



# Trans notes

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## Extended Use of ECMO Helps Lung Transplant Patient Survive After Primary Graft Failure

In a highly unusual case, the Lung Transplant Team at the Henry Ford Hospital successfully used extracorporeal membrane oxygenation (ECMO) to bridge a critically ill patient from a failed primary graft to a more successful, second lung transplantation.

The initial transplant took place in September 2012 with the second transplant following less than three weeks later. In total, the patient was on ECMO for 19 days.

"This was definitely an unusual case with the patient remaining on ECMO for so long," said Hassan Neme, M.D., surgical director of Lung Transplant, the surgeon who performed both transplantation procedures and a number of other surgical interventions while waiting for the second pair of donor lungs. The patient, 39-year-old Heather Wendt from St. Clair Shores, Mich., even spent a significant amount of time on a mechanical ventilator, which often excludes patients from consideration for lung transplantation.

"But she was young and strong and she obviously tolerated ECMO well, so after careful deliberation with many colleagues, the team decided to re-list her for a second transplant," said Lisa Allenspach, M.D., the medical

director of the Lung Transplant program.

The second transplant went very well, but Heather faced a long road to recovery. In total, she spent more than six months in the Intensive Care Unit (ICU) at Henry Ford Hospital.

"The nurses and doctors were the best at Henry Ford – absolutely the best. After so much time in the ICU, they became like a second family to me," Heather said.

Over the years, Heather had met a lot of nurses and doctors. Diagnosed with agammaglobulinemia at age 19, she'd spent years receiving bi-weekly intravenous treatments and suffered severe recurrent respiratory infections and pneumonia. After 20 years her lungs had been severely damaged, which led to her respiratory failure and the need for a lung transplant.

"I was really very close to dying," Heather said. "Near the end, it didn't look like we were going to find a second donor and some of the doctors told my family to be prepared for the worst."

But even then the transplant team didn't give up hope. "I'm so thankful to all of my doctors and nurses. I honestly believe a lot of other hospitals would have given up on me," she said. "And, of course, I'm very thankful to the organ

donors and their families."

Today, less than a year after her transplants, Heather continues to recover. But she feels better than she has in years. She's able to do household chores, play with her granddaughter and take walks without any shortness of breath. She's even looking forward to getting a job – maybe a desk job in an office setting – for the first time in almost 20 years.

"Here I am almost 40 years old and I'm getting a chance to restart my life," she said. "It's very exciting."



Lung Program Profile  
page 2



Graft Outcome Criteria  
page 3



Have We Met?  
page 5

Welcome to the Fall 2013 issue of *TransNotes*, a newsletter produced by the Henry Ford Transplant Institute. As always, our goal is to share our research and important advances in the field of transplantation with our colleagues.

In this issue, you'll find an article about a rare double lung transplant performed twice on the same 39-year-old patient.

She had suffered for 20 years with IV treatments and infections, often on a mechanical ventilator, all of which could have excluded her from transplantation. Young and strong, she tolerated the transplants and ECMO well and today she continues to recover feeling better than she has in years.

Three studies that focused on liver, kidney and cell transplantation continue to advance our work. The liver research identified patients with a higher recurrence of non-alcoholic steatohepatitis and cryptogenic cirrhosis associated with the presence of metabolic syndrome, hypertension and insulin use. The kidney study identified factors and their numerical percentage when applied to a deceased donor kidney value indicating a risk ratio for graft failure. And, the cell study evaluated the impact of pre-transplant therapy on post hematopoietic cell transplantation outcomes, including overall survival and progression-free survival.

Each edition of *TransNotes* highlights a specific program. This month, we feature the Lung Transplant program, led by Hassan Nemeh, M.D., surgical director and Lisa Allenspach, M.D., medical director.

Patients and referring physicians also have available to them the Inflammatory Bowel Disease Center in Novi. The Center offers many services IBD patients often need with the experts to support those needs.

I hope you find these articles and other information in *TransNotes* thought-provoking and valuable in your own research and practice. As always, referring physicians should feel free to contact us at our toll-free number, 1-877-434-7470, or to contact me directly at (313) 916-2941, for your patient or practice needs.

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# Lung Transplant Program Offers a Better Quality of Life

Only half of the adults on the national lung transplant waiting list will ever receive a lung transplant due to the limited number of donations. The other half will never experience a transplant. These are people between the ages of 18 and 65 who suffer from complex lung diseases.

In 2012, 14 lung transplants were performed at Henry Ford Hospital. Each lung transplant recipient is recovering very well. Despite the limited donations, approximately 1,800 lung transplants are performed annually throughout the United States.

The lung was the last organ to be transplanted, starting in 90s, due to the extreme complexity of the procedure. The Lung Transplant program at Henry Ford began in 1994. To date, 178 lung transplants have been performed. "Survival rates among Henry Ford Hospital patients have achieved the national average, with a one-year survival rate of 86 percent," says Hassan Nemeh, M.D., Henry Ford transplant surgeon, "The majority of Henry Ford lung transplant patients recover to lead active, normal lives."

Advancing technology, improved surgical skills and pharmacology work together to provide the patient with better survival rates and improved quality of life among double lung transplants. "Nationally, more double lung transplants are done than single-lung transplants, because the overall health and quality of life is significantly improved," says Dr. Nemeh. (*See cover story.*)

Research at Henry Ford Hospital has brought about new therapies for lung transplant patients. Transplants may be done with or without cardiopulmonary bypass machines and at the same time as heart surgeries, if warranted. Infection is a chief concern for the recipients of transplanted lungs, so



many patients participate in clinical trials of new medications aimed at preventing and fighting such events.

Lisa Allenspach, M.D., medical director of the Lung Transplant program explains, "Special services include the FAST Track program where qualifying lung transplant candidates may have the entire pre-transplant evaluation completed in two weeks or less." She adds that "the pulmonary division offers advanced therapy in pulmonary hypertension, interstitial lung disease, sarcoidosis and interventional bronchoscopy." In addition, the lung transplant program is certified by the Centers for Medicare and Medicaid Services (CMS) and the United Network for Organ Sharing (UNOS).

After transplantation, patients also have access to the Transplant Living Community (TLC program). This community is comprised of transplant recipients and families who have known and experienced the tribulations of living with life-threatening illness prior to transplant, and have had success in the healing period that follows. Their experiences, reflections and practical tips are helpful and comforting to those just starting this journey.

To request an evaluation for lung transplant candidates, call the Henry Ford Referring Physician Office at 1-877-434-7470.

# Graft Outcomes Linked To Standard and Expanded Criteria

## for Donor Kidney Co-Morbidities

Studies of Expanded Criteria Donor (ECD) kidney transplantation confirm lower allograft survival compared to Standard Criteria Donor (SCD). Interestingly, donor age has been strongly implicated as a risk factor. Graft outcomes of recipients of SCD kidneys with risk factors of ECD are poorly understood and hence were studied.

Among adult deceased donor kidney recipients from the UNOS database, those recipients (R) whose donors were 40-49 and 30-39 years of age and met two of the three ECD criteria: history of hypertension, serum creatinine of >1.5 mg/dl and who died of cerebrovascular accident were identified as ECD40sR and ECD30sR respectively. Control groups were ECDR, SCDR and SCD50sR (recipients of kidneys from deceased donors aged 50-59 without ECD criteria or hypertension). Excluded were re-transplant, dual and multi-organ transplant recipients. Median follow up was four years. Cox regression analyses for graft survival (GS) were performed to compare ECD40sR and ECD30sR with ECDR, SCDR and SCD50sR. The variables used for Cox regression analysis were: the recipient's age, race, gender, BMI, cause of ESRD, co-morbidities of hypertension, diabetes, cardiovascular disease, peripheral vascular disease, cerebrovascular disease, organ procurement organization wait time, preemptive transplantation, and duration of hemodialysis. Also considered were: the donor's age, race, gender, hypertension, donor/recipient HLA mismatch, ischemia times, delayed graft function, and acute rejection. Graft failure was defined as re-transplantation or return to dialysis and censored for death.

Anita Patel, M.D., medical director, Kidney and Pancreas Program, says "On Cox regression analysis, there appeared to be no difference in graft survival between ECD40sR and ECDR as well as ECD30sR and ECDR after adjusting for all study variables."

Cox Regression Analysis for Graft Failure			
Variable	Hazard Ratio	95% Confidence	p-value
ECDR vs ECD40sR	1.02	0.91-1.15	0.69
ECDR vs ECD30sR	0.92	0.76- 1.11	0.37
ECD40sR vs SCDR	1.11	1.03-1.19	0.005
ECD30sR vs SCDR	1.16	1.03-1.31	0.01

When compared with SCDR, ECD40sR and ECD30sR appeared to have decreased graft survival on Cox regression analyses regardless of other study variables, 11 percent and 16 percent lower graft survival respectively.

Cox Regression Analysis Results for Graft Loss			
Study Groups	Hazard Ratio	95% Confidence Interval	p-value
SCD50sR vs ECD40sR	0.75	0.64-0.88	0.0003
ECDR vs ECD30sR	0.65	0.47-0.9	0.01

Graft survival appeared to be significantly higher in SCD50sR (33 percent) compared to ECD40sR. SCD50sR appeared to have significantly higher graft survival (53 percent) compared to ECD30sR.

"There appeared to be no graft survival benefit for recipients receiving ECD like SCD kidneys. These organs given as SCD kidneys had inferior graft survival compared to SCD organs. It appears that hypertension and or cerebrovascular accident (correlate of hypertension) and not donor age seems to determine graft failure risk," says Dr. Patel. It also appears that

recipients of younger donor kidneys with ECD defined comorbidities have inferior graft survival when compared to recipients of older SCD kidneys without comorbidities raising the possibility of arteriosclerosis in donor kidneys with its effects on glomerulosclerosis, interstitial fibrosis and tubular atrophy. Influence of other risk factors including components of the metabolic syndrome needs to be studied in this group of donors.

To better define the outcomes of deceased donor kidneys, the Kidney Donor Profile Index (KDPI) and Kidney Donor Recipient Index (KDRI)

*Continued on page 5*

## Lecture Series Groundbreaking Topics

The Henry Ford Transplant Institute hosts a series of monthly educational lectures throughout the year, which are also broadcast via Livestream on the web. These one-credit CME lectures are led by Henry Ford Transplant Institute physicians and surgeons as well as visiting professors who present a collection of groundbreaking transplant-related topics you won't find

anywhere else. Medical students and residents may also find these lectures valuable. Learn about future topics or view past presentations when it's most convenient for you or as a teaching aide.

For details about upcoming Livestream or recorded lectures, visit [henryford.com/transplanttalk](http://henryford.com/transplanttalk).

# Pre-Transplant Therapy for Patients with Myelodysplastic Syndrome and Post-Transplant Outcomes

Proven to have curative potential for myelodysplastic syndrome (MDS) is Allogeneic hematopoietic cell transplantation (Allo-HSCT). However, patient relapse post-HSCT continues to be a problem. Pre-HSCT cytoreduction with either intensive chemotherapy or hypomethylating agents has been used with limited data on pre- or post-HSCT outcomes.

This study evaluated the impact of pre-transplant therapy on post-HSCT outcomes including overall survival (OS) and Progression Free Survival (PFS). The objective of this retrospective study was to determine the impact of therapy pre-HSCT on HSCT, explains Shatha Farhan, M.D., blood and marrow stem cell transplant program, Henry Ford Transplant Institute. Among the 31 patients who underwent allo-HSCT for MDS at Henry Ford Hospital between 1997 and 2012, demographics, disease-related and transplant-related variables were collected.

PFS was defined as the time from HSCT to the time of progression, death or last contact whichever occurred first. OS was defined as the time from HSCT to the time of death or last contact. The distributions of PFS and OS were estimated by the Kaplan-Meier method. The log-rank test was used to compare the survival distributions between the two groups. Regression analyses for survival data used Cox proportional hazards model.

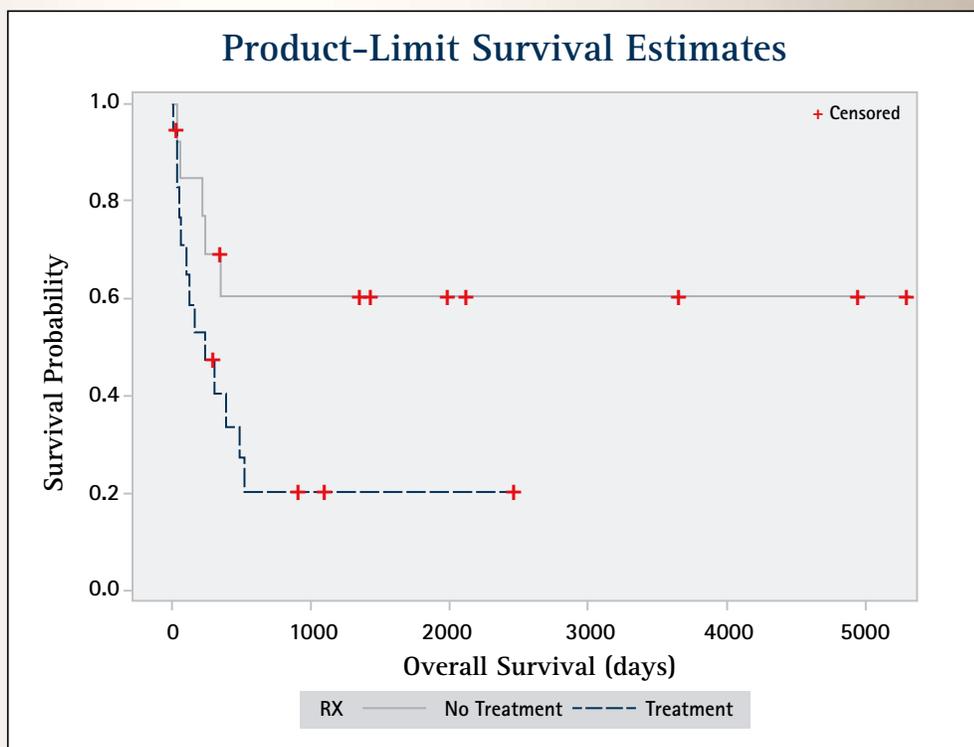
The results indicated the median age at HSCT was 58 years and median time from diagnosis to HSCT was 145 days. Of the 31 patients, 38.8 percent had poor cytogenetic abnormalities. Conditioning regimen used was high-dose in 71 percent or a reduced-intensity in 29 percent. Among the 31 patients, 18 patients (58.1 percent) received therapy before HSCT. Intensive therapy with cytarabine was used in three

patients while non-intensive therapy, with hypomethylating agents, median of four cycles, were used in 11 patients, Thalidomide or Lenalidomide in three patients and hydroxyurea in 1.13/31 (41.9 percent) did not get any therapy prior to HSCT.

On univariate analysis, the treatment prior to HSCT had adverse impact on PFS and OS (HR=2.8, P=.0404 and HR=2.8, P=.0387 respectively). In multivariate models, treatment prior to HSCT still emerged as a significant predictor of poor PFS and OS (HR=6.6, P=.0070 and HR=8.1, P=.0037 respectively) after adjusting for age, gender and WHO classification-based Prognostic Scoring System. There was no statistically significant difference in the change in percentage of blasts at

diagnosis and just before transplant for those who received therapy compared to those who did not (P=.5496).

Dr. Farhan says, "In this small cohort from a single center, the results are not in favor of MDS patients receiving therapy prior to HSCT. A prospective study with a larger cohort should be conducted to address this issue, taking into consideration disease characteristics in patients who may and may not benefit from pre-transplant therapy." As recently published, approximately 85 percent of bone marrow cells are clonal in MDS regardless of blast count (Walter et al. NEJM, 2012) which may explain the result of no difference in blast percentage before or after therapy and should not be used as a surrogate marker.



# Henry Ford Transplant Institute Outreach Clinics

In addition to the transplant clinics at Henry Ford Hospital in Detroit, 14 convenient outreach clinics are located throughout Michigan. Please contact our outreach coordinators for information: Michelle "Cookie" Crossley, R.N. at (248) 219-2326 or Dana Reissner, R.N. at (313) 218-9425.

## HEART

Advanced Heart Failure Clinic  
Henry Ford Macomb Hospital  
15855 19 Mile Road  
Clinton Township, MI 48038

Providence Heart Clinic  
22250 Providence Dr., Suite 705  
Southfield, MI 48075

Advanced Heart Failure Clinic  
St. John Hospital and Medical Center  
22201 Moross Rd., Suite 356  
Detroit, MI 48236

Advanced Heart Failure Clinic  
Henry Ford Wyandotte Hospital  
2333 Biddle Ave.  
Wyandotte, MI 48192

## KIDNEY

Lansing Kidney Clinic  
1703 E. Michigan  
Lansing, MI 48912

Pontiac Kidney Clinic  
44200 Woodward Ave., Suite 109  
Pontiac, MI 48341

Macomb Kidney Clinic  
16151 19 Mile Road, Suite 200  
Clinton Township, MI 48038

Novi Kidney & Lung Clinic  
Henry Ford Medical Center - Columbus  
39450 W. 12 Mile Road  
Novi, MI 48377

Hurley Kidney Clinic  
One Hurley Plaza, 5 West  
Flint, MI 48503

Ypsilanti Kidney Clinic  
5333 McAuly Drive, Reichert Building, Suite 403  
Ypsilanti, MI 48197

## LIVER

Borgess Liver Clinic  
1535 Gull Road, Suite 005  
Kalamazoo, MI 49048

Liver Transplant Clinic  
Spectrum Health  
41000 Lake Drive  
Grand Rapids, MI 43522

## LUNG

Grand Blanc Lung Clinic  
8220 S. Saginaw Street, Suite 800  
Grand Blanc, MI 48439

Novi Kidney & Lung Clinic  
Henry Ford Medical Center - Columbus  
39450 W. 12 Mile Road  
Novi, MI 48377

# Henry Ford Inflammatory Bowel Disease Center

The Henry Ford Inflammatory Bowel Disease (IBD) Center offers state-of-the-art medical and surgical care for patients with Crohn's disease and Ulcerative Colitis. The IBD Center offers a wide variety of services, including access to IBD subspecialists, dedicated IBD nursing, colorectal surgeons, IV infusions on-site, clinical trials, and close monitoring for patients on immunosuppressive medications.

Nirmal Kaur, M.D. and Jason Schairer, M.D., are both IBD subspecialists and are currently accepting new patients. Hours of operation are Monday through Friday, 8 a.m. to 5 p.m. The IBD Center is located within Henry Ford Medical Center - Columbus Center, in Novi. Appointments can be made by calling (248) 344-4147.

## Graft Outcomes

*continued from page 3*

were developed and these take into account the following: age, race, history of diabetes or hypertension, serum creatinine, height, weight, hepatitis C virus (HCV) result and cause of death. These factors are computed using the estimates of each factor that applies to a particular deceased donor kidney and giving a

numerical value of percentage and risk ratio for graft failure. Dr. Patel says, "UNOS is moving towards using KDPI and KDRI of a deceased donor kidney at the time of offer for transplantation giving physicians estimated risks associated with an organ. The definitions 'ECD' may soon become archaic."

## Have We Met?

### Reena J. Salgia, M.D.

#### Senior Staff Physician

#### Areas of Clinical Expertise:

Liver transplantation, hepatology, gastroenterology, and internal medicine.

#### Research Interests:

Outcomes and survival rates for liver transplant recipients, and donor factors that impact the patient.

#### Medical School Education:

University of Chicago  
Pritzker School of Medicine - Chicago, IL

#### Post Graduate Training:

University of Michigan Hospitals:  
Transplant Hepatology Fellowship -  
Department of Gastroenterology and Hepatology  
Gastroenterology Fellowship - Department of Gastroenterology  
Chief Medical Resident - Department of Internal Medicine  
Internal Medicine Residency - Department of Internal Medicine

#### Board Certifications:

Gastroenterology and Hepatology - American Board of Internal Medicine  
Internal Medicine - American Board of Internal Medicine





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## Henry Ford Transplant Institute Pledge

*To improve and extend life by meeting the  
needs of transplant patients and their  
families with compassionate, innovative  
and personalized quality care.*

# Researchers Link Metabolic Syndromes to Recurrence of Non-Alcoholic Steatohepatitis and Cryptogenic Cirrhosis Following Orthotopic Liver Transplantation

Researchers at the Henry Ford Transplant Institute are studying the recurrence of non-alcoholic steatohepatitis (NASH) and cryptogenic cirrhosis (CC) following orthotopic liver transplant (OLT). By retrospectively studying 83 patients who had liver transplants due to NASH or CC from 1996 to 2008, the researchers aimed to describe outcomes and identify predictors for recurrence of NASH and CC after transplantation.

"One of the primary outcomes of the study was identifying metabolic syndrome as a significant predictor for recurrence of NASH and CC after transplantation," said Atsushi Yoshida, M.D., surgical director of Liver Transplantation at the Henry Ford Transplant Institute and one of several

Henry Ford Transplant Institute investigators involved in the study.

Of the 83 patients included in the study, recurrence occurred in 20 patients. Thirty-four percent of patients with metabolic syndrome had recurrence of NASH or CC compared to 13 percent of patients without metabolic syndrome.

Additionally, the retrospective study revealed hypertension and insulin use to be associated with recurrence of NASH and CC after transplantation. According to the study data, recurrence occurred in 32 percent of patients with hypertension vs. 12 percent of patients without hypertension. Thirty-seven percent of patients on insulin had a recurrence vs. 6 percent of patients who were not on insulin. The research was published in a 2012

issue of the medical journal *Clinical Transplantation*.

"Our study clearly shows that there was a higher recurrence of NASH and CC associated with the presence of metabolic syndrome, hypertension and insulin use," said Dilip Moonka, M.D., hepatologist and medical director of the Liver Transplant Program, Henry Ford Transplant Institute.

Drs. Moonka and Yoshida and other researchers at the Henry Ford Transplant Institute conclude that recurrence should be further evaluated in larger studies with a special emphasis placed on understanding management of metabolic syndrome and prevention strategies.

