

# Physicians Update

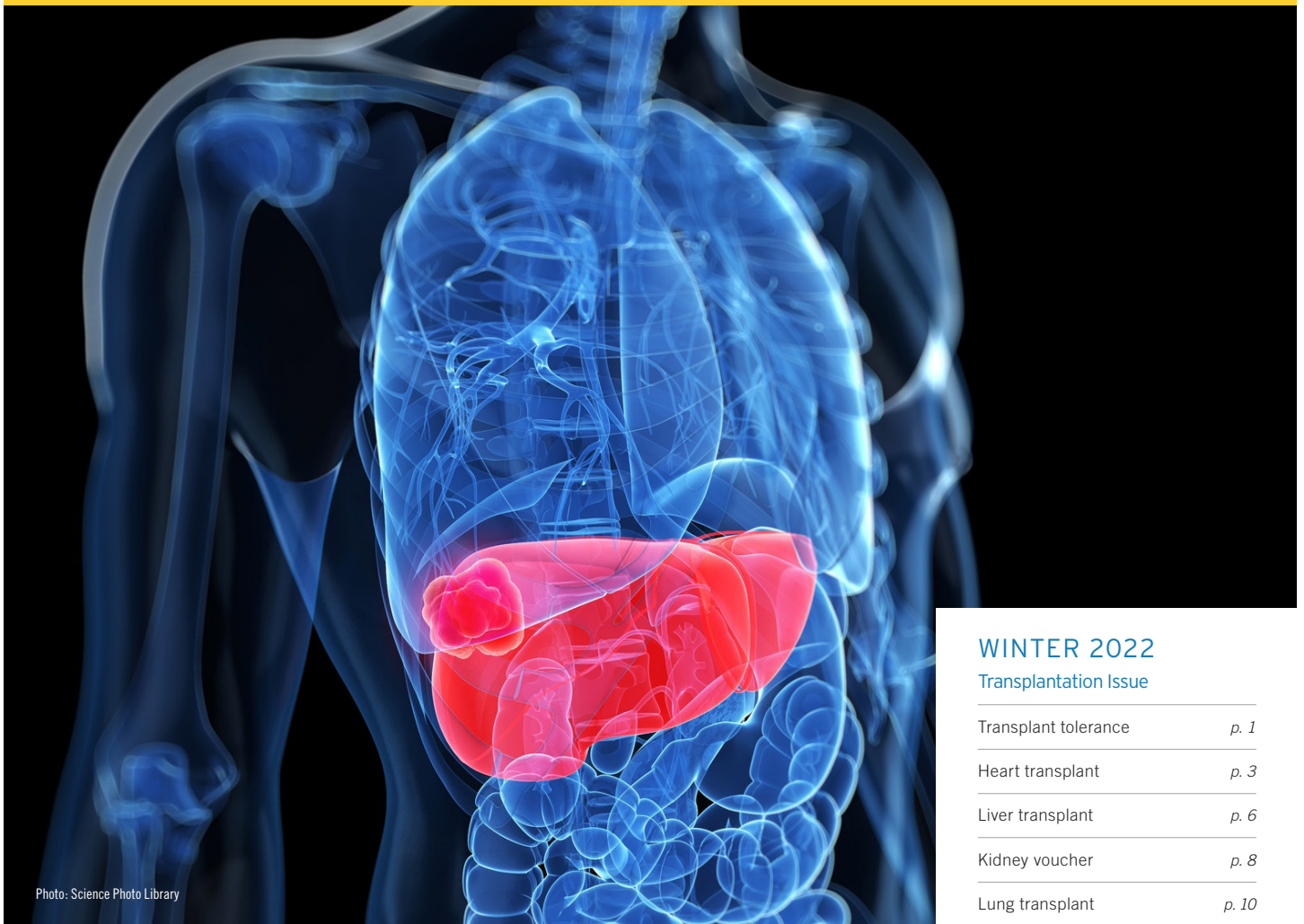


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## WINTER 2022

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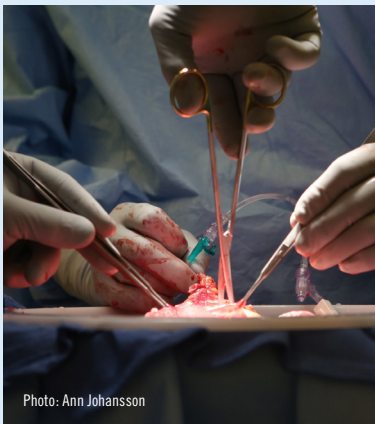


Photo: Ann Johansson

## TRANSPLANT TOLERANCE

### UCLA Health advances pioneering protocol to enable transplant recipients to thrive without antirejection drugs

Performing human-organ transplants without the necessity for a lifetime regimen of immunosuppressive drugs has been an enduring goal for transplantation medicine. Now, a new Medicare-approved protocol being implemented at UCLA Health with select living-donor kidney-transplant patients is

bringing that dream closer to reality.

“It is the Holy Grail,” says renal-transplant surgeon Jeffrey Veale, MD, who has led UCLA’s effort to develop the protocol.

Dr. Veale was at a medical conference in 2009 when he heard the celebrated immunologist David H. Sachs, MD, talk about

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**UCLA**

Health

#1

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*U.S. News & World Report Best Hospitals*

# Multidisciplinary care at the heart of UCLA's adult heart-transplant program

UCLA is among the world's busiest and most successful programs for adult heart transplantation and a major referral center of care for some of the most difficult cases. But the program's true strength is derived not merely from transplant outcomes or the ability to handle complex patients, according to the program's director.

"We have an incredibly talented multidisciplinary team that provides the full spectrum of care for patients with heart failure — from the genetic workup to pharmaceutical care for patients who need optimal medical therapy, to mechanical support with assist devices, to care for patients who need heart transplantation in conjunction with a kidney or lung transplant, to the postoperative management of any potential complications," says Abbas Ardehali, MD,

own heart, so if someone can benefit from surgery, an interventional procedure or medical therapy to postpone transplantation, then we have succeeded. And if they need the transplant, we have that option available as well."

To expand patient access to UCLA's advanced heart-failure programs, heart-failure clinics are being held at several community sites. UCLA Health heart-failure cardiologists regularly see patients at weekly clinics in Downtown Los Angeles, Torrance, Thousand Oaks and Santa Clarita, and a heart-failure clinic in Santa Barbara is set to open in early 2022. "To be able to piggyback on UCLA Health's satellite clinics for heart failure has led to meaningful relationships with our community providers and allowed us to offer advanced cardiac therapies to patients who can avoid the inconvenience of traveling to Westwood,

For patients posttransplant, UCLA's was among the first programs to use blood-based genetic testing as a noninvasive method for evaluating the risk of rejection of the transplanted heart. Advances in both surgical techniques and the use of immunosuppression have reduced complications and increased survival times.

"We have seen significant advances in the field at the level of pretransplant, peritransplant and posttransplant care that have translated to improved outcomes for patients," Dr. Ardehali says. Particularly important, Dr. Ardehali notes, has been the expansion of donor criteria that has allowed programs such as UCLA's to accept hearts that were not previously considered suitable, including the resuscitation of hearts that have stopped in patients. This has increased the available supply, reducing waiting times. UCLA's program also stands out for the frequency with which it performs combined transplantations, such as heart/lung/kidney and heart/liver procedures, for patients with end-stage liver, kidney or lung disease.

Dr. Ardehali believes that the comprehensive nature of the UCLA Heart Transplant Program has implications for referral patterns. "In the past, physicians might have waited to refer their heart-failure patient until that patient needed a transplant," he says. "But if there is any uncertainty with that patient, we recommend not waiting. We can provide advice where needed and supportive care at whatever stage the patient is in, toward the goal of referring the patient back to them — potentially without the need for a transplant."

**"We have seen significant advances in the field at the level of pretransplant, peritransplant and posttransplant care that have translated to improved outcomes for patients."**

director of the UCLA Heart, Lung, and Heart-Lung Transplant Programs. "These patients all have different needs, and by excelling in every area, we are able to provide care that is tailored to their circumstance."

The multidisciplinary heart-transplant team is poised to expand based on the depth of its offerings, Dr. Ardehali notes. In weekly calls, team members representing surgery, medicine and psychiatry, as well as social workers, case managers, advance-care planners and others take a holistic approach to each case in determining the best course of therapy. "Our team prides itself on being able to offer patients options that, in certain cases, can allow them to delay or avoid a transplant," says Ali Nsair, MD, medical director of the UCLA Heart Transplant Program. "Patients do better and live longer when we can get the maximum out of their

as well as improving continuity of care posttransplant," Dr. Nsair says.

In addition, a mobile ECMO (extracorporeal membrane oxygenation) program, which partners with outside hospitals that lack ECMO capabilities, provides life-saving mechanical support that allows patients at these facilities to be safely transported to UCLA. The program, under the direction of Peyman Benharash, MD, has grown rapidly and continues to cannulate patients at community facilities who have life-threatening heart and/or lung problems.

Overall, Dr. Nsair notes, heart-failure patients are benefiting from improved devices for getting them to transplantation safely — including mechanical pumps that allow patients to go home from the hospital while awaiting transplant, and ventricular-assist devices that improve quality of life for patients who aren't transplant candidates.



For more information about UCLA's heart-transplant program, go to: [uclahealth.org/transplants/heart](https://uclahealth.org/transplants/heart)

## STORY HIGHLIGHTS

Curbing potential risks associated with immunosuppression can extend the life of a donated organ, benefiting both the recipient and future patients by decreasing the number of people waiting for an organ.

Procedure involves extraction of donor's stem cells and infusion into recipient posttransplant to promote mixed chimerism, the blending of the donor's and recipient's immune systems to prime the recipient to recognize, rather than reject, the new organ.

UCLA aims to become the first center to advance the procedure to achieve transplant tolerance with deceased-donor organs.

# UCLA Health advances pioneering protocol to enable transplant recipients to thrive without antirejection drugs

*(continued from cover)*

how Massachusetts General Hospital was creating immune tolerance in organ-transplant recipients, eliminating the need for lifelong anti-rejection drugs. "I was mesmerized," Dr. Veale recalls. "Transplants with no immune suppression? I thought, 'That's incredible!'"

A lot has happened in the 12 years since that day in Jackson Hole, Wyoming, and today, UCLA Health is the only medical center in the U.S. practicing the tolerance protocol between well-matched siblings. The procedure has been performed at UCLA in two well-matched sibling pairs to date, with both kidney recipients successfully weaning off immunosuppression medication. In November, UCLA received approval from Medicare to provide the procedure.

While solid-organ transplants have been performed regularly since the 1950s, they always have required powerful drugs to prevent the recipient from rejecting the new organ. This is both expensive and risky for the recipient; these powerful immunosuppression drugs can have serious complications that include increased risk of cancer, infection, diabetes, hypertension and heart disease.

Curbing these potential risks by eliminating the need for immunosuppression can extend the life of a donated organ. Potentially, "it is one kidney for life," Dr. Veale says. That can have a significant impact for patients. Currently, 20% of patients on the list to receive a deceased-donor kidney are waiting for their second, third, or even fourth, organ. "Every time a patient requires a retransplant, it makes it harder and harder to get a match. In addition, the surgery itself becomes more difficult because of the scar tissue," Dr. Veale says. "If we can prolong survival of the initial graft, we make it possible for other people to receive a kidney, and we can bring down the number of patients who are waiting."

Dr. Veale talks about the procedure, who might be a good candidate and how UCLA Health plans to advance transplantation tolerance in the future.

## What does the tolerance protocol entail?

**Dr. Veale:** This protocol brings together four departments that generally don't overlap: urology, medicine (nephrology and bone-marrow transplantation), radiation oncology and pathology. The procedure begins with

**"If we can prolong survival of the initial graft, we make it possible for other people to receive a kidney, and we can bring down the number of patients who are waiting."**

extraction of stem cells from the bone marrow and blood of a well-matched donor. These stem cells will be processed and, after the recipient has received the donor organ and undergone a series of total lymphoid irradiation treatments, infused into the recipient. This infusion of the donor's stem cells promotes mixed chimerism, the blending of the donor's and recipient's immune systems to prime the recipient to recognize, rather than reject, the new organ. Once chimerism forms, the organ recipient can wean off immunosuppression drugs.

## Who is a good candidate for this procedure?

**Dr. Veale:** Right now, it is well-matched family members. The procedures we have done thus far involve sibling pairs. But we





Dr. Jeffrey Veale and UCLA's first transplant-tolerance patient before going into surgery.

now have approval from the Food and Drug Administration to perform the procedure with mismatched pairs as well. UCLA is not the first center to perform this procedure with well-matched sibling pairs, but we currently are the only one doing it.

#### **Why aren't more medical centers offering tolerance transplants?**

**Dr. Veale:** It needs to be someplace that has the infrastructure to support something like this. It requires so many different elements. UCLA has all the big pieces in place that we need. A special infusion center? UCLA has it. Cryopreservation? UCLA has it. Pheresis? UCLA has it. Advanced radiation-oncology technology? UCLA has it. UCLA's is the largest transplant program in the United States. We have all the components that are necessary to make this transplant-tolerance protocol a success. And there is such a spark among the people who are involved, such passion. When we see the patients who already have undergone the procedure, how grateful they are and how well they're doing, it gives us all some extra juice and excitement for the future.

**UCLA and its partner in this endeavor, the organ-donation nonprofit OneLegacy Foundation, want to take transplant tolerance even further. What is the future of tolerance?**

**Dr. Veale:** This is where I think UCLA will make a real difference. Up until now, tolerance

has been limited to living donors. We believe we can be the ones who will move the field forward to make the leap to tolerance with deceased-donor organs. That is where the big difference will be made. Deceased donors accounted for more than 77% of the 22,800 kidney transplants that were performed nationally in 2020. That's why OneLegacy Foundation and its CEO, Tom Mone, are working with us — they provided us with significant funding to support this effort. We want to see tolerance move from living donation to deceased donation. We would probably start with deceased-donor kidneys. Then, theoretically, we can move to other solid organs: liver, heart and potentially lungs. But also, to other areas that now are limited by immunosuppression medications, like vascular composite allograft transplantation, which would include hand, foot, uterus and face transplants. Those transplantations require very high levels of immunosuppression. If we can achieve tolerance with this group of patients, even if we aren't able to get them down 100% to no immunosuppression, we might be able to get them to immunosuppression levels that aren't so toxic.



**For more information about UCLA Health's transplant-tolerance program, go to:**  
[tinyurl.com/UCLA-Transplant-Tolerance](https://tinyurl.com/UCLA-Transplant-Tolerance)

# UCLA program improves outcomes for patients with rare liver cancer

## STORY HIGHLIGHTS

Combination of neoadjuvant chemotherapy and radiation followed by transplantation has shown great benefit for patients with cholangiocarcinoma, or bile-duct cancer.

UCLA is one of only the few centers in the United States offering liver transplantation for intrahepatic cholangiocarcinoma.

UCLA's Liver Transplant Program continues to see highly encouraging results through a protocol involving a combination of neoadjuvant chemotherapy and radiation followed by transplantation for patients with cholangiocarcinoma, or bile-duct cancer. The program has approximately 13 years of experience with the approach and remains one of only a few centers in the United States with a protocol for liver transplantation of patients with the otherwise lethal cancer — and among the only sites offering liver transplantation for intrahepatic cholangiocarcinoma, which occurs in the bile ducts within the liver.

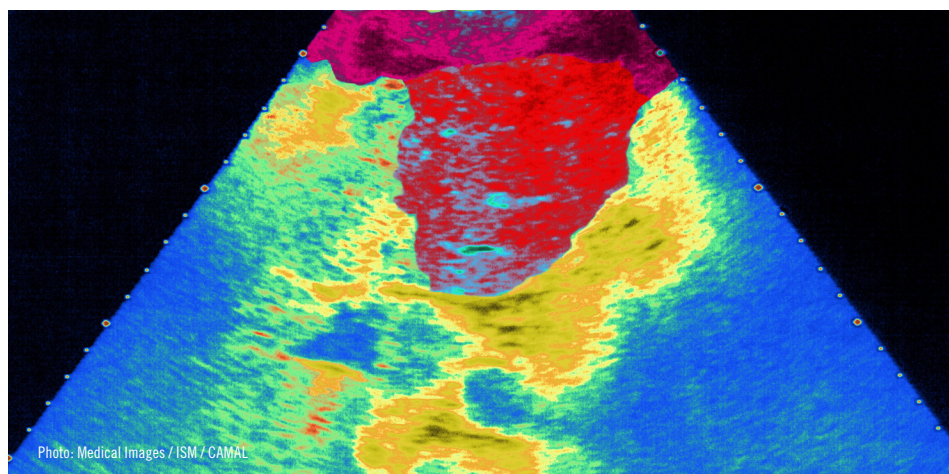
“Cholangiocarcinoma is an insidious cancer that often affects patients in the prime of their lives,” says Sammy Saab, MD, MPH, chief of transplant hepatology and medical director of the UCLA Adult Liver Transplant Program. “It tends to develop without symptoms, and there are no standardized ways of screening for people at risk, so it’s often diagnosed very late in the disease course. Many physicians in the community have considered this to be a death sentence, but the therapy provided by the multidisciplinary team at UCLA has been a game changer, and we want referring physicians to know that there is an opportunity to improve these patients’ quality of life and survival.”

Fady Kaldas, MD, associate professor of surgery and director of the UCLA Liver

Transplant Service, notes that historically, liver transplantation of cholangiocarcinoma patients has been associated with high rates of recurrence and overall outcomes so poor that they didn’t support doing the operation. That changed at UCLA with a comprehensive approach involving multidisciplinary care in which patients receive radiation therapy and chemotherapy prior to the transplant. This includes patients with intrahepatic cholangiocarcinoma as well as those with hilar cholangiocarcinoma, in which the tumor is in the bile ducts just outside the liver.

In September, the team led by Dr. Kaldas published in *Liver Transplantation* “A Three Decade Single Center Experience of Liver Transplantation for Cholangiocarcinoma; Impact of Era, Tumor Size, Location and Neoadjuvant Therapy,” covering UCLA’s experience with more than 50 intrahepatic and hilar cholangiocarcinoma patients who received transplants both before and after the current protocol was initiated. The results were striking — including a 100% survival in patients with intrahepatic cholangiocarcinoma treated with neoadjuvant chemo-radiotherapy followed by transplantation.

“We’ve learned that if patients are able to respond to chemo-radiotherapy before transplant, their outcomes are significantly better, certainly justifying the operation,” Dr. Kaldas says. “In fact, we have found that the



Ultrasound scan of the liver and bile ducts showing intrahepatic cholangiocarcinoma, bile-duct cancer.



tumor size is less relevant than previously suspected. If the patients are able to tolerate either chemotherapy or radiation — ideally both — and then get a liver transplant between six months and a little over a year after diagnosis, they tend to have the best outcomes. Obviously, this is a much less common cancer than hepatocellular carcinoma, so the numbers are small. But the outcomes continue to improve across the board.”

Drs. Saab and Kaldas believe a key to the protocol’s success is the comprehensive, multidisciplinary nature of the care,

**“We have incredible cases of survival involving patients who would have been considered untransplantable under protocols followed by most centers.”**

which involves experts in hepatology, medical oncology and radiation oncology working together in managing patients and tailoring treatment to their individual case — including not just transplantation but liver resections where appropriate.

One of the challenges the UCLA team has faced is ensuring that cholangiocarcinoma patients can get a liver once listed for transplant. “Access for these patients tends to be limited because their liver continues to work, despite it having this terrible cancer in it, and within the transplant community most centers aren’t doing liver transplants for cholangiocarcinoma — or if they are, it’s with extremely rigid criteria,” Dr. Kaldas says. “We hope our experience will support moving these patients up on the list.”

The UCLA liver-transplant team also hopes to get the word out to physicians in the community that early referral of cholangiocarcinoma patients can save lives. “Unfortunately, many of these patients show no other liver disease when they get this problem, so we are advocating having a low threshold of suspicion before imaging patients and studying them if there is any concern, especially for high-risk patients — those with primary sclerosing cholangitis, for example, and those with a family history,” Dr. Kaldas explains. “We also need to change the thinking that there is no hope for these patients once diagnosed unless they have a small lesion that can be easily resected. We have incredible cases of survival involving patients who would have been considered untransplantable under protocols followed by most centers. Hearing from such patients who, years later, are living normal lives is what motivates us to continue doing what we do.”



Photo: Medical Images / Look at Sciences



For more information about UCLA’s liver-transplant program, go to: [uclahealth.org/transplants/liver](https://uclahealth.org/transplants/liver)

# Vouchers expand reach of living-kidney donations

## STORY HIGHLIGHTS

Voucher program allows living-kidney donors to choose the most convenient time frame for their surgery, even if their intended recipient doesn't yet need a transplant, with the donated organ going to a matched recipient with an immediate need.

Nationwide program has dramatically expanded the pool of centers at which participants can donate and from which designated recipients can redeem their voucher in the future.

An innovation designed to increase living kidney donations, which started at UCLA in 2014 and is now run by the National Kidney Registry (NKR) with nearly 80 participating transplant centers, has resulted in an uptick in living donations, according to a recent UCLA-led analysis published in *JAMA Surgery*.

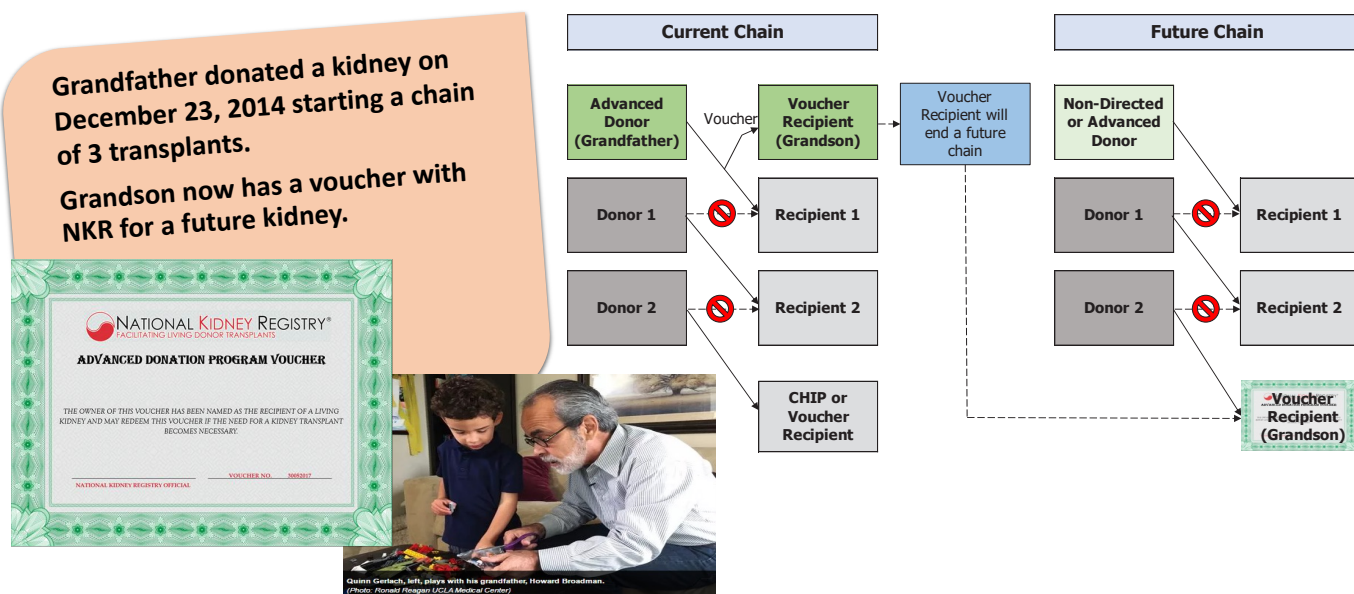
The NKR Voucher Program allows living-kidney donors to choose the most convenient time frame for their surgery, even if their intended recipient doesn't yet need a transplant. The donated kidney goes to a matched recipient on the waiting list with an immediate need, and the donor receives a voucher that can be used to prioritize a friend or family member to receive a living-donor kidney through the NKR if and when they need a transplant in the future.

In a review of data compiled by the NKR, Jeffrey L. Veale, MD, a renal-transplant surgeon who directs the UCLA Kidney Exchange Program, found that between 2014 and 2021, a total of 250

donations were made at 79 transplant centers under the voucher program, with six recipients redeeming their vouchers. During that time, the average waiting period for individuals enrolled with the NKR dropped by three months.

Dr. Veale and his colleagues concluded that the voucher program has helped otherwise willing altruistic donors overcome a hurdle to their moving forward by ensuring that loved ones who might need a kidney in the future will be taken care of. It also removes another common obstacle — when there is an intended recipient who doesn't yet need the organ at the time that an older family member is ready to give. “A new term came out of this program: chronological incompatibility,” Dr. Veale says. “Many people are incompatible not by blood type, but by time. They're able to donate now, but their relative or friend won't need the kidney for a number of years.”

Chronological incompatibility was the issue facing Howard Broadman, a 64-year-old retired San Diego County judge, when he approached the UCLA Kidney Transplant Program in 2014 with an unusual request: If he donated to a stranger now, could his



Voucher Program Solving Chronological Incompatibility



then-4-year-old grandson, Quinn, who had chronic kidney disease but didn't yet need dialysis, receive priority for a transplant if needed later in life? "Quinn wasn't likely to require dialysis for 10-to-15 years, and by that time Judge Broadman would be close to 80 and too old to qualify as a donor," Dr. Veale explains. "We thought it was a great idea, and UCLA backed us up." As an altruistic, nondirected donor, Broadman's act — and the actions of those who followed suit under the voucher program as it was launched at UCLA before going national under the NKR's administration — initiated a so-called transplant chain, in which a recipient who has an incompatible donor receives a kidney, that incompatible donor pays it forward to another person with an incompatible donor, and so on.

The voucher concept was initially met with skepticism in the transplant community, but it has since been embraced, notes H. Albin Gritsch, MD, surgical director of the UCLA Kidney Transplant Program. "There was a lot of reluctance to accept that someone would donate a kidney and not know who would receive it, but people like the judge showed that they are just trying to make the world a better place while providing some insurance for their family," Dr. Gritsch says. "This is really the ultimate philanthropic gift."

The support of the NKR has been integral to the growth of the voucher concept, Dr. Gritsch notes, since it dramatically expands the pool of centers at which participants can donate and from which designated recipients can redeem their voucher in the future. The program offers participants either a standard voucher — when a family member or friend is expected to need a kidney transplant within a year and the donor would like to donate sooner rather than later — and a family voucher, when there is not an immediate need for a kidney transplant but the donor wants to help others now, in exchange for a voucher that can be redeemed by one of five family members that donor designates.

At any given time, the number of people eligible for a life-saving kidney transplant exceeds the supply, and Drs. Gritsch and Veale note that the majority of organs still come from deceased individuals who have declared themselves as organ donors on their driver's license or discussed the matter with family members. But innovations pioneered at UCLA such as the voucher program, chain transplants, and direct exchanges among incompatible donor-recipient pairs have increased the number of living donations, and that has helped to make a dent in the waiting list, which had exceeded 105,000 and is now down to approximately 90,000.

"The demand for kidneys is going to continue," Dr. Gritsch says. "But innovations such as these are making a big difference."



Photo: Courtesy of Dr. Jeffrey L. Veale



For more information about the **UCLA Kidney Exchange Program**, go to: [uclahealth.org/transplants/kidney-exchange](https://uclahealth.org/transplants/kidney-exchange)

## STORY HIGHLIGHTS

Despite being a referral center for some of the most difficult cases — among them, patients who have been turned away at other lung-transplant centers — the UCLA Lung Transplant Program demonstrates results that are among the nation's best.

Expert utilization of extracorporeal membrane oxygenation as a bridge to transplant for many of the sickest patients has contributed to UCLA's success in the field.

A major challenge facing the field continues to be that lungs are more prone to rejection than other transplanted organs; UCLA and Duke University are launching a clinical trial of a new immune-suppression strategy designed to address this concern.

# UCLA's lung-transplant program demonstrates success with highest-risk patients

The UCLA Lung Transplant Program continues to be one of the nation's busiest — having performed 120 lung transplants in 2020, more than in any prior year in the program's history. Beyond the volume, the program has results that are among the nation's best, despite being a referral center for some of the most difficult cases — among them, patients who have been turned away at other lung-transplant centers. “We are able to bring in higher-risk patients because of the combination of having a volume that supports risks and the experience that comes with that volume, which includes dealing with very challenging medical situations and complex issues, such as patients with a heart problem who need a lung transplant or a systemic disease that's damaged their lungs,” says David Sayah, MD, PhD, the program's medical director.

One of the reasons some of the most seriously ill patients are better off awaiting a lung transplant at UCLA is the program's leadership in the use of extracorporeal membrane oxygenation (ECMO), a cardiopulmonary bypass machine that pumps oxygenated blood into the veins and arteries, allowing the lungs and heart a chance to heal. At UCLA, ECMO is employed to provide a bridge to transplant for patients who could benefit from one but become decompensated and require the intensive care treatment to keep their window to a transplant open. After doing the procedure, a team of ICU physicians provides around-the-clock care until a transplant can be performed.

“ECMO gives us the ability to stabilize patients who would otherwise not be candidates for transplantation because



Photo: Medical Images / Phanie / HOP-FOCH



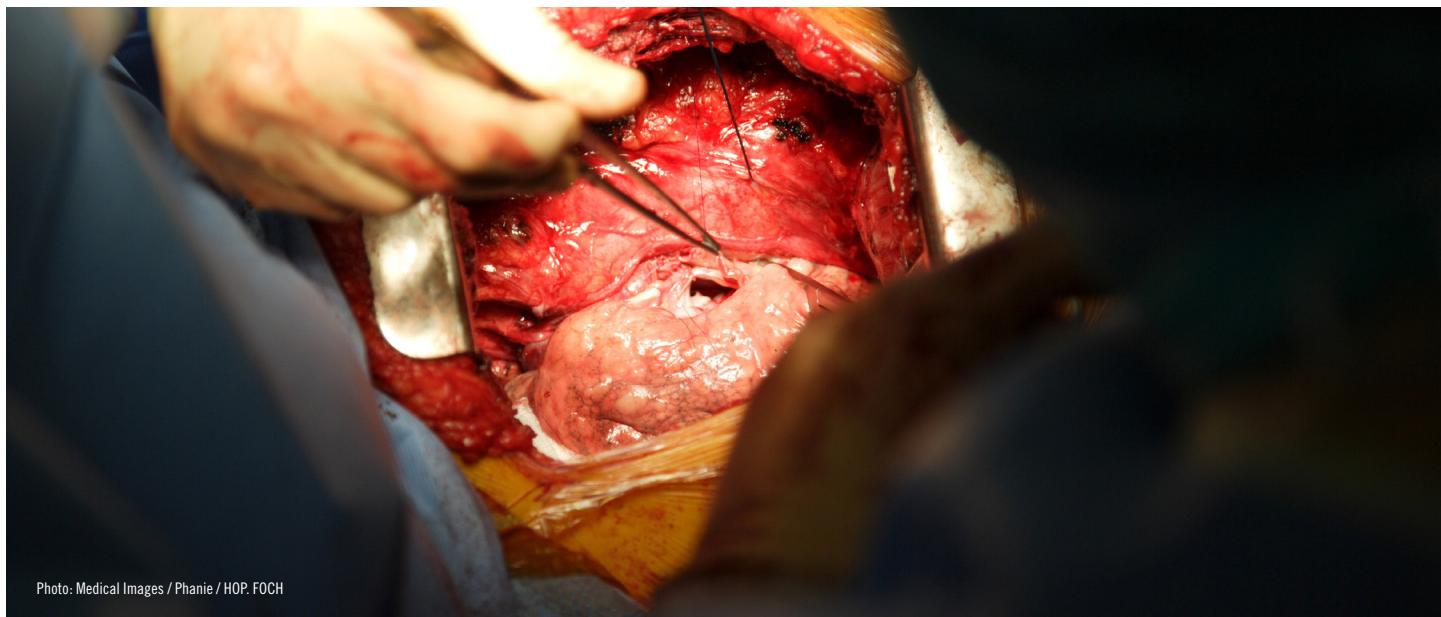


Photo: Medical Images / Phanie / HOP. FOCH

their lungs aren't working, so that they can be bridged safely to lung transplantation," says Abbas Ardehali, MD, director of the UCLA Lung Transplant Program. He notes that UCLA has one of the broadest experiences in the nation with ECMO patients going into lung transplantation, with more than 80% eventually receiving lung transplantation and nearly 100% able to return home from the hospital after the transplant. "The transplant operation is

**"We are able to bring in higher-risk patients because of the combination of having a volume that supports risks and the experience that comes with that volume..."**

much more complex because these patients are sicker and on blood thinners, but despite these adversities, they have done well, making ECMO a useful adjunct for patients who have no other options," Dr. Ardehali says. "This is a resource- and talent-rich undertaking that's only possible at an institution like UCLA."

"It's much better when patients are referred early, before they need bridging, so that we can try to avoid ECMO," Dr. Sayah

notes. "But sometimes patients decompensate so quickly that it can't be avoided, or the wait time is longer than what we anticipated, the standard ways we get patients oxygen in the hospital aren't enough and they need additional support. In such cases, ECMO gives them a chance to receive that transplant, leave the hospital and return to their lives. It fits with our overall commitment that when a patient needs a transplant, we're going to do whatever we can within our capabilities, which are considerable, to get them to that point."

Drs. Sayah and Ardehali point out that the use of ECMO as a bridge to transplantation is just one of many examples of the UCLA program's commitment to taking on high-risk cases. "As a state institution, we should be, and are, the last resort for patients without options," Dr. Ardehali says. "As such, we have expanded our indications." He notes that, for example, patients with heart conditions and those with mixed connective tissue disease, as well as patients considered too old by other centers, have been accepted for lung transplantation by the UCLA program, with good results.

Overall, Dr. Ardehali says, improvements in the surgery, as well as in perioperative and postoperative care, have meant that patients who would have had no chance at survival even 15 years ago are now able to get transplanted and go home to lead productive lives.

One of the major challenges facing the field continues to be that lungs are more prone to rejection than other transplanted organs — most likely because they are exposed to air,

activating the immune system. UCLA and Duke University will soon launch a clinical trial of a new immune-suppression strategy designed to address this concern.

Because of the rejection issue, median survival after a lung transplant is approximately six years. "That's shorter than for other solid organs, but these are patients who would otherwise have very short life expectancies," Dr. Sayah says. "And maybe even more important is the fact that their quality of life without a transplant is extremely poor. With a transplant, it's almost like watching someone be reborn. Seeing that and hearing from those patients is one of the things that keeps us doing this work."



**For more information about UCLA's lung-transplant program, go to:**  
[uclahealth.org/transplants/lung](http://uclahealth.org/transplants/lung)





U.S. News & World Report's Best Hospital Survey  
ranks UCLA No. 1 in California and No. 3 in the nation.



## UCLA Advanced Lung Disease and Lung Transplantation Symposium

The 2022 UCLA Advanced Lung Disease and Lung Transplantation Symposium is a hybrid virtual and in-person conference for pulmonologists, cardiologists, critical care physicians, internists, cardiac and thoracic surgeons, as well as allied health professionals who care for patients with advanced lung disease or who refer patients for lung transplantation. The goal of the program is to provide information on state-of-the-art therapies for patients with end-stage lung disease, including medical and interventional approaches, as well as lung transplantation.

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For more information and to register, go to:  
[tinyurl.com/2022-Lung-Transplant-Symposium](https://tinyurl.com/2022-Lung-Transplant-Symposium)

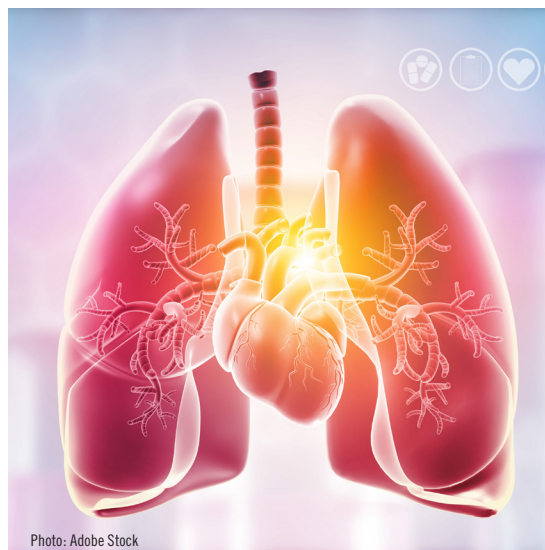


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## Physicians Update

WINTER 2022

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