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Liver transplantation at safety net hospitals: Potentially vulnerable patients with noninferior outcomes

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ABSTRACT

Background: Patients undergoing complex surgery at safety net hospitals have been shown to suffer inferior short-term outcomes. Liver transplantation, one of the most complex surgical interventions, is offered at certain safety net hospitals. We sought to identify whether patients undergoing liver transplantation at safety net hospitals have inferior outcomes compared with lower burden centers.
Methods: Using a link between the University HealthSystem Consortium and Scientific Registry of Transplant Recipient databases, we identified 11,047 patients undergoing liver transplantation at 63 centers between 2009 and 2012. Hospitals were grouped by safety net burden, defined as the proportion of Medicaid or uninsured patient encounters during that time. The highest quartile (safety net hospitals) was compared to medium- and low-burden hospitals regarding recipient and donor characteristics, perioperative outcomes, and long-term survival.
Results: Liver transplantation recipients at safety net hospitals were more often black and of lower socioeconomic status ($P < .01$), but had similar model for end-stage liver disease scores (20 vs 20 vs 18) compared with median-burden hospitals and low burden hospitals. Length of stay and readmission rates were similar; however, safety net hospitals demonstrated higher in-hospital mortality (5.2% vs 4.5% vs 2.9%, $P < .01$). Despite this, there was no significant difference in overall patient or graft survivals in patients who underwent liver transplantation at safety net hospitals and survived the perioperative setting at a median follow-up of 2 years ($P > .05$).
Conclusion: Despite differences in perioperative outcomes at safety net hospitals, these centers achieve noninferior long-term patient and graft survival for potentially vulnerable patients requiring liver transplantation. Strict care standardization, as achieved in liver transplantation, may be a mechanism by which outcomes can be improved at safety net hospitals after other complex surgical procedures.

Introduction

Advances in operative technique, perioperative care, and post-transplant management have led to improved outcomes for liver transplantation (LT) during the past several decades.[1,2] For LTs performed between 2008 to 2015, the 5-year graft survival was 72% and patient survival was 75%.[3] Demand for LT continues to increase in the United States with a total of 7,841 LT performed and 11,340 candidates added to the transplant waitlist in 2016.[1]

As the number of patients undergoing LT grows, however, variability in transplant practices owing to differences in safety net burden may have an adverse impact on post-transplant outcomes. Safety net hospitals (SNHS), that is, institutions that treat a disproportionate fraction of uninsured or Medicaid patients, have been shown previously to face challenges at the patient-level, the institutional-level, and the policy-level.[4] These centers often require costly adjunct services to address socioeconomic and cultural determinants of health when implementing initiatives targeting quality improvement. Furthermore, resource availability and utilization of various treatment modalities may differ at these hospitals.[5,6]

Regarding complex surgical care, several studies have seemed to show that patients at SNH may have inferior short-term outcomes, greater rates of failure to rescue after postoperative complications, and worse performance regarding perioperative quality measures.[7–12] Despite these putative differences in short-term outcomes, however, recent studies have demonstrated that patients receiving complex surgical care at SNHs who survive the

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perioperative period seem to have similar long-term outcomes compared with those treated at lower burden centers.[13]

Liver transplantation is rapidly growing in demand and is offered at some SNHs. Given the persistent imbalance of recipient demand and donor supply, it is important to optimize outcomes from utilization of such a precious resource. Given lack of literature regarding LT at SNHs, we sought to identify whether potentially vulnerable patients undergoing LT at SNHs have inferior outcomes compared with lower burden centers.

Methods

Data sources

This study used data from the University HealthSystem Consortium (UHC) and the Scientific Registry of Transplant Recipients (SRTR). These data were collected and analyses were completed before the merger of UHC and VHA, Inc (a national corporation of not-for-profit health care organizations) to become Vizient, Inc. The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States as submitted by the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration, US 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 Minneapolis Medical Research Foundation as the contractor for the Scientific Registry of Transplant Recipients (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 US Government. This study was approved by the Institutional Review Board of the University of Cincinnati.

Patient population

Using a link between UHC and SRTR as described previously, we identified 11,047 patients who underwent LT at 63 centers between 2009 to 2012.[14–16] The primary outcome of interest was overall patient survival. Secondary outcomes were graft survival, in-hospital mortality, and readmissions. The following recipient covariates were analyzed: age, sex, race, socioeconomic status (SES), insurance, body mass index (BMI), cause of liver disease, medical history, laboratory model for end-stage liver disease (MELD), MELD exception status, functional status, severity of illness, and employment status. Functional status was obtained from the SRTR database with those patients performing activities of daily living with no assistance defined as independent, those needing some assistance defined as dependent, and those requiring total assistance defined as severely ill. Severity of illness (SOI) was obtained from the UHC database for each recipient and grouped based on degree of organ dysfunction present on admission.[17]

The following recipient outcomes were analyzed: discharge location, hospital duration of stay, intensive care unit (ICU) duration of stay, in-hospital mortality, and readmission rate. The following donor information was collected: age, sex, race, BMI, donor type, deceased versus living donor status, graft type, cause of death, organ location, and donor risk index (DRI).

Socioeconomic status

A measure of SES was calculated using data from the US Census American Community Survey as described previously.[16] Variables included 3 measures of income (household income, value of housing unit, and percentage of households with interest, dividend, or rental income), 2 measures of education (proportion of adult residents completing high school and completing college), and 1 measure of employment (percentage of residents with management, business, science, and arts occupations). Z scores for each recipient was calculated for each variable and combined into a summary SES score. All recipients were then sorted and stratified into quintiles from lowest SES (quintile 1) to highest SES (quintile 5).

Safety net burden

The safety net burden of a hospital was defined as the proportion of total patients who had Medicaid or no insurance. Hospitals were grouped into quartiles according to safety net burden, as described previously.[7,10] Those in the first quartile (1.9–14.2%, n = 15) were defined as low burden hospitals (LBH), the middle 2 quartiles (14.5–36.4%, n = 38) made up the medium burden hospitals (MBH), and the highest quartile (36.8–100%, n = 10) indicated high burden hospitals (HBH). The HBH represented the SNH.

Transplant center characteristics

The distribution of safety net burden hospitals within each OPTN region was characterized. The volume of transplantations at each center was calculated per year using the SRTR data based on the number of recipients at each center. The volume at all centers were ranked and then divided into tertiles, with equal number of recipients in each tertile. The distribution of safety net burden hospitals within each tertile was then characterized.

Statistical analysis

We performed a retrospective, noninferiority analysis comparing survival at SNHs versus LBHs. The noninferiority margin, Δ, was set at 0.2 based on previous studies.[18,19] Noninferiority of the safety net burden would then be demonstrated if the patient (or graft) survival at SNHs is not lower by greater than 0.2 compared with patient (or graft) survival at LBHs. The 2-sided 95% confidence intervals of the outcome difference between the SNHs and LBHs used for statistical testing was calculated from the data in the table above as follows:

$$PS_1 - PS_2 \pm 1.96 \cdot \mathrm{Sqrt}\left(SD_{p1}^2/N_1 + SD_{p2}^2/N_2\right) \text{ and}$$

$$GS_1 - GS_2 \pm 1.96 \cdot \mathrm{Sqrt}\left(SD_{g1}^2/N_1 + SD_{g2}^2/N_2\right),$$

where PS_1, PS_2, GS_1, and GS_2 represent observed 3-year patient and graft survival at the SNHs and LBHs groups, respectively, SD_{p1}, SD_{p2}, SD_{g1}, and SD_{g2} are observed standard deviations in the respective groups, and N_1 and N_2 are the actual sample sizes of the respective groups. Our dataset was much greater than the sample size needed to accomplish this objective.

Missing values for specific variables were omitted from the analysis for that variable. χ^2 test and Wilcoxon rank-sum test were used for comparison of categorical and continuous variables, respectively. Kaplan-Meier survival analysis was used to compare patient and graft survival. Multiple logistic regression models were created to analyze predictors of in-hospital mortality and 30-day readmission, whereas Gamma regression techniques were used for cost and Poisson regression techniques for length of stay. The predictors of ICU and hospital duration of stay, in-hospital mortality, and 30-day readmission were adjusted using a multivariate analysis, with covariates in the final model including safety net burden, cause of disease, age, sex, race, BMI, MELD, SOI, SES, insurance, donor sex, and DRI. In addition, propensity matching was

Table I
Transplant recipient demographics according to hospital safety net burden

Recipient characteristic	Hospital safety net burden						*P* value
	LBH (Q1)		MBH (Q2,3)		HBH (Q4)		
	N (median)	% (IQR)	*N* (median)	% (IQR)	*N* (median)	% (IQR)	
No. of patients	3,162	28.6%	7,000	63.4%	885	8.0%	
No. of hospitals	15		38		10		
Sex							.16
Male	2,166	68.5%	4,667	66.7%	587	66.3%	
Female	996	31.5%	2,333	33.3%	298	33.7%	
Age							.003
18–29	112	3.5%	265	3.8%	24	2.7%	
30–39	137	4.3%	335	4.8%	41	4.6%	
40–49	406	12.8%	1,005	14.4%	142	16.1%	
50–59	1,368	43.3%	3,070	43.9%	395	44.6%	
60–69	1,018	32.2%	2,150	3.7%	261	29.5%	
≥70	121	3.8%	175	2.5%	22	2.5%	
Median (IQR)	57	51–62	56	50–61	56	50–61	<.001
Race							<.001
White	2,245	71.1%	5,116	73.1%	636	71.9%	
Black	364	11.5%	641	9.2%	119	13.4%	
Hispanic	327	1.3%	807	11.5%	105	11.9%	
Asian	199	6.3%	367	5.2%	23	2.6%	
Other	25		69		2		
SES							<.001
(lowest) Q1	527	18.2%	1,227	19.3%	239	29.0%	
Q2	550	18.9%	1,322	2.8%	165	2.0%	
Q3	530	18.2%	1,297	2.4%	145	17.6%	
Q4	642	22.1%	1,280	2.1%	142	17.2%	
(highest) Q5	655	22.6%	1,236	19.4%	132	16.0%	
Insurance							<.001
Private	1,965	62.1%	4,104	58.6%	472	53.3%	
Medicare	868	27.4%	1,857	26.5%	219	24.8%	
Medicaid	267	8.4%	920	13.1%	118	13.3%	
Uninsured	23		31		11		
Other/unknown	39		88	1.3%	65	7.3%	
BMI	27	24–32	28	24–32	28	25–32	<.001
Cause of liver disease							<.001
Alcohol	393	12.4%	997	14.3%	129	14.6%	
HCC	416	13.2%	828	11.8%	101	11.4%	
NASH	390	12.3%	997	14.3%	135	15.2%	
Viral hepatitis	1,116	35.3%	2,593	37.1%	35	39.6%	
Other	847	26.8%	1,582	22.6%	170	19.2%	
Recipient medical history							
Diabetes	765	24.4%	1,696	24.7%	237	26.8%	.33
Angina	63	2.8%	148	3.3%	45	5.4%	.002
Hemodialysis	308	9.7%	709	1.1%	78	8.8%	.44
Bacterial peritonitis	140	4.5%	451	6.6%	54	6.1%	<.001
Portal vein thrombosis	117	3.8%	288	4.3%	30	3.4%	.34
TIPS	170	5.5%	424	6.2%	56	6.4%	.30
HCV	1,385	43.8%	2,893	41.3%	396	44.8%	<.001
Approved for MELD exception	1,094	34.6%	2,032	29.0%	210	23.7%	<.001
Functional status							<.001
Independent	1,414	44.7%	2,747	39.2%	424	47.9%	
Dependent	1,057	33.4%	2,339	33.4%	291	32.9%	
Severely ill	676	21.4%	1,686	24.1%	158	17.8%	
Unknown	15	.5%	228	3.3%	12		
MELD							<.001
6–13	999	31.6%	1,798	25.7%	189	21.4%	
14–19	706	22.3%	1,647	23.5%	224	25.3%	
20–27	695	22.0%	1,661	23.7%	238	26.9%	
28–40	762	24.1%	1,894	27.1%	234	26.4%	
Median (IQR)	18	12–27	20	13–28	20	14–28	<.001
Severity of illness							<.001
Minor	41		248	3.5%	19	2.2%	
Moderate	445	14.1%	1,206	17.2%	155	17.5%	
Major	1104	34.9%	2,177	31.1%	282	31.9%	
Extreme	1572	49.7%	3,369	48.1%	429	48.5%	

HCV, hepatitis C virus; *IQR*, inter-quartile range; *TIPS*, transjugular intrahepatic portosystemic shunt.

performed based on patient characteristics (age, race, socioeconomic status, and MELD) and based separately on hospital characteristics (transplantation volume and region).

Cox proportional hazards regression was used to model long-term survival. Patients with in-hospital mortality were excluded from long-term survival analysis to adjust for the impact of perioperative mortality on overall survival. Random intercept hierarchical models were used in all analyses to account for the clustering effects of the center where the patients underwent their LT. Covariates initially entered into the Cox regression model included

Table II
Donor demographics according to safety net burden

Donor characteristic	Hospital safety net burden						P value
	LBH (Q1)		MBH (Q2,3)		HBH (Q4)		
	N (median)	% (IQR)	N (median)	% (IQR)	N (median)	% (IQR)	
Sex							.93
Male	1,855	58.7%	4,092	58.5%	523	59.1%	
Female	1,307	41.3%	2,908	41.5%	362	4.9%	
Age of donor (y)							.04
<40	650	20.6%	1,412	20.2%	191	21.6%	
40–49	648	20.5%	1,343	19.2%	173	19.6%	
50–59	357	11.3%	783	11.2%	91	10.3%	
60–69	1,353	42.8%	3,175	45.4%	407	46.0%	
>70	154	4.9%	287	4.1%	23	2.6%	
Median (IQR)	43	28–55	42	27–54	42	26–52	.03
Race							<.001
White	2,016	63.8%	4,760	68.0%	602	68.0%	
Black	634	20.1%	1,275	18.2%	180	20.3%	
Hispanic	394	12.5%	749	10.7%	79	8.9%	
Asian	101	3.2%	160	2.3%	24	2.7%	
Other	17	.5%	56		0		
Donor type							<.001
SCD	2,024	67.4%	4,608	68.8%	638	74.5%	
ECD	820	27.3%	1,735	25.9%	203	23.7%	
DCD	159	5.3%	354	5.3%	15		
DDLT vs LDLT							.06
DDLT	3,003	95.0%	6,697	95.7%	856	96.7%	
LDLT	159	5.0%	303	4.3%	29	3.3%	
Graft type							.01
Split	199	6.3%	404	5.8%	32	3.6%	
Whole	2,963	93.7%	6,596	94.2%	853	96.4%	
BMI	26	23–30	26	23–31	26	23–30	.75
Cause of death							<.001
Trauma	997	31.5%	2,249	32.1%	296	33.5%	
Anoxia	732	23.2%	1,704	24.3%	160	18.1%	
CVA	1,196	37.8%	2,561	36.6%	378	42.7%	
Other	237	7.5%	486	6.9%	51	5.8%	
Organ location							<.001
Local	2,084	69.6%	4,735	71.5%	702	82.2%	
Regional	654	21.8%	1,197	18.1%	118	13.8%	
National	255	8.5%	694	10.5%	34	4.0%	
Donor risk index							<.001
<1.2	928	29.4%	2,206	31.5%	314	35.5%	
1.2–1.49	846	26.8%	1,893	27.0%	272	30.7%	
1.5–1.79	671	21.2%	1,486	21.2%	175	19.8%	
≥1.8	717	22.7%	1,415	20.2%	124	14.0%	

CVA, cerebrovascular accident; *DCD*, donation after circulatory death; *DDLT*, deceased donor liver transplant; *ECD*, expanded criteria donor; *LDLT*, living donor liver transplant; *SCD*, standard criteria donor.

safety net burden, recipient factors (age, sex, race, BMI, cause of liver disease, MELD, bilirubin, aspartate aminotransferase, alanine aminotransferase, international normalized ratio, sodium, albumin, SOI, SES, and insurance), and donor factors (sex, DRI, cause of death). Covariates were removed if $P > .20$. Therefore, remaining covariates included safety net burden, cause of disease, age, sex, race, BMI, MELD, SOI, SES, insurance, donor sex, and DRI. An α level of 0.05 was used for all significance tests. The data were analyzed using SAS 9.4 and JMP Pro 11 (SAS Institute, Cary, NC).

Results

Demographics of the safety net transplant recipients

The demographics of the transplant recipient according to safety net burden status are demonstrated in Table I. Of all transplant recipients, 28.6% ($n = 3{,}162$) were treated at LBH, 63.4% ($n = 7{,}000$) at a MBH, and 8.0% ($n = 885$) at a HBH. Recipients treated at HBH were more likely to be of the black race, unemployed, and in the lowest socioeconomic quintile. Recipients at LBHs were more likely to have heptocellular carcinoma (HCC) whereas those at HBHs were more likely to have alcohol-induced cirrhosis, nonalcoholic steatohepatitis (NASH), and viral hepatitis as the cause of liver disease. Recipients had similar MELD score across the LBHs, MBHs, and HBHs (median 18 vs 20 vs 20), although those at LBHs had greater rate of MELD exception status (34.6% vs 29.0% vs 23.7%).

Demographics of safety net liver donor

The demographics of liver donors utilized according to safety net burden status are demonstrated in Table II. LBHs used a greater proportion of expanded criteria donors, donation after cardiac death grafts, and greater DRI grafts. There was a trend toward a greater use of living donor LTs at LBHs (5.0%) versus HBHs (3.3%), but this was not statistically significant ($P = .06$). HBHs had a greater proportion of local organ donors (82.2%) versus LBHs (69.6%, $P < .001$).

Characteristics of transplant centers

The distribution of transplant centers among OPTN regions demonstrated SNH (ie, HBHs) were present in regions 2, 3, 4, 5, 7, 10, and 11, whereas LBHs were present in regions 1, 2, 3, 4, 5, 9, and 10. Therefore, only regions 2, 3, 4, 5, and 10 had both SNHs and LBHs.

Table III
Multivariate adjustment of recipient clinical outcomes

Safety net burden	LOS		In-hospital mortality		Readmission	
	RR	*P* value	OR	*P* value	OR	*P* value
Low	Ref.		Ref.		Ref.	
Medium	1.23	.04	1.59	.04	1.11	.28
High	1.15	.27	1.93	.03	1.16	.43

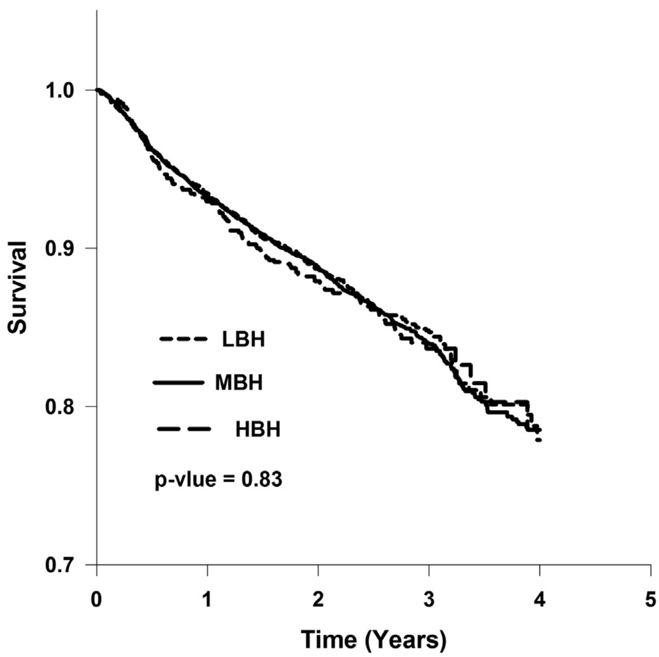

Fig 1. Kaplan-Meier curves comparing patient survival according to safety net burden.

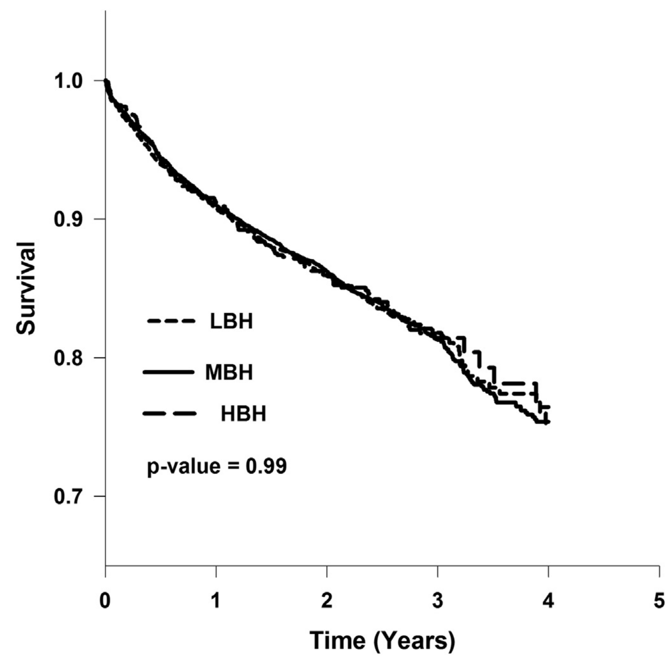

Fig 2. Kaplan-Meier curves comparing graft survival according to safety net burden.

The distribution of safety net burden status among different transplant centers according to LT volume showed that the majority of SNHs were low-volume centers (100% from 2009–2011, 90% in 2012). High-volume centers were either LBHs or MBHs. The distribution was similar throughout the study period (2009–2012).

Clinical outcomes

Median follow-up was 2.8 years. The durations of stay and readmission rates were similar across safety net burden status. HBHs and MBHs both had somewhat greater in-hospital mortality compared with LBHs (5.2% and 4.5% vs 2.9%, $P < .001$). On multivariate analysis, the odds ratio of mortality compared with LBHs was 1.58 ($P = .04$) for MBHs and 1.93 ($P = .03$) for HBHs (Table III). The difference in duration of stay between HBHs and LBHs was no longer present in the adjusted model.

Despite the difference in short-term mortality, recipients who underwent LT at a SNH and survived the perioperative setting achieved noninferior overall patient and graft survival ($P > .05$, Figs 1 and 2). Then 3-year patient survival was 82.9% at SNHs vs 84.4% at LBHs, and similarly, the 3-year graft survival was 80.4% at SNHs vs 81.3% at LBHs. Therefore, the 2-sided 95% CI of the difference in 3-year survivals between SNH and LBH was calculated to be 1.28 to 1.70 (for patient survival) and 0.77 to 1.21 (for graft survival). Because the lower limit of the 2-sided 95% CI was not less than the predefined, noninferiority margin of −0.2, noninferiority of the patient and graft survival at the SNH to the LBH was concluded.

On Cox regression analysis, factors associated with decreased patient survival included older age (HR 2.14–3.08, $P < .05$), black race (HR 1.48, $P < .05$), increased severity of illness (HR 1.62 for major and 2.38 for extreme, $P < .05$), lowest socioeconomic quintile (HR 1.25, $P < .05$), and increased DRI (HR 1.18–1.39, $P > .05$). Factors associated with improved survival included female sex (HR 0.84, $P < .05$), Asian race (HR 0.60, $P < .05$), and liver disease owing to alcohol (HR 0.49, $P < .05$) or NASH (HR 0.66, $P < .05$) versus viral cause. Factors associated with graft survival were the same as those associated with patient survival. Propensity matching based on both patient characteristics and hospital characteristics both showed no differences between SNHs and LBHs in terms of patient and graft survival.

Discussion

In this study, we demonstrated that despite differences in recipient and donor factors and perioperative outcomes, the long-term survival of LT recipients was noninferior across centers with varying safety net burden status. Although ICU and total durations of stay and readmission rates were similar across safety net burden status, both SNHs and MBHs had significantly greater in-hospital mortality rates. Median MELD scores were similar across safety net burden status, but LBHs had greater proportions of low MELD recipients and a greater rate of MELD exception status granted. Potential reasons for the lower rates of MELD exception status at SNHs may include fewer referrals to transplant centers for HCC, worse comorbidities, or more advanced liver disease at the time of referral. Although the circumstances behind this phenomenon are unknown, our findings raise the thought that perhaps LBHs are transplanting overall healthier recipients, which may contribute to a lesser perioperative mortality rate.

Another factor that may play a role in perioperative outcomes is the pretransplant care of patients with liver disease at SNHs. Previous studies have shown that patients with HCC, for example, at SNHs are less likely to undergo curative therapies and therefore, may be in worse health or have worse stage of disease at the time of LT, which could influence their perioperative outcomes.[5,6] The scope of this study, however, did not allow investigation of patients who did not undergo LT. Therefore, future studies should investigate potential disparities in access to transplantation.

The inferior short-term outcomes seen in this study are similar to previous studies investigating complex operative procedures performed at SNHs, including worse perioperative mortality after colectomy, esophagectomy, pancreatoduodenectomy, and ventral hernia repair.[7] A study looking at emergency appendectomy, cholecystectomy, and herniorrhaphy revealed greater rates of postoperative complications at SNHs, but no differences in mortality.[8] Another study of major cancer operations revealed greater readmission rates at SNHs, although this was not the case in our study.[9] These studies also demonstrated that greater comorbidity indices were associated with increased mortality and readmission rates, suggesting these inferior outcomes may be more attributable to patient factors than to the hospital setting.[8,9] Additional studies investigating care of patients with liver disease before LT, including referral patterns in the communities funneling into SNH, may provide more detailed information regarding the types of patients being evaluated for and subsequently undergoing LT. This approach may contribute potential explanations regarding patient factors associated with the inferior short-term outcomes seen at SNHs.

Our group showed previously that patients who underwent an operation for pancreatic cancer at SNHs and survived the perioperative period had similar long-term survival to those undergoing operation at non-SNHs.[13] In addition, patients with rectal cancer undergoing operations at SNHs had no difference in survival.[20] This study provides additional evidence that complex operations can be performed at SNHs with similar long-term outcomes.

A review of the SRTR adult heart, lung, liver, and kidney transplant recipients from 2002 to 2011 revealed that 8.6% of all organ transplants were insured through Medicaid, and these patients had lesser 5-year survival than patients who had private insurance.[21] In our study, overall patient and graft survivals for recipients who survived the perioperative period were noninferior at SNHs. SNHs were more likely to have recipients of black race and lowest socioeconomic status, both associated with decreased survival on multivariate analysis, but also had a lesser donor risk index and more liver disease owing to alcohol and NASH, which were protective factors. This combination of detrimental and protective factors likely balanced out the effect on overall survival. In addition, the expertise of highly trained staff at HBHs may improve the outcomes of transplant recipients. Although one might think that SNHs, which are typically academic, tertiary care centers, may have greater transplant volume, contributing to improved outcomes, our data show that SNHs were largely low-volume transplant centers. Thus, volume of transplants at SNHs does not seem to be a valid explanation for the similar outcomes seen.

The factors associated with survival from this study are largely similar to previous findings. Female sex has been shown to be associated with better survival.[22,23] Older age and donor risk index are well-known risk factors for worse survival.[22–26] Previous studies on the association of race with survival have been conflicted. Prior studies have found mixed associations between race and survival, although some of these studies did not account for SES.[27–29] In our study, Asian race was associated with better survival, whereas both SES and black race were independently associated with worse survival.

Standardized care protocols for perioperative management may contribute to improving outcomes. Gurien et al demonstrated fewer complications and reoperations after esophagectomy at their SNH compared with the NSQIP national cohort, with success attributed to their standardized clinical pathway.[30] In addition, the advent of protocol of enhanced recovery after surgery (ERAS) may help improve outcomes at SNHs. A review of ERAS protocols applied to liver surgery (though none included transplant) revealed shortened durations of stay and of functional recovery time.[31] Indeed, the ERAS Society established recommendations for hepatic surgery, which may or may not be feasible in transplant surgery.[32] The complexity of posttransplant management necessitates standardized protocols, which could partially explain the similar outcomes across centers. Similar standardized protocols may be a mechanism by which outcomes can be improved at SNHs after other complex surgical procedures.

SNH provide a substantial and important resource for patients with minority backgrounds and lower socioeconomic status. With the establishment of pay-for-performance payment structures, SNHs are at a disadvantage and often have reimbursement penalties for patient factors or their institutional infrastructure that may be out of their control.[4,33,34] Our present study demonstrates that despite inferior short-term outcomes which may reflect patient characteristics, long-term survival of LT recipients is noninferior at SNH. Instead of penalizing SNH for inferior short-term outcomes, it may be beneficial to invest in the hospital infrastructure and patient outreach so these potentially vulnerable patient populations have access to health care at earlier stages of disease, increased multidisciplinary support during the perioperative period, and resources for closer follow-up monitoring.

There are several limitations to this study. First, this is a retrospective analysis of administrative databases. We are not able to establish causality and therefore are limited to measuring associations between variables. Second, the median follow-up was only 2.8 years, and therefore our results may not be representative of longer-term outcomes. Third, our definition of safety net burden, as described in previous literature, is based on proportion of Medicaid or uninsured but does not account for differences in Medicaid coverage between states, and therefore SNH characteristics across states may not be uniform. Fourth, this study only evaluated academic centers using the University HealthSystem Consortium and therefore may not be representative of all transplant centers.

SNH are an important resource for potentially vulnerable candidates and recipients of a LT. Although short-term perioperative outcomes are inferior to non-SNH, recipients who survive the perioperative period have non-inferior, long-term patient and graft survivals. Future studies should be targeted toward improving perioperative outcomes, which may include optimizing pretransplant management of liver diseases and pathways of enhanced recovery after surgery.

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Conflict of interest/Disclosure

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References

1. Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2016 Annual Data Report: Liver. *Am J Transplant*. 2018;18(Suppl 1):172–253.
2. Stepanova M, Wai H, Saab S, Mishra A, Venkatesan C, Younossi ZM. The outcomes of adult liver transplants in the United States from 1987 to 2013. *Liver Int*. 2015;35:2036–2041.
3. Organ Procurement and Transplantation Network. United Network for Organ Sharing, 2018. https://optn.transplant.hrsa.gov/data/. Accessed July 10, 2018.
4. Macht R, McAneny D, Doherty G. Challenges in surgical quality at safety net hospitals. *JAMA Surg*. 2016;151:795–796.
5. Mokdad AA, Murphy CC, Pruitt SL, et al. Effect of hospital safety net designation on treatment use and survival in hepatocellular carcinoma. *Cancer*. 2018;124:743–751.
6. Hoehn RS, Hanseman DJ, Dhar VK, Go DE, Edwards MJ, Shah SA. Opportunities to improve care of hepatocellular carcinoma in vulnerable patient populations. *J Am Coll Surg*. 2017;224:697–704.
7. Hoehn RS, Wima K, Vestal MA, et al. Effect of hospital safety net burden on cost and outcomes after surgery. *JAMA Surg*. 2016;151:120–128.
8. Shahan CP, Bell T, Paulus E, Zarzaur BL. Emergency general surgery outcomes at safety net hospitals. *J Surg Res*. 2015;196:113–117.
9. Hong Y, Zheng C, Hechenbleikner E, Johnson LB, Shara N, Al-Refaie WB. Vulnerable hospitals and cancer surgery readmissions: Insights into the unintended consequences of the patient protection and Affordable Care Act. *J Am Coll Surg*. 2016;223:142–151.
10. Wakeam E, Hevelone ND, Maine R, et al. Failure to rescue in safety net hospitals: Availability of hospital resources and differences in performance. *JAMA Surg*. 2014;149:229–235.
11. Rosero EB, Joshi GP, Minhajuddin A, Timaran CH, Modrall JG. Effects of hospital safety net burden and hospital volume on failure to rescue after open abdominal aortic surgery. *J Vasc Surg*. 2017;66:404–412.
12. Mouch CA, Regenbogen SE, Revels SL, Wong SL, Lemak CH, Morris AM. The quality of surgical care in safety net hospitals: A systematic review. *Surgery*. 2014;155:826–838.
13. Dhar VK, Hoehn RS, Kim Y, et al. Equivalent treatment and survival after resection of pancreatic cancer at safety net hospitals. *J Gastrointest Surg*. 2018;22:98–106.
14. Hoehn RS, Singhal A, Wima K, et al. Effect of pretransplant diabetes on short-term outcomes after liver transplantation: A national cohort study. *Liver Int*. 2015;35:1902–1909.
15. Wilson GC, Quillin 3rd RC, Wima K, et al. Is liver transplantation safe and effective in elderly ($\geq$70 years) recipients? A case-controlled analysis. *HPB (Oxford)*. 2014;16:1088–1094.
16. Quillan 3rd RC, Wima K, Hohmann SF, et al. Neighborhood level effects of socioeconomic status on liver transplant selection and recipient survival. *Clin Gastroenterol Hepatol*. 2014;12:1934–1941.
17. Mortality measurement: Mortality risk adjustment methodology for University Health System Consortium. March 2009. Agency for Healthcare Research and Quality, Rockville, MD. http://archive.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/mortality/Meurer.html. Accessed July 10, 2018.
18. Christensen E. Methodology of superiority vs equivalence trials and non-inferiority trials. *J Hepatol*. 2007;46:947–954.
19. Fueglistaler P, Adamina M, Ulrich G. Non-inferiority trials in surgical oncology. *Ann Surg Onc*. 2007;14:1532–1539.
20. Hoehn RS, Go DE, Hanseman DJ, Shah SA, Paquette IM. Hospital safety net burden does not predict differences in rectal cancer treatment and outcomes. *J Surg Res*. 2018;221:204–210.
21. DuBay DA, MacLennan PA, Reed RD, et al. Insurance type and solid organ transplantation outcomes: A historical perspective on how Medicaid expansion might impact transplantation outcomes. *J Am Coll Surg*. 2016;223:611–620 e4.
22. Vrochides D, Hassanain M, Barkun J, et al. Association of preoperative parameters with postoperative mortality and long-term survival after liver transplantation. *Can J Surg*. 2011;54:101–106.
23. Waki K. UNOS Liver Registry: Ten year survivals. *Clin Transpl*. 2006:29–39.
24. Narayanan Menon KV, Nyberg SL, Harmsen WS, et al. MELD and other factors associated with survival after liver transplantation. *Am J Transplant*. 2004;4:819–825.
25. Sonny A, Kelly D, Hammel JP, Albeldawi M, Zein N, Cywinski JB. Predictors of poor outcome among older liver transplant recipients. *Clin Transplant*. 2015;29:197–203.
26. Feng S, Goodrich NP, Bragg-Gresham JL, et al. Characteristics associated with liver graft failure: The concept of a donor risk index. *Am J Transplant*. 2006;6:783–790.
27. Nair S, Eustace J, Thuluvath PJ. Effect of race on outcome of orthotopic liver transplantation: A cohort study. *Lancet*. 2002;359:287–293.
28. Hong JC, Kosari K, Benjamin E, et al. Does race influence outcomes after primary liver transplantation? A 23-year experience with 2,700 patients. *J Am Coll Surg*. 2008;206:1009–1016; discussion 1016–1018.
29. Yoo HY, Thuluvath PJ. Outcome of liver transplantation in adult recipients: Influence of neighborhood income, education, and insurance. *Liver Transpl*. 2004;10:235–243.
30. Gurien LA, Tepas 3rd JJ, Lind DS, et al. How Safe Is the Safety Net? Comparison of Ivor-Lewis esophagectomy at a safety net hospital using the NSQIP database. *J Am Coll Surg*. 2018;226:680–684.
31. Coolsen MM, Wong-Lun-Hing EM, van Dam RM, et al. A systematic review of outcomes in patients undergoing liver surgery in an enhanced recovery after surgery pathways. *HPB (Oxford)*. 2013;15:245–251.
32. Melloul E, Hubner M, Scott M, et al. Guidelines for perioperative care for liver surgery: Enhanced recovery after surgery (ERAS) society recommendations. *World J Surg*. 2016;40:2425–2440.
33. Figueroa JF, Wang DE, Jha AK. Characteristics of hospitals receiving the largest penalties by US pay-for-performance programmes. *BMJ Qual Saf*. 2016;25:898–900.
34. Woolhandler S, Himmelstein DU. Collateral damage: Pay-for-performance initiatives and safety net hospitals. *Ann Intern Med*. 2015;163:473–474.