. Based approach to the definition of stemicare.

- with the addition of more sensitive biomarkers, Ckmb. Troponin, high sensitivity, troponin, etc. As well as refined clinical approaches and increased diagnosis of myocardial injury. There have been
- updates to that definition over time.
- So this was from the 2,000 edition of the Stemi definition and Guidelines by Braunwald, who wrote one of the large cardiology textbooks that we all may have used in medical school
- thinking about it. Ecg. Was used to classify 2 types of mi. There was the Q wave mi, or the transmural infarction. The implication that the Q wave represents, through and through endocardial to epicardial necrosis, and then everyone else was non-q wave or non-transmural infarct indicating less extensive myocardial damage and increased for recurrent events.
- so this was really Ecg based definition whether or not you had Q. Waves or not. And if you didn't have any Ecg criteria and did not have biomarker elevation. You get lumped into unstable angina.
- So all 3 of these were were acute coronary, syndrome differences based off biomarkers and based off of ekg criteria
- however, more recently the
- criteria has been stemi versus n stemi rather than Q. Wave mi non q wave mi.
- We're on our 4th universal definition of mi released in 2018 very specific criteria for Stemi these days, so newer presumed. St. Elevation of the J point and 2 contiguous leads.
- 1 and all other leads than v. 2 and v. 3, for v. 2 and v. 3. It gets very nitpicky with age and sex adjusted cutoffs for St. Elevation. What is or is not allowed when there is some baseline, Ecg. J point elevation of greater than a millimeter, you're comparing it to a prior Ecg. To see if there's J point elevation of a millimeter, or more than their baseline to call it a stemi.
- It is important to note that these millimeter criteria are based off of age and sex studies back with the
- use of Ckmb as the biomarker of choice rather than troponin and
- despite this, we're still using those criteria today.
- But is it the whole picture? Because this is the most common? Ecg. We think of as a Stemi St. Elevation, J point elevation.
- But there's a whole host of other
- Ecgs that we call Stemi equivalents or high risk Ecgs that do not technically fall under the criteria of a stemi that we still sometimes treat as a stemi, which can make it challenging of who we should or shouldn't take to the Cath lab who we should or shouldn't give certain medications to.
- So these so-called stemi equivalents may have an acutely occluded coronary artery.
- People with stomach equivalents are
- less likely to get taken to the Cath lab sooner and have a delayed reperfusion. Worse prognosis, worse outcome.
- About
- 25% of patients who are diagnosed with stomach do not have an acute occlusion when we take them to the Cath lab. Similarly, we miss many people with
- not a stemi on Ekg. Who do have an occluded artery as well. So again, just getting at Stemi is not a perfect definition.
- This is just some data showing that patients diagnosed with n-stemi. So patients not having stemi on Ekg

- taken to the Cath lab at some point you can see some 40,000 patients in total, about 10,000 of them are 25%.
- Have an occluded artery when you take them to the Cath lab with increased risk of all cause mortality, both short term and long term and increased risk of major adverse cardiac events.
- So it's a it's a high risk population that we should pay attention to.
- So there's been a more recent shift.
- as there was from Q wave mi to stemi. Now from stemi to potentially occlusion, myocardial infarction as a more inclusive definition of stemi care
- kind of lumping together all of these patients with an acutely occluded artery, regardless of what their Ecg. May or may not say, taking them to the Cath lab, reperfusion them sooner, decreasing their risk of adverse cardiac events and decreased risk of morbidity and mortality.
- so this is based off of trials like the difficult trial, I promise you. That's not a misspelling. That's just the acronym in which
- 2 cardiologists took 3,000 patients blinded to any outcomes looking at current stemi, criteria, and other subtle signs of ischemia. Whether that's posterior st depressions indicative of posterior stemi.
- And I'll get to more criteria on the next slide, showing that these patients actually
- were reclassified as Omi rather than nstemi, and the patients with Omi had much larger infarcts and higher long-term mortality compared to patients without that.
- Again. This is just one study of a couple that's shown that
- bit of a busy slide, I realize. But looking at the stomach criteria in the left column rather simplistic, and the Omi column in the right.
- That is a bit more
- comprehensive, perhaps so stemming criteria. Ecg, but now we're incorporating Ekg signs whether that is St. Elevations.
- but also clinical criteria and other signs, including those high risk
- Ekgs I had shown you before on the prior couple slides
- and trying to make sure that we're doing the right thing for our patients. So it's really lumping together the current Stemi patients with your high risk, and Stemi Ekgs may be borderline, but they're having a lot of chest pain. Should I take them to the Cath Lab patients under one definition
- rather than just saying, Oh, they're an nstemi. They can wait till
- 24 to 48 h to take them to the Cath lab.
- What are our goals with this potential paradigm shift. Definition, change.
- one goal is to improve outcomes for these patients with high risk lesions. One goal is to reduce false, positive stomach activation that can lead to staph burnout
- in the in the Cath lab.
- It's to shift our decision making from just looking at the Ekg to looking at the entire clinical syndrome, involving some other imaging things. Whether that's point of care, ultrasound echocardiogram, ct.
- Perfusion, imaging whatever
- flavor, but doing more than just looking at the Ekg. And and saying, It's a Stemi. It's not a stemi to the Cath lab or not.
- There is some hope that we will be able to incorporate artificial intelligence, to screen Ekgs and pick up on some of these more subtle signs of ischemia that can be missed easily without a trained eye, or at least a comprehensive look at an Ekg.

- so jumping so questions about definition of Stemi, questions about what we do with them when we take them to the Cath lab as well as you would imagine.
- So you see an Ekg on the left side. I'll tell you it's an anterior Stemi. There's anterior St. Elevations. The patient in front of you is having chest discomfort. We take them to the Cath lab whatever time of day, and we found an occluded led that was successfully reperfused.
- What we also see, though, is this, quote unquote non-culprit lesion in the Om
- over here that is severely stenosed, and there not the culprit lesion that was causing their anterior St. Elevations and chest pain that got better once we stented it. But it's still there, and it still doesn't look great after you stent the other artery as it wouldn't.
- So what do we do with this lesion? Is revascularization of this lesion beneficial in the Stemi population. How do we think about it? How do we evaluate it? And if we're going to do something about it, at what time do we do something about it right there in the Cath lab during their index. Pci.
- do we ever do something about it? So a lot of questions surrounding that
- I'll show you some data suggesting that patients with multivessel disease at the time of their stemi do worse over time compared to patients with no non-culprit lesions or fewer number of lesions that are present
- in patients with stemi about 40 to 60% have multivessel disease, with other significant lesions and patients with acs and multivessel disease have higher rates of mortality and reinfarction. So this included this data here is from some 2,000 patients presenting with stemi undergoing primary pci
- and multivessel disease due to non-culprit lesions show with this, data is,
- leads to the question of whether we should revascularize these folks to improve outcomes.
- So we have a lot of trials to to look into this as well.
- I show here 5 major randomized clinical trials, looking at complete revascularization in patients with Stemi.
- and whether they had culprit only Pci or later on got non-culprit pci overall. They tend to support complete revascularization, regardless of whether it's during the index procedure index hospitalization or send them home, bring them back
- on a readmission so reduced.
- Mace, usually driven by reduction in myocardial infarction and need for repeat revascularization.
- Getting into some specifics of these studies. The Prami study from 2,008 to 2013, 5 centers in the United Kingdom, enrolled about 500 patients, with Stemi randomly assigned to preventative pci, or
- no preventative pci, as they called it, aka culprit only, or non-culprit only pci.
- Subsequent pci for angina was only recommended for refractory angina in those who did not receive the non-culprit pci off the bat
- primary outcome of a composite of cardiac death, non-fatal, mi refractory angina demonstrating benefit in revascularizing these patients with a preventative Pci
- upfront.
- We have a lot of things in the Cath lab to help tell us if a lesion, I think, is 70%. And Dr. Agasta thinks is 50% is significant or not. Things like fractional flow reserve or Ffr is one such test. There are many other ones. It's a pressure wire based technique that senses the functional severity of a coronary lesion to help guide our Pci strategy or not.

- showing here 2 studies that compare Acute trial and denami, 3 per multi trial that demonstrate Ffr. Guided. Complete revascularization is beneficial compared to infarct only revascularization or therapy.
- Both of these show that whether it's during the index procedure or the index admission that treating these folks is is more beneficial than not.
- But that still doesn't leave some unanswered question. We know that culprit
- only is, is inferior, perhaps, to non-culprit only. But do we? When do we do it?
- There are some
- studies looking at that as well, not as well fleshed out as as we would hope, and still an area of ongoing research and investigation.
- The complete trial was
- to determine the effect of non-culprit pci timing on major cardiovascular outcomes, and also the time course of the benefit of the revascularization.
- Some 4,000 patients with Stemi and multivessel CAD were randomized to stage non-culprit, pci, or culprit lesion only Pci.
- and that the non-culprit lesion Pci was stratified to during or after the index hospitalization.
- I think the big point of this is to just show that complete revascularization was associated with reduction in the hard outcomes of death. Recurrent mi, etc.
- Since the primary outcome was death or mi, but it was a bit unclear as to when the best time to treat them is
- at some point is better than not doing it at all.
- More studies with the multi-star ami trial. This was a open label, randomized non-inferiority trial.
- That was at 37 sites in Europe, patients with stemi and multivessel disease assigned to go on immediate Pci or Pci of a culprit lesion, followed by staged multivessel Pci of non-culprit lesions 19 to 45 days after their stemi catheterization.
- Showing benefit for the staged group over the immediate group.
- As long as they're hemodynamically stable, I think, is one of the one of the caveats there
- for cardiogenic shock patients. However, we have some pretty strong data from the culprit shock trial to demonstrate that there is harm in taking patients for multi vessel. Pci off the bat. If you have cardiogenic shock, so primary endpoint of death, severe renal failure leading to renal replacement therapy within 30 days after randomization.
- and the 30 day risk of death or renal failure was lower among those who went pci of the culprit lesion versus those who underwent immediate pci. If we're having to use more contrast and put in more stents and keeping patients in the Cath lab longer without
- Ccu therapy that we can provide, they tend to do worse.
- Sorry for that. So, looking at the guidelines we use you can see
- cardiogenic shock Stemi routine pci in in red
- down there routine pci of a non-culprit artery, that is, and kind of a flow sheet algorithm of what we keep in our heads in the Cath lab when we're looking at someone with a stemi with multivessel disease in front of us as far as timing and what we should or shouldn't be doing for these patients in the lab.
- And this is from the 2021 acc. Aha, sky guidelines for coronary artery, revascularization.

- There are some trials in the works to look at this things like the complete 2 trial and the complete 2 Oct. Trial, which is the optical coherence, tomography side of
- arm of the trial, I guess. But this is a prospective multicenter, Rct. Comparing Ffr. Guided angiography, complete revascularization in patients with CAD, who present with either stemi or n-stemi, and underwent culprit lesion Pci.
- using some composite outcomes, and then looking at the imaging characteristics of the plaque to see if there's certain things we should be looking for on those patients to determine which lesion should get revascularized versus not, or perhaps the timing of those.
- And then there's some trials from Europe like the Air Stumi trial that's using Ffr. Angio, which is an Ffr adjacent technology looking at similar outcomes and things for those patients
- switching topics. Yet again, because there are a lot of questions to help answer. For
- you see, on the left here the kind of traditional shock paradigm for cardiogenic shock. At least this was illustrated by Hollinberg, and was in Harrison's textbook.
- looking at the
- hemodynamic and inflammatory consequences, or results of myocardial infarction, and how that eventually leads to ischemia, myocardial dysfunction, death, and kind of this spiral down the pathway.
- Acute mi, as we know, is one of the leading causes of heart failure. Cardiogenic shock is one of the leading causes of death for patients with acute mi, and, despite recognition of it and treatment of it, mortality remains unacceptably elevated for these patients somewhere around 40%, despite all of the advances that have been made and we do know that every 5% increase in infarct size is a 20% increase in one year, hospitalization for heart failure and mortality.
- So is there anything we can do about that getting into the basic science. A little bit of it.
- the left figure demonstrating how ischemia, reperfusion, injury worsens infarct size. Looking at in the top, left at least in the things labeled a various modes of cardiomyocyte death that occur during acute mi ischemia, reperfusion, injury, like necrosis, apoptosis pyrroptosis etc. and in b are the different manifestations of that seen in the Myocardium itself, with
- microembolizations, interstitial edema that leads to capillary obstruction, stasis of formation of intravascular cell aggregates, impaired vasomotion of those cells. Leukocyte adherence increases. Capillary rupture causes hemorrhage. So all sorts of bad things from inflammation from ischemia, reperfusion, injury
- on the right screen i'm demonstrating how infarct size. Not only is this combination is not only just, ischemia induced and reperfusion induced injury. It's a combination of both.
- The ischemia induced. Injury depends on the duration of ischemia and amount of residual blood flow. But similarly the reperfusion, injury
- depends on the duration and severity of the preceding ischemia. The greater the ischemia induced injury. The less myocardium is salvaged, but also the less that is potentially damaged by reperfusion itself.
- So this is from a myocardial infarction model, not a cardiogenic shock model, but this was using an animal model with balloon induced occlusion of the lad left anterior descending artery for 120 min, followed by 120 min of reperfusion, with or without mechanical support. So in the they essentially tied off the lad for 120 min, and then let it reperfuse for 120 min or they tied off the led for 120 min. Did an

additional did 30 min of mechanical support, and then reperfused them for 120 min thereafter on the left group of figures you see some pressure volume loops, taking you way back to medical school, perhaps showing Lv unloading and different metrics for myocardial function like stroke work, mean wall stress, peak wall stress and wall tension, demonstrating the benefit of mechanical unloading of patients with Mi for 30 min before reperfusing them and then on the left, perhaps a more tangible group of pictures demonstrating Mi size, based off staining top group of pictures here showing larger Mi size compared to the unloading group with the smaller white blotch where the led sits.

- Also have less biomarker elevation with these patients.
- So how do we support these patients? We, of course, have many options. We have things like intra-aortic balloon pumps, and then our more continuous flow, percutaneous lv devices like impellas and tandem hearts and Ecmo and other such devices. So a lot of options or how we support them. The balloon on the bright group of pictures balloon pump provides this counter pulsation to provide circulatory support, and started usually by femoral access and then you have microaxial flow devices that traverse the aortic valve by the femoral artery, and continuously remove blood from the Lv. Into the aorta for continuous unloading of the heart.
- So with the balloon pump, you have a small reduction in Lv. Preload small increase in stroke volume, but with the microaxial pump, and impella is the brand name of of what we use.
- You have more substantial unloading, demonstrated with increased Lvn. Diastolic pressure and pulmonary capillary wedge pressure as well as decreased pressure volume area analogous to decreased myocardial oxygen consumption and you have an Lv aortic pressure uncoupling with a closed aortic valve for patients with Stemi themselves. I showed you the prior animal model, the human model. This meta-analysis from 2015 looked at balloon pump efficacy, and then later study in 2022, looking at impella, efficacy in a different meta-analysis for patients for balloon pumps. Whether it was in cardiogenic shock or not. Cardiogenic shock, it was kind of a more neutral signal perhaps similar for the impela meta-analysis
- 7,000 patients in that 3,000 of those received in pellop pre-pci, and 4,000 during or post Pci.
- This one was perhaps a little bit more convincing that Impella placement prior to Pci may have a positive impact for short and midterm mortality. Compared with Post Pci. With similar safety outcomes, these patients tended to have cardiogenic shock, although the patients in the left group for balloon pump did not all have cardiogenic shock.
- So we need some more firm data on this. We have this pre-impella Pci trial, the Dtu Stemi pilot trial involving 14 centers in the Us. To look at the feasibility and safety of mechanical unloading in patients with Stemi only included 41 patients. In the end there was demonstrated safety to early unloading, but there was no long term benefit for early unloading for patients in the Cath lab.
- There is an in the works. Dtu Stemi randomized pivotal trial because the original pilot trial was not powered for hard clinical outcomes. So this is something that's ongoing and currently recruiting. Now aiming to recruit 700 patients with an anterior Stemi, with one of their primary endpoints being Lv. Mass. Affected by infarct size, by Cmr. At 3 to 5 days.
- Post Pci. So more of an imaging metric, and then some secondary outcomes that are a bit more tangible, perhaps, or maybe a bit more important than what the

pictures look like of mortality, incidence of cardiogenic shock, if they need transplant or mechanical support more durably long term and those sort of things.

- So a lot of trials. Where do we stand with it? Unfortunately, we don't have a ton of guidelines on the use of mechanical circulatory support during acute myocardial infarction. We do have some scientific statements from the Aha, and more recently from sky expert consensus statements, saying that you should recognize patients have cardiogenic shock, you should treat them for cardiogenic shock. Whether that's a right heart, catheterization or echocardiogram showing some metrics consistent with that. And sometimes these mechanical support devices can help them before. Pci. But no, no firm recommendations, because we just don't have firm data to show any benefit as of yet.
- So where are we going from here? And there's a dozen other questions of course you could answer or ask about stemicare. These are just some of perhaps the more recent ones that have been brought up and the ones that have been investigated. More.
- There are some future approaches that may be on the horizon, things like super saturated oxygen therapy, which was recently FDA approved to reduce infarct size with anterior Stemi with it, treated within Pci. With Pci within 6 h of symptom onset so pretty narrow group of patients, if you think about it, a lot of criteria to get there. But it did reduce infarct size and was relatively safe, and some microscopy data demonstrates the endothelial structure and function improves, and there is increased microvascular flow.
- There was some high hopes for intracoronary hypothermia the thought being you cool down the coronary artery, you reduce the reperfusion, injury, you blunt inflammation and thrombosis and myocardial metabolism.
- All of the prior large studies demonstrated safety, but lacked hard endpoint benefit. The euro Ice Trial came out a couple months ago, and was supposed to be the thing that the latest and greatest it showed safety. But again, no hard clinical improvement for outcomes for these patients. Unfortunately so it's not in current cath lab use kind of routinely.
- There are, of course, a lot of new medications, and and focus on treating inflammation and the consequences of mi not just opening the artery, but treating all the inflammatory sequelae of that.
- So this pictorial here is the putative model for history of stemi and n-stemi, with the effects of Pci and anti-inflammatory drugs. So patients have some baseline level of inflammation that's more chronic, based off of their degree of immune and inflammatory activity as well as cardiovascular risk factors and other risk factors on top of this Stemi causes an acute surge of inflammation that is, higher grade, and earlier onset than in patients with an nstemi and by stemi and nstemi. For the purposes of this picture I mean current definition of it not getting back to the Omi definition I was talking about earlier.
- Pci actually elicits an additional spike in inflammation that increases more inflammatory mediators from balloon and stent expansion. You throw down distal mycoemboli, and there is reperfusion injuries however, the negative effects of all of that is far outweighed by the actual benefit of opening the occluded artery and is over time shown to decrease inflammation.
- So with certain anti-inflammatory drugs, there is some hope that we may be able to increase this or decrease excess, early inflammation, reperfusion, injury, and not only that, but decrease their residual inflammation.

- Months, days, years, however, long after the Mi event itself.
- I'm going to shout out Dr. Abate, who is a co-author of this review article, and also shout out the Virginia art. 4. Trial that he is the principal investigator for so he and and some other collaborators published a recent article on all of the prior and current and future ongoing trials for inflammation in the cardiovascular space, I threw up 2 parts of that here, looking at the future approaches for the treatment of chronic coronary disease on the left, and acute myocardial infarction on the right side. There, again, especially highlighting the Virginia air. T. 4. Trial looking at interleukin, one blockade and acute mi for the prevention of heart failure, using Anakinra versus placebo with outcomes of cardiopulmonary fitness and heart failure occurrence. So any of the health staff that have been rotating up through the Ccu may see Dr. Abate and his collaborators coming at all hours of the day and night to enroll these patients in the Anakinra study so I've talked about a lot of things for stemicare. I've said that it is highly morbid with high mortality and health care costs but I hope I've left you with the impression that the term Stemi is not perfect can be refined a little bit further, perhaps to include patients with high risk and stemi, or something. That's not a stemi on Ekg, but it's still concerning, and we should still do something about it sooner rather than later.
- I hope I've left you with the impression that non-culprit Pci has a lot of data. It is beneficial. It's just not clear what the timing of that should be. I've demonstrated that early Lv. Unloading with some sort of mechanical support is promising, but there haven't been any huge clinical trials to show really long term benefit for these patients, and there's a lot in the pipeline that we are eagerly awaiting, and I'm sure there's stuff that is in the preclinical phase that will be coming to us sooner rather than later for more investigation. So
- lot of references. But I'm happy to take any questions.
- Not as much that I came across there. There is, outside of inflammatory the inflammatory space. I'll call it, because there's a lot there. Obviously, at least the ones I'm aware of here.
- I mean, we use our usual anticoagulants, antiplatelet agents. There is an injectable antiplatelet agent solatogryl that we have been enrolling some patients in as far as a treatment for Pci after the fact but the majority of the medication space data is inflammation, inflammation, inflammation. It's been a huge focus recently and one thing I may have failed to mention is the importance of regular Gdmt for coronary disease that you should know all along aspirin, flu, vaccine and regular vaccination is among the most important things we can do for these patients and just routine healthcare otherwise. But I'm sure there is Dr. Wolf. I'm just not sure specifics other than salatagrel. As far as current ongoing like Cath Lab, Pci Stemi things we can use there. There is a thought, or perhaps there used to be a thought of decreased healing, so to speak. You're not only blunting the inflammation and the bad effects that that I showed. But you're also blunting the healing process. There was, for example, prednisone steroid medication. We use to sometimes treat inflammatory conditions like pericarditis, and a whole host of other things can lead to increased risk of myocardial rupture and mechanical complications of Mi. Thereafter a lot of the more targeted therapies other than just blasting someone with a steroid like il one blockade, il 6 blockade colchicine, etc, have not shown that signal necessarily.
- So outside of the usual things, I would think about increased risk of infection increased other non-cardiovascular things. Necessarily, there hasn't been a huge signal that it is necessarily harmful that I'm aware of at least challenges of the so

what? Help help me with that a little bit? How? How would we figure that out? Better?

- Yeah, no, absolutely. Allow me to go back to the slide for just a second. I know it's a while ago. Slide wise. But so occlusion! Mi is talking more about the pathophysiology of the underlying problem with the artery. The artery is occluded, or the artery is not occluded. We equate that to be. You have St. Elevations on your Ekg but just because you have St. Elevations on your Ekg. Does not mean your artery is occluded, and because you don't, doesn't mean your artery is not occluded.
- So it's a very Ekg based definition. The St. Elevation is not the problem right? It's it's the thrombosis. That's the problem. So I think it's it's more. Yes, you're still recognizing your stommy. Patients have have St elevations and have chest pain and need to go to the Cath lab, but it's just opening the door a little bit more to these other patients, we used to think don't need an urgent Cath so we're certainly always there as a consult service, and happy to help out with some of these more borderline cases. Your sts are 0 point 9 not one, or they had chest pain that's now gone. But it came back and it's gone. What do we do with that guy?
- Or they have some other high risk feature. It's just recognizing that there's more to an occluded artery than St. Elevation. Your patient can still have a lot of chest pain. They can have hemodynamic electrical instability. Maybe we need to do a bedside echo and see if they have a wall motion associated with it. Maybe that leads us to go to the Cath lab sooner versus later.
- Maybe there's something else that leads us to think it's pericarditis causing their St. Elevation. Not an occluded artery. So it's perhaps just a more inclusive definition to include the current stemi and your high risk and Stemi patients under one umbrella to show that they do. Similarly, if you don't treat them, Stemis, and your high risk end Stemis with with an occluded artery, do very poorly compared to. If you go in and open it.
- So it's just kind of realizing that. And and being aware that they they deserve the same care that
- your run of the mill Stemi does.
- And again, there's a lot there's there. You could go on and on about ekg. Specifics orspecifics of an angiogram. But we're here to help out with that as as much as we can. Obviously there's a lot of that station, and like counter patient sure. So for patients with culprit lesion we stent and non-culprit lesions left over.
- I find here, at least, and at some other places I've trained, and and some other places. People I know work at. Very rarely do we culprit and non-culprit pci. During the index procedure itself.
- More so for nstemi than for Stemi.
- Part of that is, we want to see how they do, what their we don't know what their ejection fraction is. Necessarily, we don't know always what the renal function is going into the lab. I don't want to blast someone with
- 300 CC's. Of contrast to put a full metal jacket down every artery. I want to put out the fire, live to fight another day, bring them back. So it's things like renal function functional status of the patient degree of ejection, fraction, impairment perhaps medication, adherence that would lead me to do it sooner rather than later. If someone's in the hospital having residual chest discomfort that I can then say, well, their led is open, but their circumflex is 99%.

- Yeah, I'm going to do that before they go home. In all likelihood, if I don't get them on, if I can't get their chest pain under control with good medical therapy. But it's the patients with perhaps not as severe stenosis, or they do have an Aki, or they're a little bit frail, and I don't want to keep potentially harming them during a procedure that that I would maybe pump the brakes a little bit, bring them back to clinic or just schedule them for the outpatient Pci within a month. Usually, again, the the data for delay on these non-culprit Pcs.
- Was only out to 45 days, so we don't have a lot of to say like, How long should you wait? The the longest time I saw was the 19 to 45 day delay post discharge. But I feel like we've been doing an increasingly good job of doing Pci on these folks before they leave the hospital, depending on their risk factors and and what's going on with them.
- But good question!
- I wish we knew it would make our. It would make it a lot easier honestly to have a more streamlined pathway with with things, because it's a lot of discussion, a lot of time on rounds and a lot of time with the patient trying to figure out what to do. And and obviously some patients, you discharge, schedule them for their visitor, Pci, and they just never show up again, and they're walking around with an untreated, severe lesion that should get treated so it can be tough.
- I do not know of current plans to get supersaturated oxygen therapy at Uva.
- I it does have some benefit. Yes, but it I I don't know if the trial data is as strong as we would like it to be it is, FDA approved. Certainly, but it's not. I don't. It doesn't seem. Even though it does have some positive data. It doesn't seem to be super widely adopted
- practically as well.
- It does increase procedure time and and cath, lab throughput, and other things that yes, we want to treat all patients as as well as we can, but then it can also affect other patients getting cath care. So it's always it's always a balance with with all these things, because it's like with the intracoronary cooling you sit there for, however long cooling their coronary, just kind of sitting, cooling their coronary, taking up a lab space and an operator and staff. And if something else happens, what what do you do then but it so good question. But not that I'm aware of.
- Earlier this week we had a talk something like nonsense.
- How often are y'all using. Like. yeah, it's a good question. There, there's a lot of you could do a legitimately a whole talk on viability testing and and looking at which lesions should or shouldn't be treated, which lesions are significant versus not. I find it less. Once they've gotten to the cath lab and something else treated that we're saying, oh, you should get a stress test on there to look at their circumflex territory or Rca. Territory, or whatever it is. Specifically, once we kind of know it's there usually want to treat it, unless sometimes we're trying to find really fine tune. And if perhaps it's a higher risk, procedure or a higher, technically challenging lesion. Maybe, then we give pause and say, Well, get a get a Cmr. See how much territory is is affected by this. What do we need to do about this rather than just launching in head 1st and and doing something there? But some things that we're perhaps using a little bit more things like perfusion echo, and and in the cath lab things ffr, Ifr, Dfr ffr Ngo, etc. That can be more helpful, perhaps, but I have seen pretty much once the lesions there. It's kind of want to go after it, so to speak, rather than trying to get another test on top of it unless there's reason to alright. No worries. Thanks, guys.