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Liver Transplantation in Patients with Sickle Cell Disease in the U.S.

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Abstract

Background: Up to 30% of patients with sickle cell disease (SCD) develop chronic liver disease via etiologies including sickle cell hepatopathy, acquired viral hepatitis, or secondary hemochromatosis. It is unclear how many patients with SCD ultimately undergo liver transplantation (LT) and what factors are associated with survival post-LT. In this study, we examined LT outcomes in these patients by reviewing the Scientific Registry of Transplant Recipients (SRTR) and our institutional experience.

Methods: Analysis of the SRTR identified 23 LT recipients and 5 simultaneous liver and kidney transplantation (SLKT) recipients with SCD. Patient demographics as well as graft and patient survival were analyzed. Two patients with SCD at our institution underwent SLKT.

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Results: Review of the SRTR revealed that recipients with SCD had significantly higher Model for End Stage Liver Disease (MELD) scores (33 vs. 21, $p = 0.004$), pre-operative intensive care unit admission (43.5% vs. 19.1%, $p = 0.007$), pre-operative dialysis (17.4% vs. 4.9%, $p = 0.009$), and were more likely to be Status 1 (26.1% vs. 12.1%, $p = 0.041$) when compared to the reference population of African American LT recipients. Despite being higher risk at the time of LT, patients with SCD had equivalent post-transplant graft and patient survival when compared to the reference population ($p=0.5$ and $p=0.2$, respectively) and a 2:1 propensity score matched group ($p=0.5$ and $p=0.2$, respectively). Two recent SLKT recipients with SCD from our institution have done well with stable allograft function.

Conclusions: Data from the SRTR demonstrate that patients with SCD can expect equivalent graft and patient survival post-LT despite exhibiting more comorbidities at the time of LT. The low number of patients with SCD who underwent LT in the SRTR in comparison to the rate of chronic liver disease in this population raises the question as to whether a disparity in access to LT exists for this complex population.

Introduction

Sickle cell disease (SCD) was one of the first human genetic diseases to be identified and is caused by the presence of pathologic hemoglobin S (HbS) in homozygous patients (HbSS), leading to the formation of sickled erythrocytes in deoxygenated conditions. This disease is most prevalent in the African American population, and intra-vascular sickling of red blood cells causes hemolysis, vaso-occlusive crises, and severe pain. While the diagnosis of SCD used to portend poor prognosis, the introduction of vaccinations for encapsulated bacteria and multidisciplinary management of these patients has resulted in improved outcomes.¹ As a consequence of chronic hemolysis and microvascular injury, patients with SCD can develop a variety of secondary end organ complications, including renal failure and chronic liver disease.² It is estimated that 25-30% or more of patients with SCD have chronic liver disease. Contributing factors include ischemic injury, and transfusion complications such as iron overload and acquired viral hepatitis (especially for transfusions received prior to 2000).^{2,3} Acute sickle intra-hepatic cholestasis is a severe condition which can progress to acute liver failure associated with a 50% mortality; some cases respond to exchange transfusion, but an estimated 17% are refractory to exchange transfusion with transplantation as the only option for survival.⁴⁻⁷ Repeated insults to the liver may lead to chronic liver disease and cirrhosis. Thus, chronic liver disease and cirrhosis is often multifactorial in these patients.^{8,9} A recent Medicare report on SCD indicated that there are presently >100,000 patients living with SCD in the U.S., with more than 25% experiencing concomitant chronic liver disease.²

Despite these data suggesting that many patients with SCD are at risk of developing liver failure, the role of liver transplantation (LT) and simultaneous liver and kidney transplantation (SLKT) in the treatment of chronic liver disease secondary to SCD is limited to case reports.^{5,7,10-12} Renal transplantation in patients with SCD and chronic kidney disease has been more commonly described in the literature, and historically, patients with SCD were associated with an increased risk of mortality post kidney transplant.^{13,14} However, more recent studies have shown comparable survival to diabetic kidney transplant recipients, with improvement in post-transplant survival.¹⁵

The objectives of this study were to review the outcomes for LT recipients with SCD, compare survival outcomes of a propensity score matched sample of LT recipients with SCD and a reference population of African American LT recipients in the Scientific Registry of Transplant Recipients (SRTR). In addition, we describe our center's approach to LT in patients with SCD by reviewing two recent cases of SLKT with positive post-transplant outcomes.

Methods

This study was approved by the Health Science Campus Institutional Review Board of the University of Southern California.

Scientific Registry of Transplant Recipients-

The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the U.S., submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. The data reported here have been supplied by the Hennepin Healthcare Research Institute (HHRI) as the contractor for the SRTR. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government. Twenty-three SCD liver transplant patients and 5 SCD SLKT patients were identified through free-text diagnosis in the OPTN data as of December 1, 2017. A reference cohort of 9,204 African American deceased donor liver transplant (DDLT) recipients age ≥ 14 was identified. First liver transplants, whole organ, and Status 1 cases were included in the reference cohort. Living donor, deceased cardiac donor, and prior organ, and multi-organ transplants were excluded. A propensity score matched sample of SCD and DDLT recipients was created by matching the variables age, sex, and transplant MELD in a ratio of 2:1. A total of 18 SCD recipients and 36 DDLT recipients were identified by propensity score matching.

Statistics-

Differences in demographic and clinical characteristics between the SCD and reference cohort were assessed using the Chi-Square test. The propensity score matching was performed without replacement using a caliper width of 0.2 of the standard deviation of the logit of the propensity score. The balance of covariates between the SCD and DDLT recipients was assessed by standardized differences. Post-transplant patient survival and graft survival were calculated using the Kaplan-Meier method. Patient survival was defined as time from transplant to death or last follow-up. Graft survival was defined as time from transplant to graft failure or death. The log-rank test or robust score test was used to assess differences in the survival curves. P-values less than 0.05 were considered statistically significant. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC) and R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

Case Series from USC-

Our center has performed SLKT in two patients with SCD out of >1500 LT procedures, both of which occurred since 2018. A retrospective review of the hospital records was conducted for two liver transplant recipients with SCD at our center for the purpose of providing case reports.

Results

Part 1: Analysis of SCD in the SRTTR

A total of 23 patients with SCD underwent LT during the study period. Compared to the reference cohort of African American LT recipients, patients with SCD were more likely to be pediatric patients ($p < 0.001$) and had significantly lower body mass index ($p > 0.001$) (Table 1). In addition, patients with SCD had significantly higher calculated MELD scores at transplantation (33 vs. 21, $p = 0.004$), were more likely to be hospitalized or be in the intensive care unit ($p = 0.007$), had significantly higher likelihood of pre-transplant dialysis (17.4% vs. 4.9%, $p = 0.009$), and were more likely to be listed as Status 1 (26.1% vs. 12.1%, $p = 0.041$). Patients with SCD were less likely to have Hepatitis B or C (4.3% vs. 25.1%; $p = 0.016$ and 8.7% vs. 41.5%, $p < 0.001$, respectively). No patients with SCD had diabetes, which was significantly lower than the reference population ($p = 0.019$) (Table 1).

The median overall survival for liver transplant in SCD was 67.7 months. The median length of stay for the SCD cohort was 24 days (Table 2). In all, 5 patients (22%) were ultimately re-transplanted at 1, 23, 45, 58, and 59 months. Three patients lost their graft due to sickle cell crisis hepatopathy, one patient lost their graft from secondary hemochromatosis, and one patient lost their graft from hepatic and portal vein thrombosis. Two patients died from cardiac arrest or cardiac complications, one patient died from hemorrhage, and one patient died from generalized sepsis.

Graft and patient survival for patients with SCD were equivalent to the reference population ($p = 0.5$ and $p = 0.2$, respectively) (Figure 1). Graft and patient survival were also equivalent between SCD patients and the propensity score matched group (Table 3 and Figure 2). One-year graft and patient survival for patients with SCD were 88.5% and 88.1% respectively. Three-year graft and patient survival were 72.1% and 70.5%, and five-year graft and patient survival were 48.1% and 58.8%, respectively.

Five patients with SCD were identified who underwent SLKT (Table 4). All of the recipients were African American. The wait list time was relatively short and ranged from 10-60 days, which was likely due to their relatively high MELD score ranging from 24-40. Despite this, only two of the five patients were hospitalized prior to transplant, and none of them were in the intensive care unit. Two of the five patients died and lost their graft at 141 days and 277 days (one due to malignancy, one unknown cause of death).

Part 2: Case Series from USC

Our center has performed SLKT in two patients with SCD out of >1500 LT procedures, both of which occurred since 2018. A retrospective review of the hospital records was conducted

for two liver transplant recipients with SCD at our center for the purpose of providing case reports.

Case 1:

A 58 year-old blood type B male with SCD and cryptogenic cirrhosis complicated by chronic kidney disease and hepatocellular carcinoma (HCC) underwent SLKT. His additional comorbidities included a reduced ejection fraction of 55%, severe protein-calorie malnutrition with a BMI of 16 kg/m², partial blindness, asplenia, gout, and venous stasis disease. He had multiple red cell antibodies requiring >8 hours' notice to prepare blood for the transplant procedure, and a pre-transplant panel reactive antibody of 51% by single antigen bead assay. His calculated MELD was 15 and with exception points for HCC rose to MELD of 30. A multidisciplinary meeting between the transplant surgeons, anesthesiologist, hepatologist, nephrologist, hematologist, transfusion medicine physician, and intensivist devised a peri-operative treatment plan, including basiliximab induction with intra-operative plasma exchange to ameliorate the effect of allo- and anti-RBC antibodies and subsequent hemolysis. The local procurement agency worked with the transplant team to allow for the time required to obtain blood and prepare the patient. He received 8 units of compatible packed red blood cells during the procedure with no further transfusion requirement postoperatively. The explant pathology demonstrated cirrhosis with sinusoidal sickling and diffuse sinusoidal dilatation with a 1.7 cm treated HCC. He was discharged on post-operative day 10 and is doing well with stable allograft function at 16 months. During his follow up period, he has been treated for a pulmonary embolus, 3 episodes of pain associated with sickle cell crisis and gout. Immunosuppression includes prednisone, mycophenolate mofetil, and tacrolimus. He was started on hydroxyurea 4 months post-transplant due to episodes of sickle cell crisis. He has had no documented episodes of rejection in either the kidney or liver allograft.

Case 2:

A blood type B, 68 year-old female with SCD and decompensated cirrhosis secondary to Hepatitis C (HCV) and chronic renal disease underwent SLKT. She had previously been treated for HCV with sofosbuvir/velpatasvir with sustained viral response. Her additional co-morbidities included a history of open cholecystectomy, asplenia, and breast cancer status post mastectomy and radiation. She had multiple red cell antibodies and a pre-transplant panel reactive antibody of 30% by single antigen bead assay. She received basiliximab and steroid induction and underwent pre-operative exchange transfusion to goal hemoglobin S<30% and to ameliorate the effect of allo- and anti-RBC antibodies and subsequent hemolysis. Intraoperatively, she required 7 units of packed red blood cells. She required 3 units of packed red blood cell transfusion in the post-operative period. Explant pathology demonstrated dilated and congested sinusoids containing clumped sickled red blood cells, cirrhosis, cholestasis, and grade 4 hemosiderin deposition (Figure 3, **panel A and B**). Her post-operative course was complicated by posterior reversible encephalopathy syndrome and seizures associated with tacrolimus prompting conversion to cyclosporine. She is maintained on cyclosporine, mycophenolate mofetil, and prednisone. She developed Stevens-Johnson syndrome in the early post-transplant period, which was thought to be associated with ciprofloxacin that she received for urinary tract infection. This resolved following

discontinuation of ciprofloxacin. She also developed a hematoma around her kidney transplant that required a return to the operating room for evacuation and washout. Her kidney transplant exhibited delayed graft function but ultimately recovered, and dialysis was discontinued during her post-transplant hospitalization. She was discharged on post-operative day 36 and required one readmission for elevated liver enzymes, which prompted a biopsy. This revealed 4/9 acute cellular rejection and congested sinusoids containing clumps of sickled red blood cells (Figure 3, **panel C and D**). This was treated with steroids and escalation of cyclosporine levels. She also had evidence of a non-occlusive deep vein thrombosis which required anticoagulation. She has otherwise had stable allograft function for >6 months post-transplant. She has had no episodes of renal transplant rejection.

Discussion

This study reports the first comprehensive analysis of outcomes of patients with SCD undergoing LT using the SRTR. In the entire dataset, only 23 patients with SCD were identified who underwent LT, along with 5 patients with SCD who underwent SLKT. Our data demonstrate that SCD patients are more likely to be African American, more likely to be children, are less likely to have diabetes, and are more likely to have lower BMI. Our data also demonstrate that SCD patients are more likely to be acutely ill going into transplant as they had significantly higher MELD, were more often in the intensive care unit, and were more likely to be receiving dialysis. In addition, SCD were more likely to be listed as Status 1. Despite these factors, patients with SCD experienced similar graft and patient survival post-LT when compared to a reference cohort of African American LT recipients with other etiologies of chronic liver disease and a 2:1 propensity score matched group. The small number of patients with SCD who underwent SLKT makes it difficult to draw conclusions; however, two of the five patients died less than one-year post-transplant. At our center, we have performed two recent SLKT in patients with SCD, both of whom have experienced excellent graft function. One patient is more than 18 months out while the other patient is only six months post-transplant but is discharged from the hospital with stable allograft function.

Despite acceptable graft and patient survival outcomes after LT, our data indicate that LT in patients with SCD occurs at a low rate. As previously stated, SCD is prevalent in the U.S. with a current population of >100,000 patients, with >25% of patients with SCD with a diagnosis of chronic liver disease in the Centers for Medicare and Medicaid Services database.² Autopsy studies in patients with SCD have reported that 91% of these patients have hepatomegaly, 34% have focal parenchymal necrosis, 20% have portal fibrosis and regenerative nodules, and 11% have cirrhosis.³ Another report from a tertiary center for SCD quotes the prevalence of acute liver failure among patients with SCD at 0.55% (11/2000).¹² Thus, our data suggests that only a small proportion of patients with SCD ultimately undergo LT.

There are several possibilities to explain why there are so few patients with SCD who underwent LT in the SRTR. First and foremost, there is no diagnostic code for SCD in the SRTR liver dataset, and thus we were only able to identify these patients through searching the free-text diagnosis of 'sickle cell' or by cross-referencing the kidney dataset to identify

SLKT patients, as a specific code for SCD exists in the kidney data. However, in keeping with a prior publication from 2013 that used the UNOS data, our review of the SRTR data for kidney transplant alone in patients with SCD identified <300 patients with SCD who underwent kidney transplant since 1987, in the face of a known incidence of chronic renal disease of 47% in the Medicare report.^{2,15} Thus, it is unlikely that the lack of a diagnostic code alone accounts for the low frequency of patients with SCD in the SRTR LT database. Another more likely possibility is that comorbidities in this population make LT seemingly high risk and thus prohibitive. A LT referral center in France with one of largest case series of LT in patients with SCD reported that 4/11 patients admitted with SCD-related hepatic failure could not be transplanted secondary to the rapid progression to multi-organ failure.¹² Thus, some centers may be reluctant to proceed with LT in patients with SCD given these results. Furthermore, it may be that while there is a significant prevalence of chronic liver disease in this population, the rate of progression to decompensated cirrhosis necessitating transplantation is less clear. The most important question that this data raises is the possibility that these patients are not referred for transplantation evaluation, and this requires further studies to investigate whether they are not being referred versus they are not accepted by the selection committees versus they have significant medical contraindications to listing and transplantation. Multiple previous studies have demonstrated disparity in access to LT amongst African American patients in general.^{16–18} Patients with SCD, particularly as they age and as demonstrated by the two patients we transplanted at our center, are complicated with multiple significant comorbidities that may prevent them from being considered transplant candidates.

The most important finding in our study is that the post-LT graft and patient survival rate for patients with SCD is equivalent to post-LT survival for other hepatic disease processes both in a reference population of African Americans and a propensity score matched group and is higher than prior case reports of LT in patients with SCD in the literature. This may be because these papers focused primarily on acute hepatic failure associated with SCD.¹² The largest case series reported a post-operative mortality of 60% with a 5-year survival of 44%, but only described cases of acute hepatic failure.¹² While we could not differentiate between patients transplanted for acute and chronic liver failure based on our data set, only 26% of patients in our series were listed as Status 1, which was significantly higher than the reference population. This would seemingly result in a greater impact on patient survival if it was a true negative association, but that is not what we observed. Furthermore, equivalent graft and patient survival outcomes were demonstrated in a propensity score matched analysis. In contrast, 2 of 5 of the patients who underwent SLKT experienced 1-year mortality and graft loss. While this is a concerning mortality rate, the number of patients in this group is too small to draw conclusions. It may be that SLKT presents added risk to this population.

Patients with SCD are considered to have increased risk of rejection secondary to increased alloimmunization from prior blood transfusion (up to 50% of SCD patients have red cell alloantibodies.^{12,19–21} Plasma exchange was primarily used in our patients to decreased hemoglobin S concentrations below 30% and to minimize hemolysis from anti-RBC antibodies; however, it may also serve to clear preformed alloantibodies to the transplanted liver. Experience with plasma exchange in LT is largely derived from ABO incompatible LT

protocols and treatment of anti-body mediated rejection.^{22–25} While there have been reports in the literature of coagulopathy and thrombocytopenia associated with plasma exchange, we did not observe increased coagulopathy or transfusion requirements as a result of plasma exchange in the two patients transplanted at our institution.^{26,27} Thus far, we have only observed mild rejection in one of our center's patients, and in the SRTR cohort, only four patients were reported to have post-LT acute rejection. One of our patients has had evidence of recurrent intrahepatic sickling on biopsy. It is possible that this would be classified as a manifestation of 'sickle cell crisis', except that the transplanted liver is functionally denervated and thus sickling may not result in pain for the recipient. Transplant physicians should have a low threshold to biopsy these patients in the face of graft dysfunction to rule out microscopic sickling. As well, both of our patients developed post-LT venous thrombosis, requiring anticoagulation. A recent study has reported that up to 20% of patients with SCD develop unprovoked venous thromboses, so transplant programs should be aware of this additional risk.²⁸

Despite equivalent graft survival rates to a reference cohort of African American patients and a propensity score matched cohort, 22% of SCD patients underwent re-transplantation. The majority of graft losses occurred beyond two years post-transplant (re-transplantation occurred at 1, 23, 45, 58, and 59 months). The causes of graft loss in this patient population are distinct from other LT recipients. Thirteen percent of patients lost their graft from recurrent sickle cell crisis, 4% from secondary hemochromatosis, and 4% from vascular complications. This is consistent with the reported complications in SCD patients after LT in other case series.^{10,12} There are strategies to mitigate these risks, but clinicians must be vigilant in managing these unique potential complications, and close follow up and communication with an experienced hematologist is likely beneficial. The available literature suggests peri-operative exchange transfusions to keep hemoglobin levels between 8-10 g/dL and Hemoglobin S <30% to minimize the risk of peri-operative hepatic vaso-occlusive crises and also suggests a transition from exchange transfusions to hydroxyurea and recombinant erythropoietin after the peri-operative period to minimize the risk of iron overload.^{10,12,29–33} The presence of multiple clinically significant red cell alloantibodies in some patients, including antibodies to high frequency red cell antigens, may pose significant challenges for perioperative transfusion support.

While not captured in the SRTR database, prior reports of post-transplant patients with SCD have also described neurologic complications in 66% of these patients, including strokes, seizures, and posterior reversible encephalopathy syndrome.^{10,12,30} One of our two patients with SCD who underwent SLKT experienced significant neurological side effects post-LT and required conversion from tacrolimus to cyclosporine. As well, both of our patients experienced clinical manifestations of sickling for the first time in many years post-LT. It is unclear what impact transplant and/or immunosuppressive medications have on the rate of sickling in these patients.

Our study is limited in that it is a retrospective review of a large database that does not have a specific diagnostic code for SCD in patients who underwent LT. Many details regarding the peri-operative care of the patients are missing, including the use of exchange transfusions, hydroxyurea or erythropoietin, frequency of red cell antibodies, and the

hemoglobin S levels peri-operatively. Furthermore, the nature of chronic liver disease is not accurately captured in the database in this population. It is difficult to distinguish those with iron overload from acute liver failure from acute sickle intra-hepatic cholestasis from cirrhosis. These various presentations may be associated with different risks and outcomes after transplantation. The small amount of SLKT patients makes it difficult to draw conclusions about this specific patient population. Finally, it is impossible to define the true denominator of patients with SCD who would benefit from LT and were never referred for evaluation. These limitations make it difficult to draw conclusions as to what extent a disparity exists.

Conclusion

In summary, this study demonstrates that the graft and patient survival outcomes of patients with SCD who undergo LT are equivalent to a propensity score matched group and the general population of LT recipients despite SCD patients presenting in more critical condition. The most common causes of graft loss are sickle cell crisis hepatopathy, secondary hemochromatosis, and hepatic and portal vein thrombosis. The overall low numbers of LT in this population compared to the observed frequency of chronic liver disease suggests that there may be disparity in access to LT for patients with SCD. There is insufficient experience with SLKT in SCD patients to evaluate outcomes, but we have had success with two patients at our center. Further studies are required to explore chronic liver disease in patients with SCD and determine if a true disparity in access exists. Experienced transplant centers should collaborate with sickle cell specialists to improve access to LT for this complex patient population.

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Abbreviations:

ESLD	End Stage Liver Disease
LT	Liver Transplantation
SCD	Sickle Cell Disease
SLKT	Simultaneous Liver and Kidney Transplantation
SRTR	Scientific Registry of Transplant Recipients

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Figure 1. Graft and Patient Survival in patients with SCD following LT.

(A) Kaplan-Meier survival curve of graft survival in 1) liver transplant in sickle cell disease and 2) DDLT reference group. Panel B illustrates patient survival in 1) liver transplant in sickle cell disease and 2) DDLT reference group by Kaplan-Meier survival analysis. Panel C shows 1, 3, and 5 years graft and patient survival rates in patients with SCD who underwent LT in the SRTR.

Figure 2. Graft and Patient Survival in patients with SCD following LT compared to a Propensity Score Matched Cohort.

(A) Kaplan-Meier survival curve of graft survival in 1) liver transplant in sickle cell disease and 2) 2:1 propensity score matched group. Panel B illustrates patient survival in 1) liver transplant in sickle cell disease and 2) 2:1 propensity score matched group by Kaplan-Meier survival analysis. Panel C shows 1, 3, and 5 years graft and patient survival rates in patients with SCD who underwent LT in the SRTR.

Figure 3. Evidence of intrahepatic sickling in both liver explant and post-transplant liver biopsy. A) Cirrhotic liver with hepatic sinusoids distended by erythrocytes, some with sickled morphology (HE X 100x). B) Hepatic sinusoids packed with sickled red blood cells (HE X 400x). C) Post-transplant liver core biopsy from the same patient showing acute cellular rejection (4/9) and hepatic sinusoids distended by erythrocytes with sickled morphology (HE X 100x). D) Post-transplant liver biopsy with hepatic sinusoids packed with sickled red blood cells (HE X 400x).

Table 1.
SRTR demographics for patients with SCD who underwent LT.

A reference cohort of African-American LT recipients was used for comparison. $P < 0.05$ was considered to be significant.

	SCD Liver Transplant (n = 23) n (%) or Median [IQR]	Ref DDLT cohort (n =9,204) n (%) or Median [IQR]	P-Value
Age (years):			
Pediatric (0-17)	7(30.4%) 14 [2-16]	281(3.1%) 16 [15-17]	<0.001
Adult (>18)	16 (69.6%) 30 [20.5-42.5]	8,923 (96.9%) 52 [42-58]	<0.001
Sex:			
Male	14 (61%)	5,071 (55%)	0.578
Female	9 (39%)	4,133 (45%)	
Race/ethnicity:			
White	2 (8.7%)	N/A	N/A
African American	20 (87.0%)	9,204 (100%)	
Multiracial	1 (4.3%)	N/A	
BMI	20.5 [17.8-22.7]	27.4 [23.9-31.6]	<0.001
Diabetes	0	1,658 (18.0%)	0.019
History of TIPSS	0	329 (3.6%)	0.305
Portal vein thrombosis	2 (8.7%)	413 (4.5%)	0.494
Donor age (years)	33 [19-48]	39 [24-52]	0.189
Lab MELD/PELD at transplant	33 [22-37]	21 [13-29]	0.004
HBV Core Ab+	1 (4.3%)	2,312 (25.1%)	0.016
HCV+	2 (8.7%)	3,778 (41.0%)	<0.001
Medical condition at transplant:			
ICU	10 (43.5%)	1,756 (19.1%)	0.007
Hospitalized, not in ICU	5 (21.7%)	1,705 (18.5%)	
Not hospitalized	8 (34.8%)	5,735 (62.4%)	
Requiring dialysis	4 (17.4%)	452 (4.9%)	0.009
Requiring ventilator	4 (17.4%)	835 (9.1%)	0.166

	SCD Liver Transplant (n = 23) n (%) or Median [IQR]	Ref DDLT cohort (n =9,204) n (%) or Median [IQR]	P-Value
Status 1	6 (26.1%)	1,116 (12.1%)	0.041
Median time on wait list in days	31 [6-80]	64 [10-236]	0.304
ABO Incompatible	0	135 (1.5%)	0.558
Deceased donor	23 (100%)	9,204 (100%)	
Whole liver	22 (95.6%)	9,204 (100%)	<0.001
Split liver	1 (4.3%)	0	
Cold ischemia time (hours)	6.6 [5.5-9]	6.8 [5-9]	0.969

Table 2.

SRTR post-LT treatment and outcomes in patients with SCD.

	Median [IQR] or n (%) (n = 23)
Immunosuppression at 6 months	
Tacrolimus	5 (22%)
Steroid	22 (96%)
Cyclosporine	0
MMF	3 (13%)
Length of stay after transplantation (days)	24 [11-35]
Rejection (n%)	4 (17%)
Biopsy-proven	4 (17%)
Causes of graft loss	
Sickle Cell Crisis, Hepatopathy	3 (13%)
Secondary Hemochromatosis	1 (4%)
Hepatic and Portal Vein Thrombosis	1 (4%)
Re-transplanted	5 (22%)
Causes of death	
Cardiac	2
Hemorrhage	1
Infection	1

Table 3:

Patient characteristics before and after propensity score matching on age, sex, and MELD, with matching ratio of 2:1 (control to case).

	Before Propensity Score Matching			After Propensity Score Matching		
	Sickle Cell	Ref DDLT cohort	Standardized difference	Sickle Cell	Ref DDLT cohort	Standardized difference
Sample size (n)	23	10977		18	36	
Age, median years (IQR)	22 (16-35)	49 (29-57)	-0.92	24 (16-35)	26.5 (16-40.5)	0.03
Sex, %						
Male	14 (60.9)	5839 (53.2)	0.16	11 (61.1)	22 (61.1)	0
Female	9 (39.1)	5138 (46.8)		7 (38.9)	14(38.9)	
Lab MELD at transplant (median, IQR)	33.5 (22-37)	21 (13-30)	0.62	33.5 (22-37)	27.5 (23.5-38)	0.03

Table 4.

SRTR Data for Patients with SCD who underwent SLKT.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Pre-transplant					
Transplantation year	2003	2006	2007	2011	2013
Age (years)/Sex	47 M	44 M	33 F	35 M	50 M
Recipient Race/ethnicity	Black	Black	Black	Black	Black
Donor Race/ethnicity	Black	White	Hispanic	Hispanic	White
Cold ischemia time (hours)	5.2	6	12.1	8	6
Warm ischemia time (minutes)	42	22	41	51	60
Donor type	Deceased	Deceased	Deceased	Deceased	Deceased
Time on wait list (days)	28	60	25	25	10
BMI	24	21	23	20	24
History of TIPS	No	No	No	No	No
Portal vein thrombosis	No	No	No	No	No
MELD or PELD at transplant	40	24	35	38	40
Albumin (g/dL)	3.4	2.1	2.9	2.7	2.6
HBV Core Ab	Neg	Neg	Neg	Neg	N/A
HCV serology status	Neg	Neg	Neg	Neg	Neg
ICU at time of transplant	none	None	None	none	none
Patient ABO/Recipient ABO	O/O	AB/B	B/B	B/O	O/O
Preliminary crossmatch done?	Not done	Yes	Yes	N/A	N/A
Peak PRA	0	0	80%	6%	N/A
HLA-A mismatch level (0-2)	2	2	1	1	N/A
HLA-B mismatch level (0-2)	2	2	2	2	N/A
HLA-DR mismatch level (0-2)	2	2	1	2	N/A
Post-transplant characteristics					
Induction	Steroids	ATG, rituximab and Steroids	Steroids	Steroids	Steroids

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Maintenance Immunosuppression	Tacrolimus, steroids	Tacrolimus, Mycophenolate	Tacrolimus, Mycophenolate, Steroids	Tacrolimus, Mycophenolate, steroids	Tacrolimus, Mycophenolate, steroids
Length of stay after transplantation (days)	17	8	8	44	9
Graft loss	Yes (0.4 yr)	Yes (0.8 yr)	No	No	No
Re-transplanted	No	No	No	No	No
Status	Died (Cause unknown)	Died (Malignancy not specified)	Alive	Lost	Alive
Follow up (years)	0.4	0.8	9.9	2.0	4.1