

Yale CANCER
CENTER
answers

WNPR Connecticut Public Radio



Hosts

Edward Chu MD

Chief of Medical Oncology

Kenneth Miller MD

Director of Supportive Care

Organ Transplantation for Cancer

Guest Expert:

Sukru Emre, MD

Chief of Organ Transplantation

Professor of Surgery, Transplantation



Yale Cancer Center Answers

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Welcome to Yale Cancer Center Answers with Drs. Ed Chu and Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and Dr. Miller, also an oncologist, specializes in pain and palliative care. If you would like to join the discussion, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This evening Ken speaks with Dr. Sukru Emre, Director of Yale-New Haven Transplantation Center and Chief of Transplant Surgery and Immunology at the Yale School of Medicine, Department of Surgery.

Miller You recently joined the faculty after leading a transplant program at Mount Sinai Hospital in New York. Tell us a little about yourself in terms of your background, training, and what brought you to New Haven.

Emre First of all, I am a native of Turkey. I grew up there and finished medical school at the University of Istanbul, School of Medicine. After that I did my residency training in the same institute and became a liver surgeon, or a hepatobiliary surgeon. I then became a Professor of Surgery at the University of Istanbul. In Europe, liver transplantation is a natural extension of hepatobiliary surgery. That was the challenge at that time and there were no liver transplant programs in Turkey so I was doing experimental liver transplantation. I came to New York in 1988 and learned clinical liver transplantation. I did research at the Downstate Medical Center and my clinical fellowship at Mount Sinai Medical Center where I was offered a job that I ended up taking. I climbed the ranks at Sinai and became Professor of Surgery and Director of Pediatric and Adult Liver Transplantation Programs. After that, I moved to Yale. Your question was why I moved to Yale. It was more of a challenge and Yale is a very reputable institution where I could bring my clinical experience and couple it with the research done here and do more translational research to create a complete package for our patients.

Miller Well welcome here. I understand that you performed over 1500 liver transplants. What's the youngest and oldest patient you operated on?

Emre The youngest patients I've had were 16 days and 18 days old. Today one is 5 years old and one is 7 years old. The oldest patient was 75 years old. She was an incredible woman until she died in a traffic accident at age 80. She went to all the dancing contests and was a really lovely woman that did very well after transplant.

Miller 16 days old; what was that like for you, performing that procedure?

Emre The emotional satisfaction is tremendous. I always say that there are certain things in life that are priceless, finishing the case successfully and talking to their family and seeing their eyes shining all of a sudden with the sadness over is one of those things that is priceless. That reward we get is what is important for me.

Miller Let me ask you a bit about the procedure because most of us really have no idea what is involved. How long of an operation is it, and in simple terms, what does a

liver transplant entail?

Emre The liver transplantation has three different aspects. One is what we call donor operation. In order to perform a liver transplantation, we need to have a donor liver. That operation should be done successfully. Then, the donor liver is brought to the center and we start the transplant operation which includes first taking the native and old diseased liver out, putting the new one in and making the connections. That operation takes somewhere between 4-6 hours, but sometimes it takes longer because as we know, the liver makes all the coagulation factors. After we put the liver in we have to wait until the liver starts making the factors. Then the field will dry and the coagulopathy, or the clotting problem, and the non-clotting problem, will be over and then we close the abdomen. If we separate it into our real operating time versus the overall operation time, it is not the same. My real operating time for taking the liver out and putting the new one in takes somewhere around 2 hours, but in between we have to wait. We have to do, what I call housekeeping, to make sure that there is no bleeding inside and then we close the abdomen; that takes somewhere around 6 hours.

Miller Thank you, that is something we talk about but don't really know much about. Let us talk about the liver a little bit. It is a fascinating organ and if you take out a part of the liver, what happens, does it grow back?

Emre Definitely. The liver grows back with what we call regeneration. It is not a budding in the sense that the part that we take out is going to be like the trees with the branches budding out, but whatever part of the liver that we left behind adjusts itself to the budding and grows together with the budding. The regeneration takes somewhere around 6-8 weeks. This is not a new thing and it has been around since the ancient Greeks. God Zeus punishes Prometheus for stealing fire by chaining him to a rock, and every morning an eagle comes and eats out his liver, but by nighttime the liver has grown back and in the morning the eagle comes again to eat the liver and it goes on and on. Since then we have known that the liver will regenerate.

Miller Why the liver and not other organs?

Emre I do not think anyone knows why, but possibly because the liver is the only organ with what we call hepatocyte growth factors, one of the main being insulin, and that is probably one of the reasons that the liver regenerates rather than other organs in the body. The liver is the only organ in the body that has a dual blood supply, or portal vein and hepatic artery. The portal vein brings the insulin which is one of the growth factors that supplies the liver and also the liver gets all the nutrients first. The liver is the entry of the body in terms of nutritional supply so when we eat something and it is absorbed by the intestine it gets into the portal vein and into the liver. The liver's job is to detoxify all this material, prepare it for the body so that the body will accept it. After that the liver gives this detoxified and cleaned up blood, nutrient-rich blood, to the heart which pumps it into all the

organs and tissues. This is the way we get all the nutrients. That is another reason that the liver can regenerate.

Miller That is amazing. People can donate a kidney to a relative or someone who needs a kidney; can they donate part of the liver?

Emre It is definitely true that someone in a family, friends, or any emotional relation, can donate a part of their liver to their loved ones. We call this living donor liver transplantation.

Miller And for the donor, will the part that they give regenerate?

Emre Yes, and again that part regenerates within 6-8 weeks and the liver reaches the same volume it was before the operation. Let's say that the liver volume before that individual donates part of his/her liver is 1600g. Within 6-8 weeks, even if we take 60% of the liver, the liver regenerates to 1600g again.

Miller Have you had patients with cancer where you have done a liver transplant?

Emre We do liver transplantation for various cancer operations, but mainly we do liver transplantation for hepatocellular carcinoma. There are two types of hepatocellular carcinoma, one is hepatocellular carcinoma that is the base of underlying liver diseases such as hepatitis C, hepatitis B and alcoholic liver diseases. These diseases can cause the development of hepatocellular carcinoma. In those cases, a liver transplantation is indicated, but sometimes we see a primary hepatocellular carcinoma without any underlying liver disease and in those cases the treatment modality is resection of the cancer, if possible. Sometimes, because of the location of the cancer, the resection is not doable. In those cases, we can offer patients the transplant operation. We also perform liver transplantation for patients with certain cancers and sarcomas like gastric sarcomas. If there is time between the original cancer operation and needing a transplant, especially if it is more than 5 years, we feel comfortable offering transplantation to those individuals. Also, we do transplantation for neuroendocrine tumors although they are metastatic liver tumors, and in those cases, because of the nature of the tumor, very slow-growing, we take the primary tumor which is usually either in the large intestine or pancreas. By taking those tumors out, together with the transplantation, we will save their lives or at least extend their lives around 7-10 years.

Miller For the very common types of cancer, colon cancer or lung cancer, which spread to the liver, is transplant used in those settings?

Emre We do not transplant in patients with metastatic lung or colon cancer. The first successful liver transplantation was performed in 1968. It was a patient with a tumor and between 1968, to somewhere around 1980, most of the cases done were with metastatic liver tumors. We learned our lessons the hard way. Since it's a metastatic disease and it's all over the body and the tumors cells are circulating in the blood and can be nested anywhere in the body, taking the liver out is not

going to cure the tumor because the tumor is systemic and everywhere. Once we give the immunosuppressive medications, immunosuppressive medications are medications that suppress the immune system, then the tumor flares up very fast. That is why we prefer not to do the transplantation with metastatic disease because we cannot gain anything but the pain and the pressure of undergoing a major procedure and the consequences.

Miller It sounds like there are some cancers where doing a transplant can be life-prolonging or curative, the primary cancer of the liver, neuroendocrine tumors or sarcomas. Can you think of any patients with sarcoma of the stomach, and what role transplant played?

Emre In the old days, because of the sarcoma operation the patient would develop hepatitis C. This was before the hepatitis C blood test became available and they developed hepatitis C as cirrhosis. In one of the cases, 7 years after the sarcoma operation, we felt that the tumor was cured so that was the reason we felt comfortable doing that. If there is an individual with colon cancer, let's say 10 years before or 12 years before, and they are developing liver cirrhosis with that tumor, we may consider that individual as well for transplantation, but if there is a metastatic liver tumor, there is no reason to do the transplant.

Miller We are going to take a break for a medical minute. Please e-mail your questions to us at canceranswers@yale.edu. We will be back in just a minute to talk more about liver transplantation and other transplantation with Dr. Sukru Emre from the Yale Cancer Center.

Medical Minute

Here in Connecticut the American Cancer Society estimates that almost a thousand people will be diagnosed with colorectal cancer every month. The good news is that when detected early, colorectal cancer is easily treated and highly curable. That means if you are over the age of 50, you should have regular colonoscopies to screen for this disease. In the case of patients that develop colorectal cancer, there are more options than ever before, thanks to increased access to advanced therapies and specialized care. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for colorectal cancer. The patients enrolled in these trials are given access to medicines not yet approved by the Food and Drug Administration.

This has been a medical minute. You will find more information at yalecancercenter.org. You are listening to the WNPR health forum from Connecticut public radio.

Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller. I am here with Dr. Sukru Emre who is an expert in transplantation surgery and Director of the Yale-New Haven Transplantation Center. Sukru, let me ask you a little bit about the team that is involved in doing a liver transplant or organ transplant.

16:52 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-09-07.mp3

Emre Liver transplantations, and any transplantation including kidney, pancreas, heart and lung, use a team approach. There is a very complex matrix rather than a single discipline. There are many disciplines and many professionals involved in the care of patients, which is the best way to provide care for our patients as well. The transplant surgeons and the transplant physicians include, a transplant hepatologist, transplant nephrologist, transplant cardiologist, transplant pulmonologist and lung specialist. Besides that, we have our core team of transplant coordinators. Also there are the nurses trained in transplantation and taking care of our patients. They facilitate and coordinate care as well as the consulting group that includes cardiology, pulmonology, intensive care, nephrologists, the blood bank, immunologist and neurologist

Miller That is a big group!

Emre And besides them we have our social workers that evaluate our patients; especially patients with substance abuse in order to help monitor them and help them clean up their act so that they can be a candidate for liver transplant.

Miller For every patient who goes through this procedure, how big is the team, how many people are backing you up and participating with you?

Emre Our core team is, surgery, hepatology, nephrology, cardiology, based on what transplants we are doing. There are consultants and all the disciplines I mentioned before. Our overall team would be somewhere around 40-50 people.

Miller Wow! That is very impressive.

Emre That is the way to give the best comprehensive care to our patients; which is the aim. I can do a perfect transplant operation but the patient may develop infection and complications. I need an infectious disease specialist helping me out and guiding me with how to treat them. After transplant there are certain infections and we need to develop protocols to help avoid or prevent those infections and complications. That ID is our right hand, and although I forgot to mention before, an ID is really an important part of the team.

Miller Let me ask you a little bit about the immunotherapy afterwards. Someone gets a transplant from a donor, whether related to them or not, what would happen if you did not intervene? How would their body react to the new liver?

Emre Unless we do an identical transplant, our immune system recognizes it as a foreign body and the immune system tries to get rid of it, the same way the immune system acts against bacteria, fungi, and viruses, what we call rejection. That usually occurs 7-10 days after transplantation and sometimes it will occur later on as well. In order to prevent these rejection episodes, we have to use certain medications, what we call immunosuppressive medications. Up until the 1980s, we did not have great immunosuppressive medications. At that time life after transplantation was extremely difficult and the survival rates were very low, somewhere around 40%. With the development of new immunosuppressive

medications that control the immune system in the way we would like without any other complications of this medication, it made the field very fruitful in terms of outcomes. Nowadays for kidney transplantation we have almost 100% patient survival and somewhere around 95% graft survival. For liver transplantation, we have, in pediatrics, somewhere around 100% patient survival, 97% graft survival. For adults, it is somewhere around 90-93% patient survival and 85-87% graft survival rates. We doubled our success rates.

Miller Those are much higher numbers than I would have thought.

Emre Our aim with a transplant patient is not to create a cripple, but make them 100% successful individuals that can resume their normal lives.

Miller This being the holiday season, how does someone indicate that they want to be an organ donor?

Emre There are many ways that someone can be an organ donor. There are websites that we can mention later on, but this really is the gift of life. People hear that we do not take our organs to heaven; heaven knows that we need them here. This is a very altruistic act for families and individuals before something happens to them. I suggest that everyone should read about organ donation and there are a couple of websites, one is www.DonateAmerica.org and www.unos.org. In Connecticut we have a web page with the group, Connecticut Coalition for Organ Donation and Tissue Donation. The web page is www.CTorganandtissuedonation.org. Individuals can read about organ donation and also at our transplant web page at the Yale Transplant Center. We have a "meet and fax" about organ donation. It is a question-answer type web page that will answer all the questions of individuals interested in donating. For example, "If I decide to donate my organs, are they are going to take my organs before I die?" Individual physicians taking caring of the patient, and individuals involved with organ donation, are totally separate teams. For the physician taking care of the patient, their job, their success, their reputation, comes from making sick patients better. They will do everything to save the lives of the patient. Sometimes, as we know, it is impossible to save a life, and at that time they invite the other individuals and those involved with organ donation to evaluate the patient and whether they are suitable for organ donation or not.

Miller We will move on to a different topic. What are some of your research interests?

Emre One of my research interests is ischemia reperfusion injury, and the other one is developing different systems to preserve organs. If we can do machine perfusions that preserve the organs longer, then we can have better quality of the organs. I have a research interest in split-liver transplantation and living donor liver transplantation as well, and I am involved heavily with psychosocial aspects of the liver transplantation; especially adherence and nonadherence and the factors affecting nonadherence.

Miller Nonadherence to what?

Emre Nonadherence to immunosuppressive medications.

Miller Right.

Emre Or resuming substance abuse.

Miller I can imagine that it is frustrating when you have gone through a liver transplant with a patient and then they start drinking again, is that common?

Emre It is not, thank God, because we do many studies before we decide to transplant them. We need at least 6 months of sobriety. They should go to alcohol rehab or be involved with rehab programs. We talk with their case managers and make sure that they develop insight about their problem. If they don't fulfill that responsibility, then we don't transplant them. That will decrease the number of recidivism after transplantation.

Miller I want to thank you for joining us tonight.

Emre It is my pleasure. Thank you for inviting me.

Miller It has been a fascinating discussion about liver transplantation, which we do not talk about much. You have brought a wonderful set of resources to Yale and to Connecticut and so we are very excited to have you.

Emre Thank you.

Miller I want to again thank Dr. Emre for joining us on Yale Cancer Center Answers. Until next week, this is Dr. Ken Miller from the Yale Cancer Center wishing you a safe and healthy week.

If you have questions, comments, or would like to subscribe to our podcast, go to yalecancercenter.org where you will also find transcripts of past broadcasts in written form. Next week, Ken speaks with Dr. Stephen Ariyan and Harriet Kluger about melanoma.