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The Path to Lung Transplantation: Roles of Extracorporeal Membrane Oxygenation (ECMO)

Narrator:
Welcome to **Medical Breakthroughs** from Penn Medicine, advancing medicine through precision diagnostics and novel therapies.

Dr. Caudle:
This is ReachMD and I'm your host, Dr. Jennifer Caudle, and with me today is Dr. Christian A. Bermudez, Surgical Director of Lung Transplantation and ECMO, Director of Thoracic Transplantation, and Associate Professor of Surgery at the Hospital of the University of Pennsylvania. The focus of our discussion today is ECMO, extracorporeal membrane oxygenation and the path to transplant. Dr. Bermudez, welcome to the program.

Dr. Bermudez:
Thank you, Jennifer. Good afternoon.

Dr. Caudle:
So, let's get started. Can you talk about what the history or background is of lung transplant and mechanical support?

Dr. Bermudez:
Absolutely. Since 1983 when the first series*:50 of lung transplant was reported by Dr. Joel Cooper, actually one of our colleagues now at Penn, lots has happened with lung transplantation. The number of patients that have been placed on the list continues to increase and we have probably about 2500 patients listed now for lung transplant every year. Unfortunately, the number of organs available has been very consistent and has not increased as we were expecting, due to multiple reasons, but the number of donors that we get every year is close to 1600, 1700 in the United States. For that reason, the number of patients on the wait list has increased and the severity of their disease has also increased. So, we're seeing now sicker patients, more frequently now on mechanical ventilation, coming to us to be evaluated for lung transplantation. Up to recently, we did not have technologies to support them, apart from mechanical ventilation. And we have seen over the last, I would say, 8 to 10 years, an increasing number of patients now being considered supported on other technologies different to mechanical ventilation, in the path to lung transplantation. One of these technologies, that is the one that we are discussing today, is called extracorporeal membrane oxygenation. That is actually an old technology that has been in use for more than 40 years. It includes an oxygenator and a pump that, fortunately for us, has had major improvements in the technology that it uses and is becoming more and more available to us to support these patients now for weeks and sometimes months as a bridge to lung transplant.

Dr. Caudle:
Great. Now, you described a little bit about ECMO, or extracorporeal membrane oxygenation. Can you tell us a little bit more about what exactly it is and how it works?

Dr. Bermudez:
This product came from the bypass machine originally used to operate patients in open heart surgery. So there were some important studies done in the early '70s with the development of the oxygenators that we used to oxygenate the blood when we're doing bypass surgery in the '50s, and one of the improvements in the technology was the creation of the membrane oxygenation, or oxygenator. And with that, we were able to decrease the size of these oxygenators in order to be able to sustain patients, not just in the operating room now, but also in the ICU. So, this technology was developed in the early-mid '70s with the first case published in 1971. And again, ECMO consists of a portable oxygenator and a centrifugal pump that basically runs blood through this oxygenator that allows the mixing between the blood and the oxygen. With this you can basically remove blood from the venous system and put it back into the arterial system now with high oxygen content, allowing patients with severe lung disease to be supported and oxygenated for a variable period of time. Unfortunately, this technology requires -- because you have fibers on the oxygenator and tubing that is connected to the patient -- requires the use of a blood thinner, heparin, and for that reason there are some complications that have been associated with the use of this technology including bleeding and thromboembolic complication. Fortunately, over the years, this technology has improved and has allowed us to support these patients now for longer periods of time, as a bridge to lung transplantation.

Dr. Caudle:
What is the role of ECMO as a path to lung transplantation?

Dr. Bermudez:
Regarding the role of ECMO today, it's probably the most advanced technology that we have to sustain patients that are not responding to the therapy with mechanical ventilation as a bridge to transplantation. This technology has become so effective that in some cases allows even to remove the patient from the ventilator and with the development of some newer cannulases (sic)*5:33, it also allows us to basically mobilize the patient, make them walk, and have some degree of rehabilitation while they're on the support, before they get to lung transplantation. So, they can walk eventually in the ICU and get stronger before the operation.

Dr. Caudle:
Can you talk about why this technology is gaining popularity in lung transplant patients?

Dr. Bermudez:
The reason why this technology is gaining popularity is because it, again, provides very efficient support and oxygenation and due to the improvement in the cannulases (sic)*6:12 especially that we are using to connect this technology to the patient. It's allowing us now to mobilize the patient, get them out of bed, and get them stronger before we do the transplant. With this, we have been able to operate on patients that we did not consider in the past that came to us in profound degree of respiratory failure and sometimes with hemodynamic involvement, meaning with hypotension and unstable. So now, with this technology, we're able to stabilize the patient, get them eventually moving, getting out of bed, and with increasing the chances of success of the surgery.

Dr. Caudle:
If you're just tuning in, you're listening to Medical Breakthroughs from Penn Medicine on ReachMD. I'm your host, Dr. Jennifer Caudle, and with me today is Dr. Christian A. Bermudez, Surgical Director of Lung Transplantation and ECMO and Associate Professor of Surgery at the Hospital of the University of Pennsylvania.

So, can you tell us how long a patient can be maintained on ECMO support?

Dr. Bermudez:
This is interesting. As we have gained experience with the use of the technology, we have been increasing the time that we're supporting these patients and we have recently had patients for more than 4 months supported on this technology waiting for a lung transplant. What 10 years ago was a few days and waiting generally for a new lung transplant, what we call re-transplant, when the organ had originally failed, with improvement in the technology, and the learning curve that we

had with this technology, now we're able to support safely some of these patients for more than 3 months waiting for lung transplantation. That gives us the opportunity to consider patients that were sicker, more debilitated, with the ability now to get them stronger, with increasing chances of succeeding at the time of the operation.

Dr. Caudle:
And what are some of the complications of extracorporeal membrane oxygenation?

Dr. Bermudez:
With any of these technologies, you have a number of complications that could appear during support. Some of them are related to bleeding due to the use of blood thinner; in this case heparin. Some of them are associated with the presence of thromboembolic complications due to the presence of a plastic material and fibers used on these devices. So, it's not infrequent if the level of heparinization, a blood thinner, is low, to get a thromboembolic complication in the form of a stroke or embolic complications in the different organs including liver, kidneys, and extremities. Fortunately, we have very sophisticated ways to maintain a good anticoagulation during the support of these patients and the reality is that we minimize these complications to less than 5 to 10% of the cases.

Dr. Caudle:
Are there any other technologies being considered or developed as an alternative to ECMO?

Dr. Bermudez:
The reality is that there has been an explosion over the last, I would say, 5 to 8 years of interest and studies that are coming with the use of different technologies to support patients with respiratory failure. The number of patients in the US hospitalized every year for different respiratory problems is more than 1.5 million, and about 10% of them require some sort of mechanical support in the form of mechanical ventilation and, in certain cases, in about 2% of the cases, the use of ECMO. Now, the use of ECMO in specifically lung transplantation is limited and the reality is, as I mentioned a few minutes ago, our ability to support patients for more than 4 months is still limited with this technology. For this reason, we are seeing a number of other devices coming that could potentially help us to support these patients for a longer period of time; sometimes not helping with the oxygenation, but helping with, for example, removal of carbon dioxide that is also a very frequent complication seen in patients with lung disease, especially in patients with cystic fibrosis and COPD. So there are some other technologies that could be beneficial and could keep these patients supported for even longer periods of time, and we have at least 2 devices available in the US that could do this, and we have a publishing in the recent past, some very successful experiences with these devices. Now, the idea would be to have a device available that could support patients for years, not just as a bridge to lung transplantation, but also to support them in what we call destination or in a permanent fashion. Unfortunately, I think we're still a few years behind, and I think there is a lot of research to be done to be able to get the devices that are biocompatible enough and that tolerate implantation for more than 6 months. Now, again, a lot of technology coming down the pipeline. I think this is a very exciting time for mechanical support, not just for lung transplant, but for all patients with respiratory failure, but still very important studies are ongoing and, unfortunately, we don't have definite result, but in the near future we should have some of these technologies able to support patients for 6 or more months.

Dr. Caudle:
Dr. Bermudez, is there anything else that you would like to add today?

Dr. Bermudez:
Again, the important comment that I want to make is that, fortunately for us and for our patients, we have now, due to the very impressive improvement of the technology and the biocompatibility of some of the devices that we have available today, the opportunity to help patients that we did not have the ability to help in the past, to get lung transplantation. So, this requires a very coordinated effort of the medical team and the nursing team, because there are still technologies that are in certain ways limited due to the need of heparin and anticoagulation, and very specific care of the devices. But the reality is that, fortunately for our patients, we have now technologies that can give us months or weeks, in certain cases, to wait for a

lung transplantation, improving the survival and the outcomes in our patients.

Dr. Caudle:
Well great. Dr. Bermudez, thank you so much for sharing your insights today.

Dr. Bermudez:
Thank you so much.

Dr. Caudle:
I am your host, Dr. Jennifer Caudle. Thank you for listening.

Narrator:
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