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Released: 10/02/2024
Valid until: 10/02/2025
Time needed to complete: 29m

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Unveiling the Reperfusion Paradox

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Patel:
This is CME on ReachMD, and I'm Dr. Manesh Patel. Thank you for joining us. I'm going to be reviewing some key information on the burden of ischemia-reperfusion injury and the molecular mechanisms underlying the inflammation response in ischemia-reperfusion injury in patients following percutaneous intervention. So let's dive right in and talk about this in hopefully an understandable way.

So just to remind us all that ischemia-reperfusion injury happens after people have had a heart attack and get the artery opened, and contributes to important pathophysiology and downstream adverse events including expansion of the heart infarct size and heart failure. So just going through our usual timeline of thinking about this process, remember, pathophysiologically, we have a coronary artery that has plaque and then has a rupture and thrombosis and then complete occlusion. And within seconds, we start to have rapid bursts of hydrogen peroxide and other reactive oxygen species, ROS sometimes on documents you've seen, resulting in a cascade of cardiac damage. And those reactive oxygen species and others start to play a role, which we'll talk about in a second, on the cellular makeup of the myocardium downstream. And then in the following minutes to hours, there's neutrophil recruitment into this damaged myocardium to try to help it heal, but that often leads to inflammation, and that, in hours to days, leads to this inflammation and sometimes infarct progression.

So just to spend a little bit more time talking about that, so when the artery is closed pretty quickly, what happens is we stop producing ATP, and the vessels and the cells start to produce these reactive oxygen species, and they're really a critical factor in the genesis of reperfusion injury. We know enzymes such as xanthine oxidase and others derive and are involved in the recruitment of actually these reactive oxygen species and recruiting leukocytes there. The mitochondria in these cells start to depolarize, and the membranes start to have what we call breakdown or pores opening in them, and so these reactive oxygen species are also then coming out. And we also know that there are a variety of other oxidases that are present that lead to neutrophils coming and leading to swelling in the epithelium and the cells of the myocardium. As that starts to happen, as I said, in the seconds to minutes, we start to have these neutrophils coming to those regions in the myocyte, and they start to try to accumulate to help with the healing. But what happens post infarct and opening of the arteries, there's sometimes plugging of these vessels, there's some thrombotic milieu, and there starts to be increased injury in these areas as there's cellular breakdown. And what starts to happen after that is, over time, that cellular breakdown leads to the infarct expansion, inflammation, and worse adverse events, leading to heart failure, and eventually adverse outcomes for our patients.

Now how many such patients are there, for example, in the United States or worldwide? I'll use some of the US data, to give you guys a sense of that. In general, there's about a million people, around 970,000 patients, who have a heart attack in the United States on a yearly basis. And that, I often tell our fellows, is about two-thirds, one-third, or about 20% to 30% ST-elevation MI, and about two-thirds

with non-ST-elevation MI, and some smaller groups that have, I'll call it, very high-risk features. So many individuals there that have ST-elevation MI [myocardial infarction] and some high-risk features, including some of those that might be a non-ST-elevation MI, that are potential patients that go on to have ischemia-reperfusion injury. So out of the million or so patients, probably somewhere between 23% to 25% are at risk of having ischemia-reperfusion injury that leads to larger infarct size and heart failure. And then that heart failure goes on in these patients in the 1 to 5 years following that, who go on to have a variety of adverse outcomes with those patients with the largest infarct size, some of them out to 5 years, having significant heart failure and mortality, sometimes up to a third to two-thirds of those patients, depending on how risky it is.

And finally, I'll just say patients having heart failure post MI are expected to not only represent a significant burden to our clinical care system, obviously adverse health for them, but it also leads to significant morbidity, mortality, and cost. So the goal for us often is to reduce the time to open the artery, to think about how we can open the artery in a way that reduces ischemia-reperfusion injury, which is driven by this generation of reactive oxygen species downstream. Hopefully you've gained some insight into how that happens and all the therapies we can think about to help with opening that.

Well, I hope you've enjoyed that. This has been brief, but I'm glad I had the opportunity to share at least some of these insights and pathophysiology. Our time is up, and thank you for listening.

Announcer:
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