Differences in Perioperative Outcomes Between Right and Left Hepatic Lobectomy

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Abstract The safety of hepatic resection is well documented, but outcome studies comparing right and left hepatic lobectomy are sparse, especially in the context of malignancy. This study analyzes the differences in outcomes between right and left hepatic lobectomy in patients with malignant diagnoses. All patients undergoing right and left hepatic lobectomies for malignancy were extracted from the National Surgical Quality Improvement Program (NSQIP) database (2005–2010). The data was analyzed to determine differences in perioperative mortality and morbidity between the two groups. A total of 1680 patients who underwent right or left hepatic lobectomy for malignant diagnoses were identified. Patients undergoing right hepatic lobectomy had a four-fold increase in perioperative mortality, compared to left lobectomy ($p < 0.0001$). Mortality in right lobectomy patients increased incrementally with age, with a 12-fold increase in patients >81 years of age. Patients undergoing right lobectomy also experienced a statistically significant increase in morbidity involving several systems (infectious, pulmonary, cardiac and renal). The results of our study demonstrate that patients undergoing right hepatic lobectomy for malignancy experience a significantly higher incidence of mortality and multi-system morbidity when compared to left lobectomy. This information will be crucial for pre-operative risk-stratification of patients undergoing hepatic resection for malignancy.

Keywords Hepatectomy · Hepatic lobectomy · Outcomes · Mortality · Morbidity

Introduction

The number of hepatic resections performed for malignant and benign diseases has been increasing, with the majority of these resections being performed for malignant diagnoses [1, 2]. Several previous studies have documented the safety of hepatic resections [3–5], with mortality after major hepatic resections ranging between 2 and 5 % in high volume centers [1, 6–9]. Although the safety of hepatic resection is well documented, the differences in outcomes after various types of major hepatic resections have not been well studied. The few published reports that analyzed the differences in outcomes between right and left hepatic lobectomy included healthy donor livers slated for transplantation, or consisted of patients that underwent extended resections. Karanjia et al. previously reported worse perioperative outcomes for right sided resections when compared to left sided resections [10], however these authors combined extended right hepatectomy (which is technically and physiologically more challenging) with right lobectomy. There is a paucity of reports that have performed a detailed analysis of the differences in perioperative outcomes between right and left hepatic lobectomy in patients undergoing hepatic resection for malignancy [10, 11].

The aim of this current study is to analyze the differences in mortality and morbidity between right and left hepatic lobectomy in patients undergoing hepatic resection for malignancy by utilizing the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database.

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Methods

All patients undergoing right hepatic lobectomy (primary CPT code 47130) and left hepatic lobectomy (primary CPT code 47125) were extracted from the ACS-NSQIP Participant Use Files (2005–2010). The subset of patients with primary and secondary malignancies of the liver were identified using ICD-9 diagnoses 155.0, 155.1 and 197.7 (155.0 and 155.1—primary liver malignancies, 197.7—secondary malignancies of the liver). Only patients with malignant diagnoses were considered for our analysis. Patients were further divided into two groups: right hepatic lobectomy and left hepatic lobectomy based on the type of hepatic resection.

Several demographic, preoperative patient-related and laboratory variables were analyzed to ensure that patients were evenly matched between the two groups of right and left hepatic lobectomies. Mortality was defined as all-cause mortality within 30 days of the procedure per the NSQIP database. The following post-operative variables were analyzed to determine the morbidity: Superficial Surgical Site Infection, Deep Incisional Surgical Site infection, Organ Space Surgical Site Infection, Wound Disruption/Dehiscence, Pneumonia, Unplanned Reintubation, Pulmonary Embolism, Failure to Wean the Ventilator (>48 h), Progressive Renal Insufficiency, Acute Renal Failure, Urinary Tract Infection, Stroke/CVA with Neurological Deficit, Coma>24 h, Peripheral Nerve Injury, Cardiac Arrest Requiring CPR, Myocardial Infarction, Bleeding/Transfusions, Graft/Prosthesis Failure, DVT/Thrombophlebitis, Sepsis and Return to OR.

The mean and standard deviations or median and ranges were used to describe the continuous variables, and percentages were reported for categorical variables. Chi-square test was used to perform univariate analyses of categorical variables whereas Mann-Whitney U test was used to compare continuous variables. Multivariate logistic regression was used to determine if right vs. left lobectomy are significant predictors of dichotomous outcomes (morbidity, mortality, and length of stay>10 days) after adjusting for covariates. Multivariate linear regression was employed to predict minutes of OR time in right vs. left lobectomy after adjusting for covariates. The multivariate model was adjusted for: age, gender, race, smoking status, BMI, Ascites, and CVA without neurological deficits. SAS software was used for the data analysis (SAS Institute Inc., Cary, NC). *p* values of <0.05 were considered significant.

Results

Patient Characteristics

Using the ACS-NSQIP database, 2311 patients who underwent a right or left hepatic lobectomy, between years

2005 and 2010 were extracted. Malignant diagnoses accounted for 73 % ($n=1680$) of the patients. Given the aims of the study, further analysis was limited to patients undergoing hepatic resection for malignant diagnoses only.

Nearly two thirds of all study patients (65 %) underwent right hepatic lobectomy. The mean age for the patients included in the study was 60.4 years. There were no differences in the mean age, BMI, gender distribution, preoperative use of cigarette smoking, alcohol consumption and preoperative weight loss between patients undergoing right or left hepatic lobectomy. Furthermore, the database was also checked for possible colectomy operations, coded as secondary procedures, done concomitantly at the time of liver resection. No differences were found in the incidence of colectomies performed during left or right hepatic lobectomies. Table 1 summarizes the demographic factors for patients undergoing right and left hepatic lobectomy for malignancy.

Preoperative comorbidities were comparable between the two groups with few exceptions. Patients undergoing left hepatic lobectomy had a higher prevalence of ascites preoperatively than those who underwent right hepatic lobectomy (2.18 vs. 0.89 %, $p=0.029$). However, patients undergoing left hepatic lobectomy had fewer episodes of cerebrovascular attacks with no neurological deficits than right hepatic lobectomy patients (0.54 vs. 1.86 % $p=0.033$). In addition, there were no significant differences in the available preoperative laboratory values between the two groups. Tables 2 and 3 summarize the preoperative comorbidities and mean laboratory values for patients undergoing right and left hepatic lobectomy for malignancy.

Perioperative Outcomes

Overall Mortality and Morbidity

The overall 30-day mortality and morbidity for the entire cohort of patients ($n=1680$) who underwent right or left hepatic lobectomy for malignancy was 3.39 % and 32.5 % respectively. Right hepatic lobectomy was associated with significantly higher 30-day mortality when compared to left hepatic lobectomy (4.52 vs. 1.09 % respectively, $p<0.001$). The influence of age on 30-day mortality within the two groups of right and left hepatic lobectomy, was analyzed by dividing the patient's age into quintiles (<50, 51–60, 61–70, 71–80 and >81 year of age) (Fig. 1). For patients undergoing right hepatic lobectomy, increasing age was associated with a significant increase in 30-day mortality (0.5 % for <50 years vs. 17.65 % for patients over 81 years of age, $p<0.001$). In contrast, increasing age was not associated with significant increase in 30-day mortality for patients undergoing left hepatic lobectomy (0.9 % for <50 years versus 1.43 % for >81 years of age, $p=0.968$).

On univariate analysis right hepatic lobectomy was associated with a higher incidence of a) overall morbidity b)

Table 1 Demographic variables for patients undergoing right and left hepatic lobectomy for malignancy

		N=1680		P value
		Right hepatic lobectomy N=1129 %	Left hepatic lobectomy N=551 %	
Age (years)	Mean±SD	60.35 (12.1)	60.77 (13.0)	0.53
Gender	Female	42.55	42.08	0.853
	Male	57.45	57.92	
BMI	Mean±SD	27.86 (5.9)	27.94 (6.2)	0.78
Current smoker within last 1 year	No	84.85	84.21	0.731
	Yes	15.15	15.79	
Alcohol intake>2 drinks per day	No	96.55	95.46	0.276
	Yes	3.45	4.54	
Weight loss>10 % in last 6 months	No	94.6	93.83	0.523
	Yes	5.4	6.17	
Concomitant partial colectomy as secondary procedure	No	98.4	98.7	0.607
	Yes	1.6	1.3	

infectious complications such as organ space infections and sepsis c) respiratory complications such as re-intubation, pulmonary embolism and failure to wean from ventilator lasting>48 h d) renal insufficiency and e) cardiac arrest. Similarly, right hepatic lobectomy was associated with longer operative times and prolonged length of stay. The worse outcomes associated with right hepatic lobectomy maintained significance on multivariate analysis. Tables 4 and 5 summarize the univariate and multivariate analyses of perioperative morbidity and 30-day mortality when comparing right vs. left hepatic lobectomy for malignancy.

Discussion

There are few reports that have performed a thorough analysis of the differences in perioperative outcomes between the right and left hepatectomy in patients undergoing hepatic resection for malignant diagnoses. The few reports published [10–13] are either from single institutions with a small number of patients or included only living donor hepatectomy with healthy livers that does not lend to general applicability. Karanjia et al. [10] compared right and extended right hepatectomy to all other liver resections and did not include a direct comparison between right and left hepatic lobectomy. Similarly the study of Zeyneloglu et al. [11] and Umeshita et al. [12] compared right versus left hepatectomy for living donor liver transplantation in younger and healthy patients which again precludes

generalization to patients with malignancy who often have multiple co-morbidities. This current study however, is a detailed analysis of the differences in perioperative outcomes between right and left hepatic lobectomies in patients undergoing hepatic resection with a specific emphasis only on malignant diagnoses by using the ACS-NSQIP database.

The results of our study demonstrate that right hepatic lobectomy is associated with a statistically significant higher rate of perioperative morbidity and 30-day mortality when compared to left hepatic lobectomy. Additionally, we noted that with increasing age, the 30-day mortality rate continued to rise in patients undergoing right hepatectomy. This age-based gradient effect on worsening 30-day mortality was evident only in patients undergoing right hepatectomy. In patients older than 81 years of age, the mortality after right hepatic lobectomy was found to be 16.75 % when compared to left hepatic lobectomy (1.43 %). These results are consistent with findings of the study by Tzeng et al. [14] which reported a higher mortality rate for patients greater than 75 years of age. Although their study documented a higher mortality rate in elderly patients, they did not perform a direct comparison of detailed perioperative outcomes between right and left hepatic lobectomy. In addition our study also highlighted an age-based gradient negative effect on 30-day mortality.

Patients undergoing right hepatic lobectomy were also noted to have a significantly higher post-operative morbidity rate than those undergoing left hepatic lobectomy. This higher morbidity extended across several systems such as infectious,

Table 2 Comorbidities of patients undergoing right vs. left hepatic lobectomy for malignancy. Statistically significant differences are indicated by asterisks ($P<0.05$)

	N=1680		
	Right N=1129 %	Left N=551 %	P value
General			
Functional status prior to surgery			0.29
Independent	98.32	98.55	
Partially dependent	1.59	1.09	
Totally dependent	0.09	0.36	
ASA classification			0.35
Class 1	0.44	0.73	
Class 2	26.48	23.59	
Class 3	68.2	70.05	
Class 4	4.87	5.44	
Class 5	0	0.18	
Cardiovascular			
CHF<30 days before surgery	0.09	0.36	0.25
MI<6 months before surgery	0	0	
Angina<1 month before surgery	0.44	0.36	1
HTN on meds	48.89	51.72	0.276
Previous percutaneous coronary intervention	4.16	6.17	0.071
Previous cardiac surgery	4.61	4.54	0.95
History of revascularization/amputation for peripheral vascular disease	1.15	1.45	0.603
Endocrine			
Diabetes			0.502
Non insulin dependent	10.72	12.16	
Insulin dependent	6.02	6.9	
Steroid use	1.95	2	0.947
Pulmonary			
COPD	2.66	2.9	0.771
Current pneumonia	0.09	0	1
Ventilator dependence for >48 h prior to surgery	0	0	
Hepatic			
Ascites	0.89	2.18	0.029*
Esophageal varices	0.09	0.54	0.11
Renal			
Acute renal failure	0	0.18	0.33
Dialysis	0.27	0.18	1
Neurological			
Transient ischemic attack	2.48	1.63	0.267
CVA with neurological deficits	1.24	1.09	0.789
CVA without neurological deficits	1.86	0.54	0.033*

pulmonary, renal and cardiovascular system. Right hepatic lobectomy patients in addition experienced a higher re-operation rate and longer length of stay.

Since the current study was a descriptive study of the database, we can only speculate on the potential causes of increased 30-day mortality and morbidity after right hepatic

lobectomy. It is likely that an increase in the rate of infectious, respiratory, renal and cardiac complications seen in patients undergoing right hepatic lobectomy could contribute to the increased mortality. Several other studies have noted the higher rate of pleural effusions, venous thromboembolism in patients undergoing right hepatic lobectomy [15–17].

Table 3 Pre-operative laboratory values of patients undergoing right and left hepatic lobectomy for malignancy

	Right hepatic lobectomy		Left hepatic lobectomy		<i>P</i> value
	Mean	SD	Mean	SD	
Sodium	139.25	2.98	139	2.88	0.066
Blood urea nitrogen	14.76	6.74	15.01	6.5	0.48
Creatinine	0.94	0.5	0.94	0.43	0.38
Albumin	3.95	0.54	3.92	0.55	0.39
Total bilirubin	0.81	1.03	0.76	0.82	0.9
SGOT	42.37	45.3	42.36	47.89	0.91
Hematocrit	39.03	4.62	39.13	4.9	0.72
Platelets	242.05	95.19	245.96	100.07	0.47
PTT	29.44	5.16	29.66	5.44	0.49
INR	1.03	0.12	1.06	0.43	0.15
PT	12.52	2.49	12.62	2.41	0.49

Furthermore, it is known that morbidity and mortality after hepatic resection for malignancy is strongly associated with volume of the future liver remnant [18]. It is likely that the smaller future liver remnant following right hepatic lobectomy contributes to the worse perioperative outcomes as echoed by many other studies involving living donors undergoing right hepatectomies [13, 19, 20]. Given the limitations of the ACS-NSQIP database we could not factor in the details on the size of future liver remnant or rates of post-hepatectomy liver failure. In addition it has been shown that longer operating time incrementally increases multisystem morbidity, as well as mortality, with an effect more noticeable in the elderly population as seen in a study of 7696 major surgical procedures [21]. Similar to the published literature, we also noted that right hepatic lobectomy was associated with longer operative times which could contribute to the worse outcomes in our study.

The difference in outcomes between right and left hepatic lobectomy can have a significant bearing on several aspects of our clinical practice. An important aspect relates to obtaining consent for hepatic resections. In our discussions with the patients we generally quote the acceptable mortality rate of low-single digits for any type of lobectomy regardless of the laterality and age. The findings of our study suggest that quoting a uniform blanket mortality rate does not reflect the true mortality rates for the two operations, particularly in elderly patients. Instead, in our discussions with our patients we should highlight the differences in mortality and morbidity based on the laterality of hepatic lobectomy and age. However, these findings need to be validated in other studies.

There are several strengths associated with this study. The data analyzed in this report includes a large number of patients derived from several hospitals across the nation, which attests to the generalizability of the study findings. A large database

Fig. 1 Representation of the 30-day mortality of right and left hepatic lobectomy across different age categories

Table 4 Univariate analysis of post-operative outcomes in right vs left hepatic lobectomy. Statistically significant differences are indicated by asterisks ($P<0.05$)

	<i>N</i> =1680 %	Right hepatic lobectomy <i>N</i> =1129 %	Left hepatic lobectomy <i>N</i> =551 %	<i>P</i> value
Superficial surgical site infection	4.76	5.14	3.99	0.301
Deep incisional surgical site infection	0.6	0.8	0.18	0.124
Organ space infection	7.08	8.15	4.9	0.015*
Wound disruption/dehiscence	1.01	1.15	0.73	0.413
Pneumonia	5.24	5.67	4.36	0.257
Unplanned reintubation	5.24	6.02	3.63	0.039*
PE/DVT	3.69	4.34	2.36	0.043*
Failure to wean the ventilator (>48 h)	6.01	7.17	3.63	0.0041*
Renal insufficiency	3.87	5.14	1.27	0.0001*
Urinary tract infection	3.93	4.43	2.9	0.131
Stroke/CVA with neurological deficit	0.48	0.62	0.18	0.29
Coma>24 h	0.48	0.53	0.36	1
Peripheral nerve injury	0.18	0.27	0	0.56
Cardiac arrest requiring CPR	1.73	2.3	0.54	0.0094*
Myocardial infarction	0.42	0.53	0.18	0.44
Bleeding/transfusions	8.04	8.77	6.53	0.114
Graft/prosthesis failure	0.06	0	0.18	0.33
Sepsis	6.55	7.97	3.63	0.0007*
Return to OR	5.42	5.93	4.36	0.18
30 day mortality	3.39	4.52	1.09	0.0003*
Total morbidity	32.5	36.49	24.32	<0.0001*
Median (range) OR time, minutes	256 (36–881)	263 (65–881)	244 (36–875)	0.003*
Hospital stay>10 days	18.84	21.31	13.79	0.0002*

such as that of NSQIP, which takes into account more than 400 academic and non-academic institutions, provides the

benefit of obtaining a more generalizable understanding of national outcomes of hepatectomies rather than looking at

Table 5 Multivariate analysis of post-operative outcomes in right vs left hepatic lobectomy. Statistically significant differences are indicated by asterisks ($P<0.05$)

		OR	95 % confidence interval		<i>P</i> value ^a
			Lower	Upper	
Organ space surgical site infection	Right vs. left hepatic lobectomy	1.73	1.11	2.69	0.016*
Unplanned reintubation	Right vs. left hepatic lobectomy	1.79	1.07	3.00	0.027*
PE/DVT	Right vs. left hepatic lobectomy	1.82	0.98	3.41	0.06
Failure to wean the ventilator (>48 h)	Right vs. left hepatic lobectomy	2.19	1.32	3.65	0.0026*
Renal insufficiency	Right vs. left hepatic lobectomy	4.70	2.09	10.58	0.0002*
Cardiac arrest requiring CPR	Right vs. left hepatic lobectomy	4.77	1.42	15.96	0.011*
Sepsis	Right vs. left hepatic lobectomy	2.59	1.55	4.32	0.0003*
30 day mortality	Right vs. left hepatic lobectomy	4.55	1.92	10.75	0.0006*
Total morbidity	Right vs. left hepatic lobectomy	1.83	1.45	2.31	<0.0001*
Hospital stay>10 days	Right vs. left hepatic lobectomy	1.88	1.41	2.52	<0.0001*
			95 % CI	95 % CI	
		<i>β</i> estimate	Lower	Upper	<i>P</i> value ^a
OR time, minutes	Right vs. left hepatic lobectomy	18.25	7.81	28.69	0.0006*

^a Adjusted for: age, gender, race, smoking status, BMI, Ascites, CVA without neuro deficits

outcomes from single institutional reports which may not be as representative. Secondly, patients in the groups of right and left hepatic lobectomy were evenly matched for demographics, general variables, functional status, pre-operative co-morbidities and pre-operative laboratory values specific for hepatic and renal function. Finally, the overall 30-day mortality and morbidity rate noted for the entire cohort of patients was 3.12 and 32.11 % respectively, which is congruent with the currently accepted standards and similar to other seminal published reports [6, 22, 23]. This similarity in the rates of mortality and morbidity attests to the robustness of the included data, which thereby adds strength to the conclusions derived from this study.

A study of this kind that utilizes a national database has several limitations. The study does not include data on the specific type of malignant diagnosis or extent of disease such a tumor burden etc. The current study does not include any information on pre-operative chemotherapy, which can have an influence on perioperative outcomes following hepatic resection for malignancy. Although we were able to control for some of the pre-operative laboratory values that signify hepatic and renal function, crucial information on the size of future liver remnant was not available for inclusion. It is also likely that some left lateral hepatectomies may have been miscoded as left hepatic lobectomy contributing to the better outcomes. Nonetheless, since NSQIP is a surgical database that is maintained by surgeons with an institutional surgical champion the errors should be minimal. Lastly, we were unable to analyze the influence of the type of operative approach (open, laparoscopic or robotic) on perioperative outcomes.

In summary, the results of our study demonstrate that patients undergoing right hepatic lobectomy for a malignant diagnosis have significantly worse outcomes when compared to left hepatic lobectomy. This includes a significantly higher mortality rate, which is worse in the elderly. Patients undergoing right hepatic lobectomy are also noted to have a higher post-operative morbidity rates that affect several systems. These findings need to be validated in other studies. Efforts directed at improving outcomes and controlling costs in patients undergoing hepatic resections for malignancy need to be cognizant of this vital information.

ACS-NSQIP Disclosure Statement The American College of Surgeons National Surgical Quality Improvement Program and the hospitals participating in the ACS NSQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

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