Rural-Urban Differences in In-Hospital Mortality Among Admissions for End-Stage Liver Disease in the United States

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Access to quality hospital care is a persistent problem for rural patients. Little is known about disparities between rural and urban populations regarding in-hospital outcomes for end-stage liver disease (ESLD) patients. We aimed to determine whether rural ESLD patients experienced higher in-hospital mortality than urban patients and whether disparities were attributable to the rurality of the patient or the center. This was a retrospective study of patient admissions in the National Inpatient Sample, a population-based sample of hospitals in the United States. Admissions were included if they were from adult patients who had an ESLD-related admission defined by codes from the International Classification of Diseases, Ninth Revision, between January 2012 and December 2014. The primary exposures of interest were patient-level rurality and hospital-level rurality. The main outcome was in-hospital mortality. We stratified our analysis by disease severity score. After accounting for patient- and hospital-level covariates, ESLD admissions to rural hospitals in every category of disease severity had significantly higher odds of in-hospital mortality than patient admissions to urban hospitals. Those with moderate or major risk of dying had more than twice the odds of in-hospital mortality (odds ratio [OR] for moderate risk, 2.41; 95% confidence interval [CI], 1.62-3.59; OR for major risk, 2.49; 95% CI, 1.97-3.14). There was no association between patient-level rurality and mortality in the adjusted models. In conclusion, ESLD patients admitted to rural hospitals had increased odds of in-hospital mortality compared with those admitted to urban hospitals, and the differences were not attributable to patient-level rurality. Our results suggest that interventions to improve outcomes in this population should focus on the level of the health system.

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Patients with end-stage liver disease (ESLD) are often critically ill and require hospital admission for the management of complications. Consistent with a general trend of improvement in outcomes across other common chronic conditions,[1-3] there has been a substantial reduction of in-hospital mortality rates among patients with cirrhosis over the past decade.[4,5] This trend has been attributed to improved medical care aimed at prolonging life among patients with cirrhosis and increased attention to health care delivery, including quality improvement initiatives.[6]

Abbreviations: AMA, against medical advice; APR-DRG, all patient refined diagnosis-related group; CI, confidence interval; ESLD, end-stage liver disease; GEE, generalized estimating equation; HCUP, Healthcare Cost and Utilization Project; ICD-9, International Classification of Diseases, Ninth Revision; ICF, intermediate care facility; NIS, National Inpatient Sample; OR, odds ratio; SD, standard deviation; SNF, skilled nursing facility.

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Characteristics of the treating hospital play a large role in the outcomes of patients with cirrhosis. Inpatient mortality varies substantially among hospitals[7] and is partially attributable to differences in resource intensity at the hospital level.[8] Little is known about treatment outcomes in rural hospitals, where outcomes for other conditions, such as acute myocardial infarction and congestive heart failure, are known to be inferior.[9] The quality of rural hospital care is particularly relevant for patients with ESLD because rural areas experience a disproportionate burden of ESLD mortality.[10] Improving outcomes for these patients requires consideration of both the patient-level and health systems–level factors that affect care in rural areas.

To clarify the role of the hospital setting on outcomes among ESLD patients, we used national-level hospital admissions data to examine whether rural ESLD patients experienced higher in-hospital mortality than urban patients. We also sought to discern whether observed disparities were primarily attributable to the rurality of the patient or to the center. Finally, we examined patterns of intensity of care that may potentially explain observed differences in outcomes.

Patients and Methods

DATA SOURCE

This study was a secondary analysis of the 2012-2014 National Inpatient Sample (NIS), collected as a part of the Healthcare Cost and Utilization Project (HCUP) at the Agency for Healthcare Research and Quality. The NIS is a 20% stratified random sample of discharge records from general, community, and academic medical centers in the United States from 46 participating states. Patients admitted to longterm care or rehabilitation facilities are not represented in the NIS. NIS data can be weighted to represent national estimates of health care utilization, access, charges, quality, and outcomes.[11] This study was exempt from review by the Emory Institutional Review Board.

STUDY POPULATION

The unit of analysis was hospital admission. Admitted patients were classified on the basis of International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes and put into 3 groups: cirrhosis (571.2, 571.5); portal hypertensive complications (portal hypertension [572.3], ascites [78959], hepatic encephalopathy [572.2], upper gastrointestinal bleed [456.0, 456.2, 578.0, 578.1, or 578.9], or hepatorenal syndrome [572.4]); or primary liver tumor (155.0). Admissions were considered to be related to ESLD if they met 1 of 3 criteria:

1. Primary diagnosis of cirrhosis with a secondary diagnosis of portal hypertensive complications.
2. Primary diagnosis of portal hypertensive complications with a secondary diagnosis of cirrhosis.
3. Primary liver tumor as either the primary or secondary diagnosis.

This algorithm has been previously shown to have a high positive predictive value for identifying ESLD patients.[12] Admissions were included if they were from adult patients (>18 years of age) who had an ESLD-related admission between January 1, 2012, and December 31, 2014.

STUDY VARIABLES

The primary outcome was in-hospital mortality, obtained from the discharge disposition of the patient. Patients with this outcome were those who died while admitted to the hospital. Patients without this outcome were alive at the time of discharge, even if they died outside of the hospital later. As a secondary outcome, we used ICD-9 procedural codes to determine whether an admitted patient had a paracentesis (549.1) or endoscopy (451.3, 441.3, 422.3, or 423.3) performed. Paracentesis and endoscopy serve diagnostic and therapeutic roles in ESLD patients with suspected peritonitis and gastrointestinal bleeding.

The primary exposures of interest were patient-level rurality, which was assessed using the county of patient residence, and hospital-level rurality. Patient rurality was assessed using the National Center for Health Statistics classification scheme for counties and was dichotomized into rural counties (micropolitan or noncore county) and urban counties (counties in metropolitan areas of a population >50,000). Hospital rurality was based on the core-based statistical area of the hospital. Hospitals with a core-based statistical area type of being a micropolitan or noncore county were considered rural, whereas urban nonteaching and teaching hospitals were collapsed into 1 urban category. We assessed whether this affected results in a sensitivity

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analysis that compared rural hospitals and urban nonteaching hospitals with urban teaching hospitals.

Because patients with more severe disease tend to have a higher risk of mortality and to self-select or be transferred into hospitals with more resources, we stratified our analysis by disease severity to account for this potential bias. Disease severity was classified according to the all patient refined diagnosis-related group (APR-DRG) risk of mortality scheme, developed for HCUP databases and previously found to be the strongest predictors of in-hospital mortality among admitted patients with cirrhosis.[13] The APR-DRG is a 4-category scale: 1, minor risk of dying; 2, moderate risk of dying; 3, major risk of dying; or 4, extreme risk of dying. Patient-level covariates collected at the time of hospital admission included age, sex, race, primary payer, zip code–level income, Elixhauser comorbidity index, and whether the patient was transferred into the hospital. Hospital-level covariates included region and number of beds.

STATISTICAL ANALYSES

We used the provided survey weights for NIS to account for the stratified sampling. Descriptive statistics for our population, including means, medians, and proportions, were calculated. Bivariate analyses were used to compare discharge-level categorical variables by patient- and hospital-level rurality. We used multivariate logistic regression to estimate the association between rurality and in-hospital mortality, accounting for patient- and hospital-level factors. Generalized estimating equations (GEEs) were used to account for correlations between patients in the same hospitals. We chose to use the GEE model because it is considered an appropriate method to obtain the average effect of both patient- and hospital-level covariates on an outcome in a population in the presence of correlated data.[14] All models were stratified by APR-DRG mortality risk group. Because of our interest in identifying the relative importance of patient- and hospital-level rurality, we examined effects 1 at a time.

First, we separately estimated the crude association between hospital rurality (model 1A) and patient rurality (model 1B) with in-hospital mortality. Second, we included both hospital rurality and patient rurality in the model (model 2). Finally, we included all identified patient- and hospital-level covariates in a fully adjusted model (model 3). To accomplish our secondary aim, we used the chi-square test to compare the frequency of receiving paracentesis, endoscopy, or either, by hospital rurality. We then included paracentesis and endoscopy into the fully adjusted model mentioned here to determine whether their inclusion explained the association between rurality and in-hospital mortality (model 4). We conducted a complete case analysis, and 8685 (7.8%) patients were excluded for missing covariate or outcome information. All analyses were conducted in SAS, version 9.4 (SAS Institute, Cary, NC).

Results

We identified 111,044 ESLD-related admissions between January 1, 2012, and December 31, 2014. Demographic characteristics are provided in Table 1. Approximately 15.9% of ESLD admissions resided in a rural area (n = 17,559), whereas 8.1% of admissions were at a rural hospital (n = 8992). Admitted patients were predominantly male (65.6%, n = 72,839) and white (64%, n = 67,815), with a mean age of 59.5 years (SD = 26.6 years). Medicare was the most frequent primary payer (42.9%, n = 47,478), followed by Medicaid (22.6%, n = 25,089) and private insurance (22.0%, n = 24,332). Approximately one-third of ESLD admissions were patients who lived in zip codes in the lowest income quartile (33%, n = 36,073). The South was the most common hospital region of admissions (40.3%, n = 44,737), and most admissions were to large hospitals (60.9%, n = 67,596). Approximately 7% of ESLD admissions resulted in an in-hospital death (n = 7178), and over half of the sample was at a major or extreme risk of dying as measured by the APR-DRG mortality risk classification (59.8%, n = 66,434; Table 1).

Demographic characteristics varied by both hospital- and patient-level rurality (Table 2). Over 90% of admissions to rural hospitals were patients who lived in rural areas, but over half of the admissions among patients who lived in rural areas were to urban hospitals. Patients admitted to rural hospitals were more likely to be white (82.2% versus 62.2%), have Medicare as the primary payer (50.4% versus 42.2%), and live in zip codes in the lowest income quartile (54.2% versus 31.7%). Over half of the admissions to rural hospitals were in the South (52.3% versus 39.2%). Patients admitted to rural hospitals were less likely to be at an extreme risk of dying (11.9% versus 17.4%) or major risk of dying (39.7% versus 43.1%). The crude difference of in-hospital mortality among admissions to rural hospitals was small (7.1% versus 6.4%). These patients at rural hospitals were more likely to be transferred to another short-term facility

TABLE 1. Demographic Characteristics of ESLD Hospital Admissions in the NIS, United States (2012-2014)

	Frequency (n = 111,044)	Weighted Frequency (n = 555,220)	Percent of Weighted Frequency
Hospital rurality			
Rural	8992	44,960	8.1
Urban	102,052	510,260	91.9
Patient rurality			
Rural	17,559	87,795	15.9
Urban	92,657	463,285	84.1
Missing	828	—	
Sex			
Male	72,839	364,195	65.6
Female	38,191	190,955	34.4
Missing	14	—	
Race			
White	67,815	339,075	63.8
Black	11,142	55,710	10.5
Hispanic	18,776	93,880	17.7
Asian/Pacific Islander	3274	16,370	3.1
Native American	1476	7380	1.4
Other	3820	19,100	3.6
Missing	4741	—	
Primary payer			
Medicare	47,478	237,390	42.9
Medicaid	25,089	125,445	22.6
Private insurance	24,332	121,660	22.0
Self-pay	8591	42,955	7.8
No charge	796	3980	0.7
Other	4464	22,320	4.0
Missing	294	—	
Median household income			
US $1-$38,999	36,073	180,365	33.5
US $39,000-$47,999	28,388	141,940	26.4
US $48,000-$63,999	24,389	121,945	22.6
US $64,000+	18,884	94,420	17.5
Missing	3310	—	
Hospital region			
Northeast	20,600	103,000	18.6
Midwest	20,491	102,455	18.5
South	44,737	223,685	40.3
West	25,216	126,080	22.7
Hospital size (by number of beds)			
Small	14,136	70,680	12.7
Medium	29,312	146,560	26.4
Large	67,596	337,980	60.9
APR-DRG mortality risk			
Minor risk of dying	7122	35,610	6.4
Moderate risk of dying	37,477	187,385	33.8
Major risk of dying	47,565	237,825	42.8
Extreme risk of dying	18,869	94,345	17.0
Missing	11	—	

TABLE 1. *Continued*

	Frequency (n = 111,044)	Weighted Frequency (n = 555,220)	Percent of Weighted Frequency
Died in hospital			
Yes	7178	35,890	6.5
No	103,823	519,115	93.5
Missing	43	—	
Age, years, mean ± SD	59.5 ± 26.6		
Elixhauser index, mean ± SD	12.9 ± 25.0		

TABLE 2. Demographic Characteristics of ESLD Admissions Stratified by Hospital-Level and Patient-Level Rurality, NIS, United States (2012-2014)

	Hospital Rurality			Patient Rurality			Among Rural Patients		
	Rural Hospital (n = 8,992, 8.1%)	Urban Hospital (n = 102,052, 91.9%)	*P* Value	Rural Patient (n = 17,559, 15.8%)	Urban Patient (n = 92,657, 83.4%)	*P* Value	Rural Hospital (n = 8,356, 47.6%)	Urban Hospital (n = 9,203, 52.4%)	*P* Value
Hospital rurality						<0.001			
Rural				8356 (47.6)	623 (0.7)				
Urban				9203 (52.4)	92,034 (99.3)				
Patient rurality			<0.001						
Rural	8356 (93.1)	9203 (9.1)							
Urban	623 (6.9)	92,034 (90.9)							
Sex			<0.001			<0.001			<0.001
Male	5626 (62.6)	67,203 (65.9)		11,269 (64.2)	60,928 (65.8)		5224 (62.5)	6045 (65.7)	
Female	3356 (37.4)	34,835 (34.1)		6289 (35.8)	31,717 (34.2)		3132 (37.5)	3157 (34.3)	
Race			<0.001			<0.001			<0.001
White	6853 (82.2)	60,962 (62.2)		13,028 (80.4)	54,424 (61.0)		6330 (82.0)	6698 (78.9)	
Black	479 (5.7)	10,663 (10.9)		892 (5.5)	10,115 (11.3)		442 (5.7)	450 (5.3)	
Hispanic	566 (6.8)	18,210 (18.6)		1262 (7.8)	17,324 (19.4)		528 (6.8)	734 (8.6)	
Asian/Pacific Islander	65 (0.8)	3209 (3.3)		114 (0.7)	3134 (3.5)		63 (0.8)	51 (0.6)	
Native American	237 (2.8)	1239 (1.3)		589 (3.6)	886 (1.0)		222 (2.9)	367 (4.3)	
Other	142 (1.7)	3678 (3.8)		319 (2.0)	3403 (3.8)		133 (1.7)	186 (2.2)	
Primary payer			<0.001			<0.001			<0.001
Medicare	4516 (50.4)	42,962 (42.2)		8283 (47.4)	38,996 (42.2)		4230 (50.8)	4053 (44.2)	
Medicaid	1852 (20.7)	23,237 (22.8)		3524 (20.2)	21,271 (23.0)		1724 (20.7)	1800 (19.6)	
Private insurance	1552 (17.3)	22,780 (22.4)		3405 (19.5)	20,804 (22.5)		1426 (17.1)	1979 (21.6)	
Self-pay	652 (7.3)	7939 (7.8)		1344 (7.7)	7120 (7.7)		594 (7.1)	750 (8.2)	
No charge	41 (0.5)	755 (0.7)		80 (0.5)	704 (0.8)		41 (0.5)	39 (0.4)	
Other	344 (3.8)	4120 (4.0)		848 (4.9)	3545 (3.8)		307 (3.7)	541 (5.9)	
Median household income			<0.001			<0.001			0.001
$1-$38,999	4697 (54.2)	31,376 (31.7)		9251 (54.6)	26,822 (29.5)		4520 (56.0)	4731 (53.3)	
$39,000-$47,999	2921 (33.7)	25,467 (25.7)		5733 (33.8)	22,655 (25.0)		2688 (33.3)	3045 (34.3)	
$48,000-$63,999	859 (9.9)	23,530 (23.8)		1687 (10.0)	22,702 (25.0)		738 (9.1)	949 (10.7)	
$64,000+	195 (2.2)	18,689 (18.9)		271 (1.6)	18,613 (20.5)		120 (1.5)	151 (1.7)	
Hospital region			<0.001			<0.001			<0.001
Northeast	1161 (12.9)	19,439 (19.0)		1594 (9.1)	18,674 (20.2)		1032 (12.4)	562 (6.1)	
Midwest	1912 (21.3)	18,579 (18.2)		4234 (24.1)	16,221 (17.5)		1829 (21.9)	2405 (26.1)	
South	4706 (52.3)	40,031 (39.2)		9338 (53.2)	35,146 (37.9)		4330 (51.8)	5008 (54.4)	
West	1213 (13.5)	24,003 (23.5)		2393 (13.6)	22,616 (24.4)		1165 (13.9)	1228 (13.3)	

TABLE 2. *Continued*

	Hospital Rurality			Patient Rurality			Among Rural Patients		
	Rural Hospital (n = 8,992, 8.1%)	Urban Hospital (n = 102,052, 91.9%)	*P* Value	Rural Patient (n = 17,559, 15.8%)	Urban Patient (n = 92,657, 83.4%)	*P* Value	Rural Hospital (n = 8,356, 47.6%)	Urban Hospital (n = 9,203, 52.4%)	*P* Value
Hospital size (by number of beds)			<0.001						<0.001
Small	995 (11.1)	13,141 (12.9)		1735 (9.9)	12,336 (13.3)		917 (11.0)	818 (8.9)	
Medium	1798 (20.0)	27,514 (27.0)		3884 (22.1)	25,243 (27.2)		1664 (19.9)	2220 (24.1)	
Large	6199 (68.9)	61,397 (60.2)		11,940 (68.0)	55,078 (59.4)		5775 (69.1)	6165 (67.0)	
APR-DRG mortality risk			<0.001			<0.001			<0.001
Minor risk of dying	830 (9.2)	6292 (6.2)		1237 (7.0)	5825 (6.3)		781 (9.3)	456 (5.0)	
Moderate risk of dying	3525 (39.2)	33,952 (33.3)		6089 (34.7)	31,106 (33.6)		3283 (39.3)	2806 (30.5)	
Major risk of dying	3570 (39.7)	43,995 (43.1)		7272 (41.4)	39,945 (43.1)		3300 (39.5)	3972 (43.2)	
Extreme risk of dying	1067 (11.9)	17,802 (17.4)		2957 (16.8)	15,774 (17.0)		992 (11.9)	1965 (21.4)	
Died in hospital			0.02			<0.001			0.86
Yes	635 (7.1)	6543 (6.4)		1248 (7.1)	5862 (6.3)		591 (7.1)	657 (7.1)	
No	8353 (92.9)	95,470 (93.6)		16,302 (92.9)	86,761 (93.7)		7761 (92.9)	8541 (92.9)	
Discharge location			<0.001			<0.001			<0.001
Routine	4763 (53.1)	60,768 (59.7)		10,104 (57.6)	54,914 (59.4)		4409 (52.9)	5695 (61.9)	
Transfer to short-term facility	702 (7.8)	2760 (2.7)		884 (5.0)	2561 (2.8)		649 (7.8)	235 (2.6)	
Transfer to SNF, ICF, other	1427 (15.9)	14,933 (14.70)		2525 (14.4)	13,748 (14.9)		1353 (16.2)	1172 (12.7)	
Home health	1298 (14.5)	14,827 (14.6)		2523 (14.4)	13,502 (14.6)		1197 (14.4)	1327 (14.4)	
AMA	148 (1.6)	2032 (2.0)		248 (1.4)	1888 (2.0)		140 (1.7)	108 (1.2)	
Died	635 (7.1)	6543 (6.4)		1248 (7.1)	5862 (6.3)		591 (7.1)	657 (7.1)	
Portal hypertensive complication									
Portal hypertension	2489 (27.7)	38,598 (37.8)	<0.001	6139 (35.0)	34,645 (37.4)	<0.001	2301 (27.5)	3838 (41.7)	<0.001
Ascites	4177 (46.5)	50,464 (49.5)	<0.001	8593 (48.9)	45,654 (49.3)	0.42	3860 (46.2)	4733 (51.4)	<0.001
Hepatic encephalopathy	3901 (43.4)	34,557 (33.9)	<0.001	6775 (38.6)	31,476 (34.0)	<0.001	3645 (43.6)	3130 (34.0)	<0.001
Upper gastrointestinal bleed	1652 (18.4)	17,347 (17.0)	0.001	3212 (18.3)	15,627 (16.9)	<0.001	1534 (18.4)	1678 (18.2)	0.83
Hepatorenal syndrome	518 (5.8)	6609 (6.5)	0.001	1188 (6.8)	5893 (6.4)	0.04	486 (5.8)	702 (7.6)	<0.001
Primary liver tumor	1631 (18.1)	29,490 (28.9)	<0.001	3984 (22.7)	26,839 (29.0)	<0.001	1524 (18.2)	2460 (26.7)	<0.001
Length of stay, days, mean ± SD	4.4 ± 4.5	5.6 ± 6.9	<0.001	5.2 ± 5.8	5.6 ± 6.9	<0.001	4.4 ± 4.4	5.9 ± 6.7	<0.001
Age, years, mean ± SD	60.7 ± 11.8	59.4 ± 11.9	<0.001	59.7 ± 11.8	59.5 ± 11.9	0.04	60.7 ± 11.8	58.8 ± 11.8	<0.001
Comorbidity score, mean ± SD	11.7 ± 10.8	13.0 ± 11.2	<0.001	12.6 ± 11.0	12.9 ± 11.2	<0.001	11.8 ± 10.8	13.3 ± 11.1	<0.001

NOTE: Data are given as mean ± SD and n (%).

(7.8% versus 2.7%) or to a skilled nursing facility (SNF; 15.9% versus 14.6%) than admissions to urban hospitals. Patients admitted to rural hospitals were less likely than those admitted to urban hospitals to have portal hypertension (27.7% versus 37.8%) or a primary liver tumor (18.1% versus 28.9%). However, they were more likely to have hepatic encephalopathy (43.4% versus 33.9%). Patients admitted to rural hospitals had a shorter mean length of stay than patients admitted to urban hospitals (4.4 versus 5.6 days). Demographic and clinical characteristics among patients living in rural areas were essentially identical to admissions to rural hospitals with the exception of disease severity, comorbidity score, and portal hypertensive complications. The distribution of these characteristics was similar between rural and urban patients.

Among rural patients, 47.6% were admitted to a rural hospital, and 52.4% were admitted to an urban hospital. Among rural patients, admissions to rural hospitals were more likely to have Medicare (50.8% versus 44.2%), to live in a zip code in the lowest quartile of income (56.0% versus 53.3%) and to live in the Northeast (12.4% versus 6.1%) than admissions to urban hospitals. There were substantial differences in admission location among rural patients by disease severity, with admissions to rural hospitals less likely to be at extreme (11.9% versus 21.4%) or major (39.5% versus 43.2%) risk of dying. Similar to the overall population, among rural patients, those admitted to rural hospitals were less likely to have portal hypertension (27.5% versus 41.7%) or a primary liver tumor (18.2% versus 26.7%) but were more likely to have hepatic encephalopathy (43.6% versus 34.0%). Although there was not a meaningful difference in length of stay between rural and urban patients (5.2 days versus 5.6 days), among rural patients, those in rural hospitals had a shorter length of stay than those in urban hospitals (4.4 days versus 5.9 days). Rural patients seen in rural hospitals had a lower comorbidity score than rural patients seen in urban hospitals (11.8 versus 13.3).

In stratified bivariate analyses (Fig. 1), hospital rurality was significantly associated with in-hospital mortality among every category of disease severity. Among patients at minor, moderate, or major risk of dying, those admitted to rural hospitals had double the proportion of in-hospital mortality (2% versus 1%, 2% versus 1%, 6% versus 3%, respectively). Patient rurality was significantly associated with in-hospital mortality among every category of disease severity with the exception of those at extreme risk of mortality ($P = 0.86$). When limited to admissions to urban hospitals, there were no statistically significant differences between in-hospital mortality rates for rural and urban patients in any category of disease severity.

The multivariate logistic regression analyses examining the association between rurality and in-hospital mortality, accounting for other patient- and hospital-level covariates, are presented in Table 3. Model 1 presents the crude association of both hospital-level and patient-level rurality with in-hospital mortality. Rural admissions of either classification had significantly increased odds of in-hospital mortality than urban patients, with the exception of rural patients at an extreme risk of dying (OR, 0.99; 95% CI, 0.91-1.08).

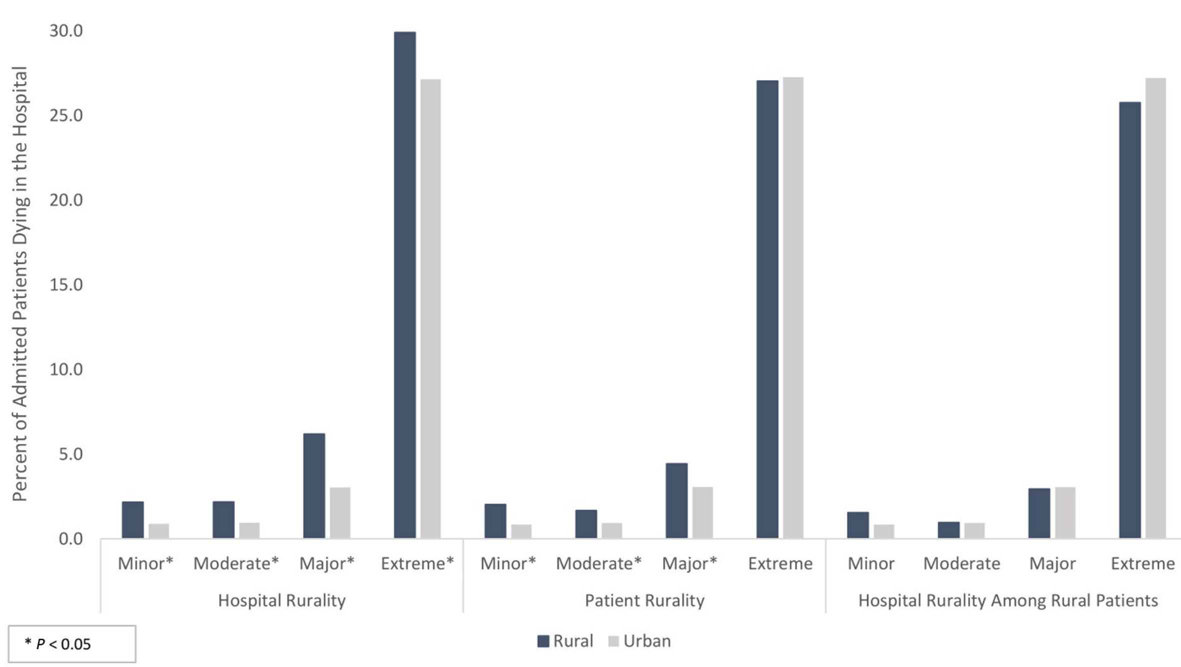

FIG. 1. Proportion of admissions for ESLD patients who died in the hospital, stratified by disease severity, hospital rurality, and patient rurality, NIS (2012-2014).

TABLE 3. Multivariate Logistic Regression Examining the Effect of Rurality on In-Hospital Mortality Among Admissions for ESLD (2012-2014)

	Model 1A/B*		Model 2†		Model 3‡		Model 4§	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Minor risk of dying								
Rural hospital	2.47	1.44-4.22	1.35	0.63-2.91	2.73	1.20-6.20	2.67	1.18-6.07
Urban hospital‖	—	—	—	—	—	—	—	—
Rural patient	2.44	1.50-3.96	1.99	1.00-4.00	1.36	0.64-2.92	1.36	0.64-2.90
Urban patient‖	—	—	—	—	—	—	—	—
Moderate risk of dying								
Rural hospital	2.34	1.82-3.00	2.12	1.47-3.05	2.39	1.61-3.58	2.15	1.43-3.23
Urban hospital‖	—	—	—	—	—	—	—	—
Rural patient	1.8	1.44-2.26	1.14	0.82-1.58	1.05	0.72-1.54	1.05	0.71-1.55
Urban patient‖	—	—	—	—	—	—	—	—
Major risk of dying								
Rural hospital	2.11	1.82-2.44	2.16	1.75-2.66	2.48	1.97-3.14	2.29	1.81-2.89
Urban hospital‖	—	—	—	—	—	—	—	—
Rural patient	1.47	1.29-1.66	0.97	0.82-1.17	0.89	0.73-1.10	0.91	0.74-1.12
Urban patient‖	—	—	—	—	—	—	—	—
Extreme risk of dying								
Rural hospital	1.15	1.00-1.31	1.23	1.05-1.45	1.32	1.01-1.57	1.23	1.03-1.47
Urban hospital‖	—	—	—	—	—	—	—	—
Rural patient	0.99	0.91-1.08	0.92	0.83-1.02	0.91	0.81-1.03	0.92	0.82-1.05
Urban patient‖	—	—	—	—	—	—	—	—

*Model includes either hospital-level or patient-level rurality.
†Model includes both hospital-level and patient-level rurality.
‡Model includes hospital-level rurality, patient-level rurality, age, race, sex, comorbidity score, primary payer zip code–level income quartile, transfer status, hospital region, and number of hospital beds.
§Model includes hospital-level rurality, patient-level rurality, age, race, sex, comorbidity score, primary payer zip code–level income quartile, transfer status, hospital region, number of hospital beds, receipt of paracentesis, and receipt of endoscopy.
‖Reference category.

In model 2, we examined the association of hospital-level and patient-level rurality on in-hospital mortality together. Among patients at a minor risk of dying, there were no significant associations between rurality and in-hospital mortality. Among patients at a moderate or major risk of dying, patients admitted to rural hospitals had over twice the odds of experiencing in-hospital mortality as patients in urban hospitals (OR for moderate risk, 2.12; 95% CI, 1.47-3.05; OR for major risk, 2.16; 95% CI, 1.75-2.66). The association between patient-level rurality and in-hospital mortality was not significant for moderate (OR, 1.14; 95% CI, 0.82-1.58) or for major risk (OR, 0.97; 95% CI, 0.82-1.17).

In model 3, after adjustment for age, race, sex, comorbidity score, primary payer zip code–level income quartile, transfer status, hospital region, and number of hospital beds, there was a significant association between hospital rurality and in-hospital mortality in every strata of disease severity. The strength of the association decreased as disease severity increased. Admissions among patients with a minor risk of dying had nearly 3 times the odds of in-hospital mortality at rural hospitals than at urban hospitals (OR, 2.73; 95% CI, 1.20-6.22). Patients admitted to rural hospitals who were at a moderate (OR, 2.39; 95% CI, 1.61-3.58) or major (OR, 2.48; 95% CI, 1.97-3.14) risk of dying had more than twice the odds of experiencing in-hospital mortality as those admitted to urban hospitals. Among patients who were at an extreme risk of dying, admissions to rural hospitals had a 32% increased odds of in-hospital mortality compared with urban hospitals (95% CI, 1.01-1.57), even after adjustment for patient- and hospital-level covariates. There were no significant associations between patient-level rurality and likelihood of inpatient hospital mortality in any strata of disease severity.

Table 4 presents the frequency of access to liver-disease specific procedures, including paracentesis and endoscopy by hospital-level rurality, stratified by disease severity. For each procedure and in every strata of disease severity, with the exception of patients at a minor risk of death, patients admitted to urban hospitals were statistically significantly more likely to have the procedure than those admitted to rural hospitals. Inclusion of paracentesis and endoscopy to the fully adjusted model only partially attenuated the association between hospital rurality and in-hospital mortality (Table 3, model 4). The attenuation was strongest for patients in the moderate (OR, 2.15; 95% CI, 1.43-3.23) and major (OR, 2.29; 95% CI, 1.81-2.89) risk categories.

In a sensitivity analysis, we compared patient admissions to rural and to urban nonteaching hospitals with patient admissions to urban teaching hospitals accounting for the covariates described previously. In every strata of disease severity except for severe disease, patients admitted to rural hospitals were significantly more likely to experience in-hospital mortality than those admitted to urban teaching hospitals for minor risk (OR, 2.82; 95% CI, 1.18-6.74), moderate risk (OR, 2.73; 95% CI, 1.78-4.19), major risk (OR, 2.39; 95% CI, 1.88-3.04), and extreme risk (OR, 1.15; 95% CI, 0.96-1.38). Patients admitted to urban nonteaching hospitals also had a significantly higher likelihood of in-hospital mortality among patients at a moderate (OR, 1.89; 95% CI, 1.49-2.42) or major (OR, 1.28; 95% CI, 1.14-1.45) risk of dying, although the magnitude of the association was lower. We also conducted a sensitivity analysis to evaluate whether results differed among the Medicare population or after adjustment for portal hypertensive complications or primary liver tumor, and we found no significant differences (data not shown).

To explore whether the effect of hospital location on mortality among rural patients could be explained by differences in referral patterns to urban hospitals (eg, if patients retained in rural hospitals were sicker or had lower socioeconomic status), we compared demographic and clinical characteristics between rural patients admitted to rural hospitals and rural patients admitted to urban hospitals (Supporting Table 1). Rural patients admitted to rural hospitals were more likely to live in the lowest income zip codes (56.0% versus 53.3%), have Medicare (50.8% versus 44.2%), and be at minor (9.4% versus 5.0%) or moderate (39.3% versus 30.5%) risk of dying compared with rural patients admitted to urban hospitals. On average, rural patients admitted to rural hospitals were older (60.7 years versus 58.8 years) but had a lower comorbidity index (11.8 versus 13.3) compared with those admitted to urban hospitals. On the basis of these findings, it does not appear that the reason why rural patients in rural hospitals are not being referred to urban hospitals is because their situation is futile; rather, patients in rural hospitals have less severe disease (based on APR-DRG mortality risk) and similar comorbidity scores. Socioeconomic status could play a role in referral because rural patients in rural hospitals had a higher proportion of patients in the lowest income zip codes, but the absolute difference between the 2 groups appears to be small and not likely to explain our findings.

TABLE 4. Receipt of Procedures Among Admissions for ESLD by Hospital Rurality in the NIS (2012-2014)

	Paracentesis			Endoscopy			Either		
	Rural	Urban	*P* Value	Rural	Urban	*P* Value	Rural	Urban	*P* Value
Minor risk of dying			0.50			0.02			0.06
Procedure	109 (13.1)	880 (14.0)		40 (4.8)	434 (6.9)		148 (17.8)	1300 (20.7)	
No procedure	721 (86.9)	5412 (86.0)		790 (95.2)	5858 (93.1)		682 (82.2)	4992 (79.3)	
Moderate risk of dying			<0.001			<0.001			<0.001
Procedure	957 (27.1)	11,343 (33.4)		329 (9.3)	5545 (16.3)		1217 (34.5)	15,703 (46.3)	
No procedure	2568 (72.9)	22,609 (66.6)		3196 (90.7)	28,407 (83.7)		2308 (65.5)	18,249 (53.7)	
Major risk of dying			<0.001			<0.001			<0.001
Procedure	979 (27.4)	14,634 (33.3)		662 (18.5)	10,771 (24.5)		1516 (42.5)	22,608 (51.4)	
No procedure	2591 (72.6)	29,361 (66.7)		2908 (81.5)	33,224 (75.5)		2054 (57.5)	21,387 (48.6)	
Extreme risk of dying			<0.001			<0.001			<0.001
Procedure	361 (33.8)	7492 (42.1)		183 (17.2)	4622 (26.0)		498 (46.7)	10,229 (57.5)	
No procedure	706 (66.2)	10,310 (57.9)		884 (82.8)	13,180 (74.0)		569 (53.3)	7573 (42.5)	

Discussion

In this analysis of a representative sample of ESLD admissions in the United States, we found that admission to a rural hospital compared with admission to an urban hospital was associated with increased in-hospital mortality, independent of patient-level rurality and other covariates. This association was strongest among patients with scores on admission of moderate or major disease severity, who had more than twice the odds of experiencing in-hospital mortality as their urban counterparts, and it was not explained by receipt of paracentesis or endoscopy. After accounting for hospital-level rurality, patient-level rurality was not significantly associated with in-hospital mortality in any strata of disease severity. Our findings are relevant to the 1800 rural community hospitals in the United States[15] and imply that interventions to improve outcomes among rural ESLD patients may need to focus on intensity or quality of care at the health system level. Because nearly half of the ESLD admissions in our study were covered by Medicare and similar associations between hospital rurality and mortality were observed in the Medicare population, our findings may also be relevant to the Centers for Medicare and Medicaid Services.

Rural areas in the United States have experienced higher mortality rates and excess death for the past 2 decades.[16] Although prevalence estimates for ESLD are unavailable, rural areas have higher age-adjusted ESLD mortality rates than urban areas.[10] However, in our study, rural patients made up 15.3% of ESLD admissions despite making up 19.3% of the US population. This underrepresentation in admissions, combined with an overrepresentation in mortality, signals that that there may be a disparity in access to care for rural ESLD patients that contributes to poor outcomes in this population.

Our results offer an important insight into care and outcomes for patients with cirrhosis. Potential reasons for excess mortality in rural hospitals include a low volume of invasive procedures[17,18] and less access to subspecialists, such as gastroenterologists, which has been associated with poor outcomes for liver disease patients.[19-21] One immediate implication of our findings is that liver disease patients benefit from care at urban centers, either due to resources or personnel that are more commonly available than in rural settings. Previous studies have shown that rural patients prefer hospitals with greater service capacity,[22] and they are more likely to bypass closer, rural hospitals for urban hospitals if they have acute medical conditions,[23] such as decompensated cirrhosis. Although expedited transfer of ESLD patients to urban centers could potentially reduce mortality risks in the short term, such a policy would be costly and risk further partitioning quality care away from rural communities where hospital closures already threaten access to care.[24] A more inclusive and ultimately effective approach would be to leverage technologies, such as telemedicine, which has been applied to other facets of rural health care delivery including preventing emergency room transfers,[25] providing pediatric subspecialty care,[26] and providing time-sensitive care to stroke patients.[27] Clinical decision support systems[28] and regional collaborations and support networks[29] have also been successfully implemented to improve quality of care in rural hospitals. One such pilot program using Veterans Health Administration referrals to a central subspecialty service found similar survival with telepresence consultations and in-person visits and a marked reduction in patient mortality across early- and late-stage liver disease in propensity-matched cohorts without any visit, particularly for rural patients.[30] Subspecialty care through dispersed networks have shown telemedicine and spoke-and-hub referral systems to be highly cost-effective in other disease settings.[31-33] Another strategy to contain costs and facilitate patient referral and follow-up would be the employment of patient navigators, who have been proven to reduce unnecessary emergency department visits and readmissions in other settings.[34,35]

Our findings support those of previous studies that demonstrated the importance of hospital-level characteristics to outcomes among patients with cirrhosis.[7,8] Mellinger et al. found that patients admitted to rural hospitals had a 27% higher odds of in-hospital mortality than patients admitted to urban hospitals after accounting for patient-level factors. However, in their cohort, this effect was not statistically significant.[7] However, this analysis was restricted to 1 year of data from a high-volume cohort of hospitals, potentially skewing the association between rurality and mortality due to differential exclusion of rural hospitals with less experience treating patients with cirrhosis and higher in-hospital mortality rates. Our results are also consistent with findings from other diseases, including rural-urban disparities in the quality of care and mortality rates for cardiopulmonary conditions including acute myocardial infarction, pneumonia, and congestive heart failure.[9,36] Disparities in care quality for inpatients in the rural setting reflect environmental considerations that extend beyond the hospital itself,[37] but key contributors within the health system framework are lesser engagement of multidisciplinary teams outside of teaching and high-volume centers,[38] less timely access to procedural specialists, such as interventional radiologists,[39] and even structural considerations, such as the size and experience of health care informatics and administrative staff.[40,41] Although the manifold drivers of rural disparity are challenging, they represent numerous domains in which quality improvement projects may identify and ameliorate excess risks in this population.

This analysis is constrained by limitations common to retrospective review of administrative data. Patient-specific risks are not captured in registry data so that considerations, such as clinical stability for transfer and proximity of the admitting hospital to a tertiary referral center, cannot be adjusted for in models. As a sample of admissions, the NIS lacks any patient identifier to follow patients across admissions. The redesign of the NIS after 2011 does not allow for hospital identification or linkage to other data sets. This lack of hospital identifiers restricts our ability to explore hospital-specific characteristics, such as care processes, that might differ between rural and urban hospitals and account for the observed disparity as well as factors that occur before the admission, such as access to primary or specialty care. Because of these limitations, NIS data must be taken as a stand-alone depiction of hospitalization, with limited context and no ability to imply causality. Despite these constraints, however, NIS represents the largest all-payer inpatient care database in the United States, containing data on more than 7 million hospital stays. As a result, our nationally representative sample of patients with ESLD offers insights into patterns of disease and care at a level not obtainable through other data sources.

In conclusion, ESLD patients admitted to rural hospitals had increased odds of in-hospital mortality compared with those admitted to urban hospitals, particularly among patients with lower APR-DRG expected mortality scores. After accounting for hospital rurality, patient-level rurality was not associated with increased in-hospital mortality. These findings suggest that excess mortality associated with rural hospitals may not be due to patient-level factors but rather to features of the admitting center. Further research is needed to identify potential hospital-level mediators and targets for improved care of liver disease patients in rural settings.

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