Yale CANCER CENTER answers

WNPR Connecticut Public Radio

Organ Transplantation

Guest Expert:
Sanjay Kulkarni, MD

Associate Professor of Surgery, Transplant, and of Medicine Nephrology, Yale School of Medicine.

Hosts

Anees Chagpar MD

Associate Professor of Surgical Oncology

Susan Higgins MD

Professor of Therapeutic Radiology, Obstetrics, Gynecology, and Reproductive Sciences

Steven Gore MD

Director of Hematologic Malignancies

Yale Cancer Center Answers is a weekly broadcast on **WNPR** Connecticut Public Radio Sunday Evenings at 6:00PM

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Welcome to Yale Cancer Center Answers with your hosts doctors, Anees Chagpar, Susan Higgns, and Steven Gore. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale, New Haven. Dr. Higgins is Professor of Therapeutic Radiology and of Obstetrics, Gynecology and Reproductive Sciences and Dr. Gore is Director of Hematological Malignancies at Smilow and an expert in Myelodysplastic Syndromes. Yale Cancer Center Answers features weekly conversations about the research diagnosis and treatment of cancer and if you would like to join the conversation, you can submit questions and comments to canceranswers@yale.edu *or you can leave a voicemail message at 888-234-4YCC. This week it is a conversation about organ transplantation with Dr. Sanjay Kulkarni. Dr. Kulkarni is Associate Professor of Surgery, Transplant, and of Medicine Nephrology at Yale School of Medicine. Here is Dr. Anees Chagpar.*

Chagpar Sanjay, let's start by talking about organ transplantation. I know that this is a show called Yale Cancer Center Answers, but let's start with the basics of transplantation. How many people in this country get transplants, how many need transplants, and what are some of the big problems in terms of making sure that we are meeting those needs?

Sanjay You probably hit the most important question first because we are in a public health crisis as far as people needing both kidney, liver, and heart transplants and it really comes down to the fact that our lists are burgeoning with people as there are over 120,000 people in the country waiting for organ transplantation and only 10% of them get transplanted every single year, so these lists continue to increase, people are continuing to die on these waiting lists, so it is critical that we find a solution to the organ shortage problem.

Chagpar Right off the top, how do people become organ donors, what can you do if you want to help this crisis?

Sanjay Well, there are 2 types of organ donors, there is what we call deceased donors and these are unfortunate people, who are hospitalized, brain dead, they may actually not be brain dead in certain circumstances or have no chance of neurological recovery, and their families are approached to consent for them to donate. Now, I don't know if you know this, but Connecticut has historically been one of the poor states in the country as far as the number of deceased donors available for transplant. There are multiple factors for that, but we continue to suffer from an organ transplant perspective on the number of organs available for transplant and on the other side, there are of course living donors and these are individuals that are just remarkable people, I'm primarily a living donor surgeon and I do most of the living donor kidney procurements at Yale and it is just an honor meeting these people because they are unique individuals and these people come forward, they may come forward to be a directed donor, so let's say I want to donate to you or they sometimes come and say, I just want to help and I don't

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care who the kidney goes to and those are called altruistic donors. So the simple answer to your question is there are deceased donors and then there are living donors and at Yale, we are really trying to emphasize to be a program more geared towards living donation given the healthcare crisis.

Chagpar And even on the deceased donor side, I would think that it is not that difficult to sign your driver's license, tell your family that is your wish because if it is something that you want after you pass to be able to help other people, you need to tell somebody that is what you want.

Sanjay That is so important, yes, you should sign your driver's licence, but during that process, you really want your family members to know what your wishes are and that makes it a lot less complex because ultimately the family members are there and they are going to be approached and they are going to get consented for that organ procurement and in spite of signing that license, for your family to comprehend your true feeling is imperative to making this process work.

Chagpar I wanted to a lay that groundwork at the top because this is a show on organ transplantation, but it is also a show called Yale Cancer Center Answers, so tell me a little bit more about the connection between organ transplantation and cancer. Many people feel that if you have cancer you are not eligible for a transplant, so why are we talking about this?

Sanjay The two are actually very close and very interrelated and there are several examples, but I think the most prominent example is in liver transplantation, so patients who suffer from end-stage liver disease, some of them do develop small cancers and the way the liver transplantation works is that the sicker you are, that is based on something called a MELD score, the higher priority you get to get an organ, so the people who tend not to be so sick, it is unfortunate, but they end up going to the back of the line and the sicker people get the transplants first. Interestingly, there is an exception for people with liver cancer, so if your liver cancer meets a specific criteria and that criteria is usually based on imaging or a CAT scan and so forth, then you can get special priority in the United States and particularly our region, where you get elevated on the list, so your probability of getting a liver transplant increases and we interface very closely with Smilow Cancer

Hospital on this, there is a multidisciplinary meeting where transplant surgeons, surgical oncologists, radiologists, medical oncologists all interface to discuss these cases and to determine what is the most appropriate therapy for these patients.

Chagpar So what are their choices?

Sanjay It depends on the size and the advancement of the disease and the choices go from being placed on the transplant list to local therapy that our radiologists perform, something called radiofrequency ablation or chemoembolization. There is certainly chemotherapy that can be provided and then surgical resection.

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Chagpar And can people have multiple things at once, for example, you try your best at chemo ablation or resection while you are on the transplant list, because if the stats that you gave us at the top of the show are true, 10% of people actually get the organ that they need in any given year, so you better be doing something about your cancer while you are waiting.

Sanjay That is absolutely true and that is why we have that meeting because many of these patients even if they are on the list, they have cancer that needs to be treated, so we make a decision amongst all of us, what is the appropriate therapy and the therapy can be staged. I think you are absolutely right. There are even instances where somebody may undergo a surgical resection and then down the road, still need a transplant and it is so important for the professionals in our field to discuss each patient individually at this multidisciplinary meeting and develop a comprehensive treatment plan because you are right, it is complex.

Chagpar One of the things, Sanjay, that I think is intriguing that you mentioned and I want to ask you this because I think that some of our listeners may be intrigued by this as well, is that you said that some liver cancer patients get priority, now some people who may sadly be on a liver transplant list may be wondering why is it that cancer patients get priority, I mean if you have got cancer and that cancer has the potential to metastasize and your life expectancy may be determined in part by that cancer, why would you get priority over somebody who has liver disease that is not malignant?

Sanjay It is all evidence based and it is all based on clinical studies on patients who are randomized to different treatments and the patients with liver cancer, I am talking about, the liver cancer tends to be a very early stage, it does not tend to be advanced and we go through great strides to assure that is not the case and even during the transplant, we

make an assessment clinically in the operation to make sure that patient has a very early stage cancer and in the event that it is beyond that stage, we won't proceed with the transplant. So a lot of these clinical studies, the major one which was primarily from Italy a while back, established something called the Milan criteria and these patients did better with transplant than other forms of treatment.

Chagpar You talked a little bit about deceased donors and living donors and you made the comment that Yale was particularly interested in developing a living donor program, why is that?

Sanjay Well the status of patients with chronic kidney disease and chronic liver disease is a public health crisis and I think the United States should think of it that way as well and over the past two decades the number of deceased donors simply has not improved and it is not for lack of trying, there is a fair amount of education involved, outreach people working very very hard and committed to increasing organ donation, but you have to also look at our demographics, our country is getting older and patients who are older tend to have more comorbidities and so many of these organs, you can still transplant them, but they tend to be suboptimal, particularly when you are comparing them to a living donor. So given the fact that we have so many patients on our list, we feel really compelled as a fiduciary responsibility to our patients to find methods

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to save their lives and it just so happens that at Yale, we have a lot of experience with living donation. If you look at the number of surgeons we have and the number of cases they have done, for both kidney procurement and liver procurement, they are top 3 in the country. So we certainly have the resources to do it. We just want to develop a comprehensive program to implement it and get the word out.

Chagpar Is living donation primarily liver and kidney, because I would think that you cannot really be a living donor of a heart.

Sanjay It is primarily kidney and liver, there are cases of living donor lung transplants where a segment of lung has been taken, they have done living donor pancreas transplants, but that is extremely rare and there have actually been cases of living donor intestinal transplants. So the latter three are extremely rare, but predominantly in the United States we concentrate on living donor kidney and living donor liver transplants.

Chagpar So tell us a little bit more about each of those two. Living donor kidney, most of our listeners would understand how that works, you have got two kidneys, you give one to somebody else, what about your liver?

Sanjay Well, you only have one liver, but fortunately the liver regenerates and I think it is important to make the comment for both kidney and for liver donation, just because somebody wants to be a donor, it does not mean that they automatically can be. The evaluation is very extensive for both kidney donors and even more so for living donors. So we have to have strict assurances that if we take a portion of their liver or we take a portion of their kidney that long-term they are going to be able to lead the same type of life as they did prior to donation and that is really what our aim is.

Chagpar Tell us more about that because certainly it is an intriguing possibility. What is donation like, what is that process? How do you get involved and what is the evaluation like? What are your long-term outcomes? You have already kind of spoken to the last point, but what about the first three, because I can see how some people may be intimidated to get involved in this process albeit for altruistic purposes.

Sanjay Yes, I think it is important to understand that if you are interested in being an organ donor what we emphasize is education more than anything else and that is why the process is extensive. So when people are interested, the first thing we do is we bring them in and we talk to them, so they understand exactly what they are getting into and what we emphasize to donors is they should not feel any pressure, that they can back out at any time, that this is meant to be a very comfortable process for them and at the end of it, they should feel rewarded and they should feel gratitude and it should not limit their lives in any way.

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Chagpar We are going to learn a lot more about living donation and how this can really make a big difference to cancer survivors after we take a short break for a medical minute. Please stay tuned to learn more information with my guest, Dr. Sanjay Kulkarni.

Medical Minute *This year over 200,000 Americans will be diagnosed with lung cancer. More than 85% of lung cancer diagnoses are related to smoking and quitting even after decades of use can significantly reduce your risk of developing lung cancer. Clinical trials are currently underway at federally designated comprehensive cancer centers, such as Yale Cancer*

Center and at Smilow Cancer Hospital at Yale-New Haven to test innovative new treatments for lung cancer. Advances are being made by utilizing targeted therapies and immunotherapies. The BATTLE-2 trial at Yale aims to learn if a drug or combination of drugs based on personal biomarkers can help to control non-small cell lung cancer. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. More information is available at yalecancercenter.org. *You are listening to WNPR, Connecticut's Public Media Source for news and ideas.*

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Sanjay Kulkarni. We are talking about organ transplantation. Right before the break Sanjay you were talking about how people get involved, how they can become living donors, the process of education, the process of knowing what to expect. What if you have cancer, can you still donate a kidney, and can you still donate part of your liver?

Sanjay That is a really intriguing question and I am going to say it is very intriguing because there is a shift that is occurring in healthcare in the United States where there are more opportunities for people with cancer to become potential donors, but in general, the answer is no, again, if you are going to side by the welfare of the person donating, you do not want to remove any portion of the vital organ because down the road that cancer may be causing greater difficulty, so in general, 99% of the time, the answer is no, you cannot be a donor. Interestingly enough, there is a new field in transplantation that is something called therapeutic donors and this has really been spurred on by the healthcare crisis, we are trying to find ways to provide transplants to people in need and one of the important things that has come to fruitions is, we have always known that kidney recipients or recipients of living donor kidneys do better than recipients of deceased donor kidneys, but this year we have also recognized that recipients of living donor livers do better than recipients of deceased donor livers. So getting back to the therapeutic donation topic, what some centers are doing is, let's say you have a small cancer on your kidney and you may need that removed by removing the whole kidney or you may just need a portion of that kidney removed. Well, what people are doing is approaching these people and asking them, would you be willing, as a process of getting treatment for the cancer, also being a donor, so we would remove the kidney with the cancer, we would remove the cancer after the kidney has been removed and then implant that as a transplant. So this field is just emerging, it is really in its infancy, and we really need to have a strong

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ethical debate and a strong consensus as a community whether this is an option for potential people, but yes, I think in the future you are going to find that more people with cancers are actually going to be donors.

Chagpar It is interesting, this whole concept of therapeutic donors because potentially if you could just take out that portion of the kidney that has the tumor in it instead of the whole kidney, then couldn't the donor have a smaller operation than removing the whole kidney?

Sanjay They could and that is where informed consent really comes into play and that is why we really need to have a strong ethical debate on how we are going to approach this as a society. You know, there are some tumors just simply based on their location on a kidney, that may be small enough that it is safe to transplant, but in a location where removal of the whole kidney is required.

Chagpar You would wonder though if you were the donor whether you would want a cancerous kidney.

Sanjay A lot of studies in Japan have looked at that and we have a fair amount of experience with that as well. As long as the cancers are very small and as long as they are localized, removing them is essentially curative and what you are looking at is, potentially getting a living donor kidney with a very very small risk of developing cancer long-term versus staying on the waiting list with a predicted mortality every single year and a five- to six-year waiting time. So it is really prompted by the public health crisis and by the number of people waiting for organ transplantation to try to find new and innovative ways to provide life-saving treatments for these people.

Chagpar And I guess the last question on this whole therapeutic transplantation thing is, if you get a transplant, you need to have immunosuppression, right?

Sanjay Correct.

Chagpar Wouldn't immunosuppression increase your risk of a cancer going awry?

Sanjay It actually does increase your risk of certain cancers and one of the things that we need to realize about immunosuppression is immunosuppression has revolutionized transplant and immunosuppression that we use nowadays is quite different than transplantation in the 80s and 90s. The dosage is far less, the overall immunosuppressive load is far less, and the steroids are far more reduced, so we have gotten pretty good at modified immune suppression and personalizing it to a particular person. As far as cancer risk, if you look at people who are transplant patients, who are on immunosuppression and you compare them

to people in general population, it is true that they do have a higher risk of cancer. They typically are head and neck cancers or certain virally mediated cancers that they are at the highest risk for. Now, again, it is all about weighing risks,

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yes, I potentially could have a slightly higher risk of developing kidney cancer from a kidney that has been removed where the cancer has been excised, but on the other hand, I am going to wait six years and the faster I get transplanted, I know I am going to have better results. As long as the surveillance is there afterwards, I think it is actually very safe to do.

Chagpar One thing that tweaked a question from me when you talked about the increased risk being virally mediated cancers, head and neck cancers, and other cancers in large part in transplant recipients, what if people had had an HPV vaccine prior to being transplanted and being immunosuppressed, do those people have a lower risk than if they would never have been vaccinated?

Sanjay This is a great question and to my knowledge, there is no clinical study, but that is something we should definitely investigate.

Chagpar Just another reason to think about vaccination, okay off the soapbox, tell me about some of the research that is ongoing, I am sure there are a lot of great innovative studies going on in the transplant field.

Sanjay There really are and at Yale we have really concentrated on living donors again because we want to really get the word out and develop a comprehensive program where living donors get cutting-edge treatments and the only way to be cutting edge is to be involved in research. One other thing is that we have been on the forefront of developing more donor-centered approaches and if I can elaborate on that a little bit, the Institute of Medicine came out with a recommendation that the practice of medicine should be more focused to patient-centered models, involving patients and understanding what their motivations are, understanding the different elements of life and how for them certain treatments may be advantageous versus others and we are trying to apply that same model to living donors and to my understanding, we are the only center that is currently doing this. So when there is some medical uncertainty, for example, the risk of developing kidney disease long-term if you have hypertension, let's say, what we are

trying to do is develop a systematic way of involving donors in the decision making process and I think the only way we can justifiably do that is to pair that with very comprehensive long-term donor follow-up to make sure that donors are not getting hurt when they may be taking a slightly incremental risk based on their motivations and I think a really good example of something like this is, parents giving to children or other instances where the bond is very tight such as an elderly wife giving to her husband, so they can travel, they can do things and many of these instances we do consider motivations, but we have not really formulized it. So, we are doing a fair amount of research and trying to develop new models of donor care.

Chagpar That sounds like it is more a clinical kind of programmatic advance. What about other clinical trials, for example, are there new cutting edge things on the horizon in terms of certain immunosuppressants or certain surgical techniques or things that make it more possible to either donate or receive?

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Sanjay There are a couple of things I can think about. On the liver side, the medical director of our liver transplant program, Dr. Schilsky is working with Dr. Israel in radiology to develop expedited ways to determine whether certain people who want to donate are suitable and to try to make that decision very very quickly, efficiently, and cost effective. On the kidney transplant side, we are about to complete a randomized clinical trial and a device by a local company called SurgiQuest, it is actually made right here in Milford, and what they have done is they have developed a way to finally regulate the pressure that we have to use in the abdomen. All laparoscopy surgery requires you to add air so you can actually see and what this new device does, which is called AirSeal, is it finely regulates the pressure so you use less of it and what our hypothesis in the clinical study is, that by using less pressure, can we somehow improve the comfort afterwards? Maybe somehow the two are related and maybe patients will use less pain medication, so that is exactly what our primary outcome is, it is the narcotic use afterwards and I hope to have answers by another month or so when we complete the study.

Chagpar That is very cool. How much transplant surgery is done laparoscopically? I think most of us, at least I always thought, about transplant surgery being this massive operation with a huge incision, is it not that way anymore?

Sanjay No, with donors in particular, we do a 100% of our kidneys donors laparoscopically.

Chagpar Wow!

Sanjay And that has really shifted over the last ten years or so. The liver donors are still done open, though. Dr. Mulligan, who is the director of our transplant program, he is committed to bringing minimally invasive surgical techniques to living donors and I fully anticipate that coming to fruiting within the next 12 months.

Chagpar It is so interesting when we talk about living donors. I can imagine how it is as you say an elderly wife giving to her husband or parents giving to children. The other side that you mentioned before the break was this altruistic general population just wanting to do something incredible. How many people are out there who actually do that?

Sanjay Very few, but I think that the reason is lack of education, more than anything else, and the altruistic donors, in addition to being just amazing individuals, I mean can you imagine, just coming forward to say I am going to donate my kidney because I want to help somebody, it really goes against a lot of skepticism we have as human beings and again, that is why I have the best job in the world. I interact with these individuals and it is very humbling and it really is the better side of human nature, but the altruistic donors, in particular, make a tremendous impact, because what we do nowadays is we have a computerized matching system. It was actually developed by a professor who won the Nobel Prize for it and there are many people on our list who have living donors, but they cannot donate to each other.

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Chagpar Because they are not a match.

Sanjay They are not a match, they are different blood types, and there could be other compatibility issues. Let's say for an instance we have four of those individuals, what we do with these altruistic donors is we put them into the matching algorithm to see whether they can initiate a chain, so the altruistic donor will donate to one of the recipients, in exchange for that that donor who is not compatible donates to the next recipient on the list and recently at Yale, we had a wonderful story that had a fair amount of media attention, where an altruistic donator donated and triggered a chain reaction and we had four people transplanted, so that one gift translated into four people being transplanted. Interestingly enough, it was all wives giving to husbands, which was just a great story, because you probably know that the vast majority of people who donate are actually women.

Dr. Sanjay Kulkarni is Associate Professor of Surgery, Transplant, and of Medicine Nephrology at Yale School of Medicine. We invite you to share your questions and comments, you can send

them to canceranswers@yale.edu *or you can leave a voicemail message at 888-234-4YCC and as an additional resource, archived programs are available in both audio and written format at* yalecancercenter.org. *I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another edition of Yale Cancer Center Answers here on WNPR, Connecticut's Public Media Source for news and ideas.*