Transplant Rounds
NEWSLETTER
Baylor St. Luke's Medical Center
Baylor College of Medicine
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In This Issue:

Transplant by the Numbers

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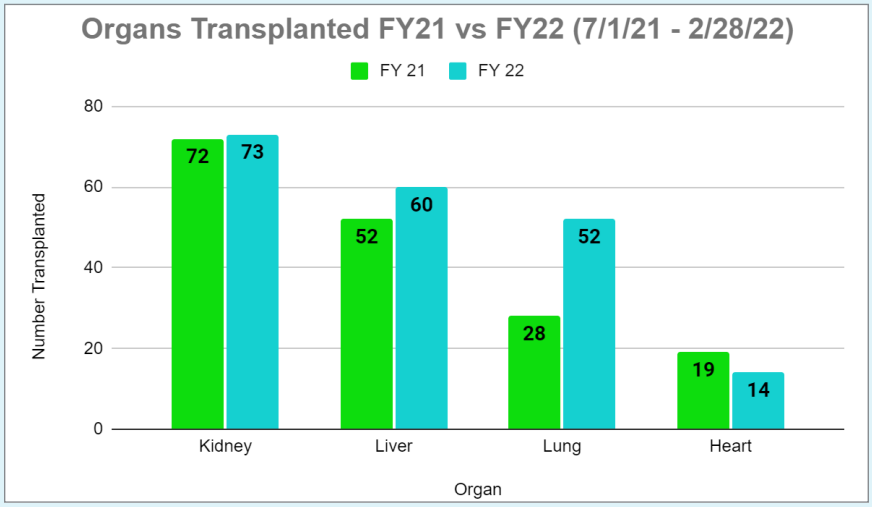

Transplant Hot Topics:

Baylor St. Luke's Medical Center and Life Gift Celebrate Lifesaving Gifts of Donation During April National Donate Life Month

LAUREN QUINN
Vice President of External Relations
Life Gift

National Donate Life Month was established by **Donate Life America** and its partnering organizations in 2003. Observed in April, National Donate Life Month supports and encourages Americans to **register as organ, eye and tissue donors** and to honor those that have saved lives through the gift of donation.

In support of Donate Life Month, Baylor St. Luke's Medical Center will be lighting up in blue and green throughout the month of April as part of Life Gift's Shine a Light of Hope campaign. City buildings, hospitals and other organizations throughout Houston, Fort Worth and Lubbock will shine in the Donate Life colors to honor donors and raise awareness of the importance of donation.

"We are deeply appreciative of our partnership with BSLMC in offering hope to donor families and transplant recipients through organ, eye and tissue donation," said Kevin Myer, CEO and president of Life Gift. "We are grateful to all of the hospital staff who have worked so hard to help us fulfill our mission to save lives."

Be sure to join **Life Gift** during the month of April on **Facebook**, **LinkedIn**, **Twitter** and **Instagram** to help celebrate Donate Life Month. And if you haven't yet joined the **Donate Life Texas donor registry**, you can register online and leave a legacy of life.

Transplant Contact: **HEART**: 832.355.2285 **KIDNEY**: 832.355.4100 **LIVER**: 832.355.1471 **LUNG**: 832.355.2285
Newsletter Contact: melissa.nugent@commonspirit.org norma.flores@commonspirit.org

Quality Corner: OPTN CHANGES TO TRANSPLANT PROGRAM MONITORING SYSTEM

SUSAN BOURGEOIS, MSN, RN, CCRN-K, CPHQ, CCTN, CENP
Director of Transplant Quality—Patient Safety, Baylor St. Luke's Medical Center (BSLMC)

The Membership and Professional Standards Committee (MPSC) of the United Network for Organ Sharing (UNOS) reviews transplant center performance under the authority of the Organ Procurement and Transplantation Network (OPTN). Currently, the MPSC uses a single metric, one-year post-transplant graft and patient survival, for identifying underperforming transplant centers. These criteria have been in the OPTN Bylaws since as early as 1987.

The MPSC has recently modified the OPTN Bylaws to create a more holistic approach to evaluation of transplant program performance. New metrics were selected to evaluate both pre-transplant and post-transplant aspects of patient care.

The MPSC has established new pre-transplant and post-transplant metrics and set boundaries for each. Under the new metrics, a transplant program will enter review if it fails to meet any of the thresholds set for each.

The new metrics address two main areas for review along the transplant continuum—waitlist management and post-transplant outcomes. The waitlist management metrics include waitlist patient care and organ offer acceptance practices, and the post-transplant metrics include 90-day graft survival and one-year graft survival. The first new metric will become effective in July 2022 and monitoring will begin in real-time moving forward (the new metrics will not be applied retroactively). The new metrics will be phased in one-at-a-time over a period of years. Proposed new metrics are shown in the table below:

Metric	Anticipated Implementation
90-day Graft Survival (2 ½ yr cohort)	July 2022 (JAN 2019 – JUN 2021)
1-year Graft Survival (excluding graft losses within 90 days) (2 ½ yr cohort)	July 2022 (JAN 2019 – JUN 2021)
Organ Acceptance Rate Ratio (1 yr cohort)	July 2023 (JAN 2022 – DEC 2022)
Pre-Transplant Mortality Rate Ratio (2 yr cohort)	July 2024 (JAN 2022 – DEC 2023)

In July 2022, the MPSC will consider program performance on these two metrics for transplants occurring January 2019 through June 2021. These two new metrics will replace the current 1-year post-transplant graft and patient survival criteria used by the MPSC to identify programs for performance review.

- 90-day graft survival hazard ratio: A program's rate of graft failure from date of transplant to 90 days post-transplant, relative to the expected based on transplants with similar recipient and donor organ characteristics across the nation
- 1-year conditional on 90-day graft survival hazard ratio: A program's rate of graft failure from day 90 post-transplant to day 365 post-transplant, conditional on the graft surviving for the first 90 days post-transplant, relative to the expected based on transplants with similar recipient and donor organ characteristics across the nation

Two other metrics will be added over the coming 2 ½ years. These will address pre-transplant program performance:

- The offer acceptance rate ratio is the most complex of the models built by the Scientific Registry of Transplant Recipients (SRTR) for transplant center data reports. The model adjusts for an extensive number of donor factors and recipient factors, sequence number of the candidate for which the offer is received, and candidate's distance from the donor hospital. Programs are only evaluated on offers they receive and decline that another program accepts and transplants. The Offer Acceptance Rate Ratio only evaluates offers for which at some point the center became the primary potential recipient. *When implemented in July 2023, the MPSC will examine offers received from January 2022 through December 2022.*
- Pre-transplant mortality rate will measure a program's rate of candidate mortality from registration date and before transplant relative to the expected risk-adjusted mortality at the time of registration. All candidates on the list at any time during the cohort are included (even if removed for reasons other than transplant, transfer, or recovery) if the death occurred during the cohort. If a patient is removed for recovery, they will remain included in the cohort until 60 days post recovery during the cohort. *When implemented in July 2024, the MPSC will examine deaths of candidates registered from January 2022 through December 2023.*

Transplant Program Performance

The MPSC will conduct reviews of transplant program performance to identify potential risks to patient health or public safety, as evidenced by a program failing to meet these thresholds:

1. The transplant program's 90-day post-transplant graft survival hazard ratio is **greater than 1.75 during a 2.5 year time period**. **(1.60 for pediatrics)**
2. The transplant program's 1-year post-transplant graft survival conditional on 90-day post-transplant graft survival hazard ratio is **greater than 1.75 during a 2.5 year period. (1.60 for pediatrics)**
3. The transplant program's offer acceptance rate ratio is **less than 0.30 during a 1 year period (0.35 for pediatrics)**.
4. The transplant program's pre-transplant mortality rate ratio is **greater than 1.75 during a 2 year period**.

Stay tuned to see the new outcomes reports in July 2022 at **srtr.org**!

RESEARCH NEWS

Simultaneous Liver-Kidney Transplantation for Highly HLA-Sensitized Patients

PETER JINDRA, PHD D(ACHI)

HLA Lab Director, Baylor Immune Evaluation Laboratory, Assistant Professor of Surgery, Division of Abdominal Transplantation, Department of Surgery

—and—

BHAMIDIPATI V. R. MURTHY, MD,DM.

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The role of HLA molecules is to present small protein pieces called antigens to T cells that initiate an immune response. The sequence of amino acids that creates the structure of the HLA molecule is very diverse among the human race and allows for the presentation of many different antigens to host T cells. In the presence of a foreign HLA molecule a person can develop anti-HLA antibodies and become sensitized. A high level of sensitization renders the patient unable to receive an organ to which they have made an anti-HLA antibody. Patients become highly sensitized after exposure to HLA antigens through blood transfusions, pregnancy or prior transplantation. HLA-sensitized patients now represent an ever increasing number of transplant candidates. In particular, women and various ethnic groups with less common ABO blood types are at risk for sensitization. HLA-sensitized patients pose major challenges both pre and post kidney transplantation. Patients with high titer of anti-HLA donor-specific antibodies (DSA) have a potential risk of hyperacute rejection, antibody-mediated rejection (AMR) and allograft loss. A positive complement-dependent cytotoxicity (CDC) crossmatch suggests a high titer of these antibodies, and is traditionally considered a contraindication for kidney transplantation.

In general, liver appears to be immunologically privileged having the ability to withstand high levels of DSA. Hence, pre-transplant sensitization, either through measurement of DSA or a pre-transplant CDC crossmatch, are not considered important for liver transplant alone. In case of simultaneous liver and kidney transplantation (SLKT), the significance of pre-sensitization has been a topic of debate. Our current research determines the intra-operative kinetics of anti-HLA antibody in SLKT. The duration and exact mechanism(s) of this protection is an active area of research we are engaged in. The order in which the organs are transplanted is critical. The liver needs to precede the kidney. As soon as the clamps are released the transplanted liver starts removing anti-HLA antibodies allowing for successful transplantation even in the face of a positive CDC crossmatch or high level of DSA without the need for desensitization. Pre-transplant DSA to class I antigens have been shown to decrease following SLKT. However, removal of preformed DSA to class II antigens may be variable and incomplete and can be associated with early graft rejection.

In our series of SLKT recipients transplanted between September 2016 and December 2018 with pre-formed DSA we found a marked reduction in DSA within one hour of reperfusion of the liver allograft which most likely-prevented hyperactue rejection of the renal allograft. Positive CDC crossmatch results pre-transplant were repeat tested after the liver transplant was complete and found to be negative. (Table 1) (Mol Genet Metab Rep 2021 (26) 100705) We observed within the patient sera a significant decrease of DSA while non-DSA antibodies remained strong emphasizing the specificity of this mechanism to remove only donor specific antibodies from the circulation. (Table 2) To measure if this effect was long-lasting, we repeated DSA assessment at 11 months post-transplant. At this timepoint there was no de-novo DSA and anti-HLA class I DSA suppression persisted. Interestingly, we found that anti-HLA class II DSA were not cleared as readily as anti-HLA class I DSA which fell to undetectable levels soon after reperfusion of the liver allograft although we did see reductions of up to 82%. This incomplete penetrance of the protective effect of the liver allograft against anti-HLA class II DSA may have its answer in the antigen expression of HLA class II molecules compared to HLA class I in the liver which is expressed on all somatic cells. HLA class II molecules are specifically expressed on antigen presenting cells (B cells, Macrophages and Dendritic Cells). Without the high concentration of cells in the liver expressing donor HLA Class II antigens, antibodies to HLA class II remain in the circulation.

These data (next page) have shown that it is possible to transplant immunologically high-risk patients with a prohibitive degree of sensitization that would otherwise have decreased access to transplant if unacceptable antigens were listed. All of our SLK transplants in this study have maintained excellent dual graft function with minimal immunologic inductions and represent a procedure that should be considered versus death on the waitlist. The timing of kidney transplant after the liver transplant has also been a subject of debate. Some centers have suggested waiting 6 to 24 hours after the liver transplant for the kidney transplant. However, we have found in our study no immunological compromise of the kidney even if transplanted immediately. Thus, the optimal timing of renal transplant during SLKT is immediate without delay, as long as patient is stable after the liver transplant. This will also not lead to increased cold ischemia time on the kidney, inflammation and stress on the patient.

RESEARCH NEWS *continued*

Table 1
Patient demographics and crossmatch results.

Patient	age	liver dz	kidney dz	Sex	Prior Txp	ABO, recipient	ABO, donor	PRA-I	PRA-II	Flow B cell	Flow T cell	CDC	CIT
1	56	HCV[¥]	HTN	M	YES	B	O	0	41	NEG	NEG	NEG	8 h 38 min
2	48	NASH	DM, HTN	M	NO	O	O	5	0	NEG	NEG	NEG	6 h 59 min
3	56	HCV[£]	HTN, DM	F	YES	A	A	99	80	POS	POS	POS	14 h 34 min
4	17	Hyper-oxaluria	Hyper-oxaluria	M	NO	B	O	0	0	NEG	NEG	NEG	9 h 25 min
5	70	NASH	DM	M	NO	B	B	93	50	POS	POS	NEG	12 h 0 min
6	57	NASH	DM	F	NO	B	B	87	22	POS	POS	NEG	10 h 51 min
7	63	HCV[¥]	DM	F	NO	A	A	100	80	POS	POS	POS	14 h 3 min

Dz, disease; txp, transplant; NASH, non-alcoholic steatohepatitis; HCV, hepatitis C virus; DM, diabetes mellitus; HTN, hypertension; txp, transplant; ABO, ABO blood group system; PRA, panel reactive antibody; CDC, complement-dependent cytotoxic crossmatch (retrospective, pre-transplant); *prior kidney transplant, [£]untreated; [¥]treated with sustained viral response.

Table 2
Anti-HLA antibody specificities and intensities.

	Anti-HLA Antibodies[a]					
		MFI				
	Antibody	PRE-OP	POST-LIVER	POST-KIDNEY	POD1	Transfusion RBC/FFP
Patient 1	A*01:01	12,072	311	258	241	700/1000
	A*02:01	**6851**	**8703**	**8651**	**9252**	
	B*07:02	**13,702**	**14,305**	**12,964**	**12,186**	
	B*35:01	14,378	285	229	168	
	B*41:01	14,794	2771	2461	1662	
	C*17:01	3653	482	383	242	
	DRB1*08:01	1279	366	316	226	
	DRB1*04	**9546**	**6849**	**6102**	**5357**	
Patient 2	B*57:01	3181	581	405	338	1050/0
Patient 3	DQ8	6935	5424	3698	2119	700/0
Patient 4	A*24:01	2145	785	984	556	0/0
	Bw4	Present	Absent	Absent	Absent	
Patient 5	**A*68:01**	**9020**			**12,003**	2100/750
	B*07:02	11,220			75	
	B*49:01	**8115**			**11,015**	
Patient 6	A*01:01	14,720			195	1050/250
	A*24:01	**6796**			**11,062**	
	B*44:03	10,479			119	
	B*57:01	**12,133**			**3242**	
Patient 7	A*33:01	19,308			2274	700/0
	B*53:01	19,201			1158	
	B*15:03	23,082			2431	
	C*02:02	10,725			1697	
	DRB1*14:01	2963			3772	
	DPB1*13:01	3400			1355	

Bold indicates non-DSA anti-HLA.
HLA, human leukocyte antigen complex; MFI, mean fluorescent intensity; PRE-OP, pre-transplant sample; POST-LIVER, post-liver reperfusion sample; POST-KIDNEY, post-kidney reperfusion sample; POD1, first post-operative day sample; transfusion, intra-operative transfusion requirements during transplant; RBC, packed red blood cells (mL); FFP, fresh frozen plasma (mL).

We hope the continued research in this field will lead to a greater understanding of how high titer anti-HLA antibodies can be significantly removed before and during transplant to promote long lived graft survival.

Normothermic Perfusion: DCD HEART DONATION AND TRANSPLANTATION

KEN LIAO, MD
Professor and Chief, Division of Cardiac Transplantation and Circulatory Support
Michael E. DeBakey Department of Surgery, Baylor College of Medicine

Heart transplantation has established itself as the best therapeutic option for patients with end-stage heart failure, with the opportunity to provide these patients with a near-normal quality of life. However, this treatment is severely limited by the availability of suitable donor hearts. Traditional cardiac donations are from brain death donors and every year about 3500 donor hearts are available for transplantation. Donation after Circulatory Death (DCD), previously referred to as donation after cardiac death or non-heart beating organ donation, refers to the retrieval of organs for the purpose of transplantation from patients whose death is diagnosed and confirmed using cardio-respiratory criteria. DCD has opened new perspectives and could be a valuable option to expand the brain-dead donors. It is estimated that DCD can potentially increase the heart donations for transplant by 20-30% yearly.

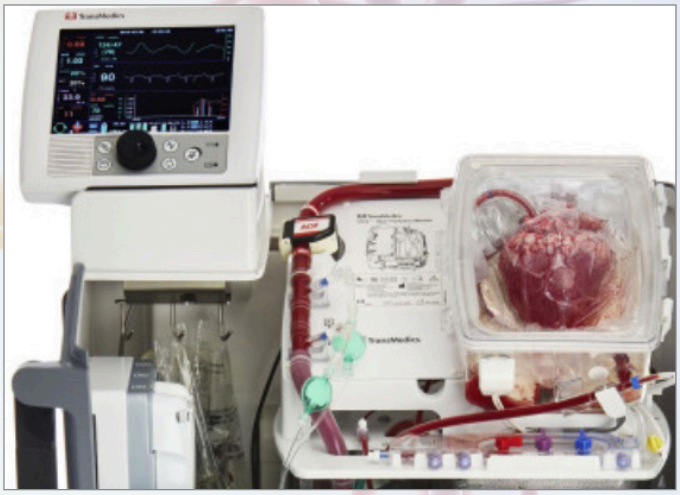
During DCD heart donation, the hearts are retrieved from those who have died because their hearts stopped because physicians discontinued life support as part of DCD donation protocol. The use of donor hearts from DCD had been thought to be associated with high risk and poor outcomes until recent developments in organ perfusion and retrieval techniques have shown that DCD heart can be safely transplanted. A couple of new methods and devices of "reanimating" donor hearts from those who have died from cardiac arrest before accepting them for heart transplant are currently undergoing clinical trials in the U.S.

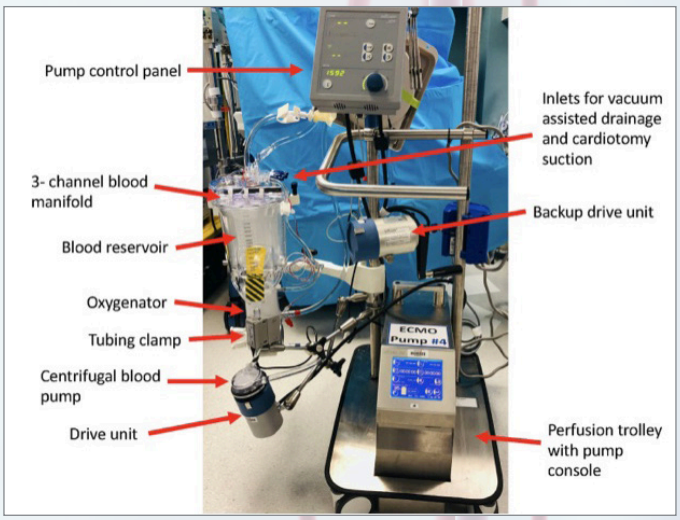
The first technology uses an ex vivo device (Trans medic OCS) that allows the heart to be perfused with warm blood after it has been removed from the donor, keeping the heart beating, functional and "alive" enough to be transported and transplanted several hours after retrieval until the moment of the recipient heart is removed. This device allows surgeons to assess the heart's functionality, including biochemical changes in a way that wasn't previously possible. (Figure 1)

The 2nd technology also called normothermic regional perfusion (NRP) utilizes Extracorporeal Membrane Oxygenation (ECMO) or cardiopulmonary bypass to reperfuse the heart and other organs in situ after isolation and ligation of the cerebral vessels. In situ resuscitation of the heart has the added advantage of allowing full hemodynamic and echocardiographic assessment of the donor heart prior to final acceptance for transplantation without the imminent danger of ongoing warm ischemia.

Once blood flow to the heart is established, the heart will start beating. At 30 minute intervals, the donor will be separated from cardiopulmonary bypass and the heart will be assessed for functionality. If accepted standard DBD procurement will commence. (Figure 2).

The major challenge or uncertainty of using DCD hearts is the donor heart warm ischemic interval prior to cardiac arrest. It is unclear what warm ischemic interval time is safe to accept the DCD heart before it develops irreversible myocardium damage. At present 30 minutes warm ischemic time in DCD hearts are considered acceptable though there is little scientific evidence to support this arbitrarily set time and it's unclear if DCD hearts with warm ischemic time longer than 30 minutes can still be safely used for transplant, which subgroup can represent additional donors. At the Division of Cardiothoracic Transplant at Balor St Luke's Dr Liao's team is currently conducting original research to provide the answers to these challenging but important questions in DCD heart donation and transplantation. The research is supported by the research grant from The Brockman Foundation.





Staff Spotlight: MIN JOO KO, RN, BSN

I am Min Joo Ko and I am a clinical surgery coordinator in the cardiovascular operating room at Baylor St. Luke's Medical Center.

I started my nursing career at St. Luke's CVOR and have not left since. I fell in love with the fast-paced, high intensity environment, all while working as a team. My role in the operating room is the circulating nurse. I make sure that the room has everything each surgical procedure needs, as well as being the problem solver when issues arise. It is important for me to speak up for my patients since they are not able to under anesthesia.

I am a member of the liver transplant team. When a liver transplant candidate gets an offer, the OR team is notified. I come in hours before the scheduled case and start my preparation for the transplant. If I could say it in three words, it would be ice, blood, and sutures! The most important step that is part of my routine is to make sure that the expected liver arrives in the OR. The surgeon and myself compare the unique identifier along with the ABO so that we know that it is the correct organ designated for this patient. It is always satisfying when the liver turns bright pink after the surgeon completes all of the anastomosis to the liver.

A liver transplant is not possible without all of the pieces to the puzzle. We have a pretty awesome team here at St. Luke's. From our surgeons, anesthesiologists, perfusionists, nurses, surgical techs, and patient care assistants. We come together and put in our best every time so that our patients get the care that they deserve. From the coordinators who guide our transplant patients all the way to day of surgery, to our surgical team, to the team in recovery that takes care of them post-op, and the donors who make all of this possible. I am so thankful and honored to be part of this team and proud to say this is what I do as my profession.

PHARMACY TIPS

RAYMOND YAU, PHARMD
Clinical Pharmacist II
Liver Transplant/Hepatology
Department of Pharmacy

Tacrolimus is the main immunosuppressive agent used after solid organ transplant. It is metabolized in the liver via the cytochrome P450 3A4 (CYP3A4) enzyme system. Drug interactions that we worry about consist of CYP3A4 inducers and inhibitors. CYP3A4 inducers lead to lower serum tacrolimus levels while inhibitors lead to increased levels. Some common inducers and inhibitors of the CYP3A4 system are listed here:

INHIBITORS (ELEVATE TACROLIMUS LEVELS)

Antifungals:
Fluconazole, voriconazole, posaconazole, isavuconazonium

Antibiotics:
Clarithromycin, erythromycin

Antihypertensives:
Verapamil, diltiazem

Drugs containing ritonavir (sometimes in HIV and HCV meds, or Paxlovid)

INDUCERS (LOWER TACROLIMUS LEVELS)

Antiepileptics:
carbamazepine, phenytoin, phenobarbital, primidone

Antibiotics:
Rifamycin products

NUTRITION TIPS
FOOD SAFETY

Good nutrition is extremely important throughout the transplant process and post-transplant to promote health and healing.

ALICIA DEGRAFTENREED, RD, LD
Liver Transplant Dietitian
Food and Nutrition Services

After transplantation you will be put on medications that lower your immune system. To avoid becoming sick it is very important to practice good food safety habits.

- Thoroughly wash all fresh fruits and vegetables before consuming them.
- Only consume pasteurized dairy products, and avoid all moldy cheeses.
- Do not use the same cutting board for fruits and vegetables as for raw meat.
- Cook all meat to the correct internal temperature:
  - Beef, veal, pork, lamb to 145°F
  - Poultry to 165°F
  - Fish to 145°F
  - Casseroles to 160°F
  - Eggs: whites & yolks should be firm

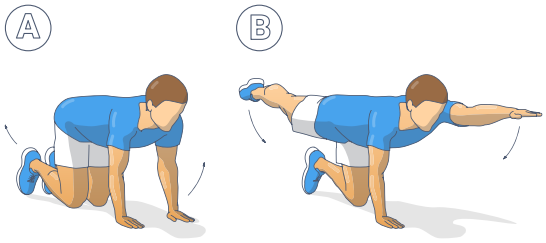
EXERCISE TIPS

Exercise is an important part of the road to recovery, both pre-and post-transplant.

GIL SPITZ, MS, CSCS
Exercise Physiologist
Liver Transplant Program
Baylor St. Luke's Medical Center

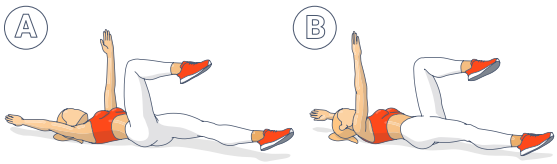
Abdominal surgery patients with strong core muscles tend to recover more quickly. To the right are two effective/accessible core exercises.

BIRD-DOG



DEAD BUG

ABS EXERCISE



CORE TRAINING

Bird-dog

From all fours, brace the core (think of pulling your navel up and back towards your spine), and extend opposite arm and leg forming a straight line from fingertip to heel; pause, return to starting position; repeat other side (X10).

Dead-bug

Lying supine, arms extending straight up, feet off the ground, hips and knees bent 90° so that torso, thighs and legs form right angles. Brace your core, fully extend opposite arm and leg; pause, return to starting position; repeat other side (X10).

Upcoming Events

Transplant Grand Rounds

MONTHLY

https://CommonSpirit-VirtualCareAnywhere.zoom.us/meeting/register/tJAtceCspjMjHtHiVJpUinsN3M1m8EpZfdss