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Borderline Operability in Hepatectomy Patients Is Associated with Higher Rates of Failure to Rescue after Severe Complications

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Abstract

Introduction: To understand the influence of age and comorbidities, this study analyzed the incidence and risk factors for post-hepatectomy morbidity/mortality in patients with "borderline" (BL) operability, defined as age≥75, dependent function, lung disease, ascites/varices, myocardial infarction, stroke, steroids, weight loss>10%, and/or sepsis.

Methods: All elective hepatectomies were identified in the 2005–13 ACS-NSQIP database. Predictors of 30-day morbidity/mortality in BL patients were analyzed.

Results: 3,574/15,920 (22.4%) patients met BL criteria. Despite non-BL and BL patients undergoing similar magnitude hepatectomies ($p>0.4$), BL patients had higher severe complication (SC, 23.3% vs. 15.3%) and mortality rates (3.7% vs. 1.2%, $p<0.001$). BL patients with any SC experienced a 14.1% mortality rate (vs. 7.3%, non-BL, $p<0.001$). The mortality disparity was more pronounced with ≥2 and ≥3 SC (24.6% vs. 14.1%; 34.4% vs. 23.4%, $p<0.001$). Independent risk factors for SC in BL patients included anesthesia score>3 (odds ratio, OR-1.29), smoking (OR-1.41), albumin<3.5g/dL (OR-1.36), bilirubin >1 (OR-2.21), operative time>240min (OR-1.58), additional colorectal procedure (OR-1.78), and concurrent procedure (OR-1.73, all $p<0.05$). Independent predictors of mortality included disseminated cancer (OR-0.44), albumin<3.5g/dL (OR-1.94), thrombocytopenia (OR-1.95), and extended/right hepatectomy (OR-2.81, all $p<0.01$).

Conclusions: Hepatectomy patients meeting BL criteria have an overall post-hepatectomy mortality rate that is triple that of non-BL patients. With less clinical reserve, BL patients who suffer SC are at greater risk of post-hepatectomy death, reflecting their low tolerance for

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physiologic insults. To improve outcomes, hepatobiliary surgeons should emphasize the preoperative identification of BL operable patients in order to optimize modifiable medical risk factors and to choose appropriate magnitude operations.

Keywords

Comorbidity; Surgical Outcomes; Patient Selection

INTRODUCTION

Over the past 2–3 decades, liver surgery has become significantly safer due to improved patient selection,[1–3] optimization of preoperative risk factors (anatomic[4] and physiologic[5,6]), advanced surgical techniques,[7,8] parenchyma-sparing operations,[9–14] targeted perioperative care,[15] personalized treatment sequencing,[16–19] and modern strategies for clinical rescue after complications.[1,20–22] With these advances, surgeons are pushing the envelope and expanding the limits of both technical resectability[22] and medical operability,[2] thus offering surgery to medically borderline (BL) patients who likely would not have been offered surgery prior to the contemporary era.[23]

BL operability has been previously described by the current authors in the context of pancreatic surgery.[24] Within this context, the population of BL patients defined as a subset of patients who have modifiable comorbidities (with exception of age), which can be targeted for intervention before a hepatectomy. These surgical risk factors can be addressed with medical optimization, immunonutrition programs, and formal prehabilitation, before a hepatectomy to potentially prevent morbidity and improve the failure to rescue rate in BL patients.

This study hypothesized that BL patients are at greater risk for post-hepatectomy morbidity/mortality compared to their non-BL counter parts. To address this question, the current study analyzed the national rates of post-hepatectomy morbidity/mortality in the growing cohort of BL patients from the most recent version of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database. Furthermore, the relationship between BL status and ability/failure to rescue these patients after major morbidity was examined. Within this context, the primary aim was to identify risk factors for severe complications and mortality in order to find potentially modifiable risk factors in the borderline patient population undergoing hepatectomy.

PATIENTS AND METHODS

Patients and data collection

From the 2005–2013 NSQIP participant use file, all hepatectomy procedures were initially extracted. Emergency operations and wedge biopsies (current procedural terminology [CPT] code 47100) were eliminated to focus on elective and substantive liver resections. The extent of hepatectomy was classified by the primary CPT code and included the following liver resections by order of increasing magnitude: partial (CPT 47120), left (47125), right (47130), and extended (47122) hepatectomies. The patients with the following preoperative conditions were excluded in order to select a population the authors felt could reasonably undergo elective surgery under non-urgent circumstances: ventilator dependence, coma, altered mental status, congestive heart failure in the past month, peripheral vascular disease with rest pain or requiring operation, dialysis or current acute renal failure, bleeding disorder, angina in past month, and dyspnea at rest. Risk factors for major morbidity/mortality were derived from analyses of NSQIP-collected perioperative clinical factors, as previously described.[1,2,25,26]

Preoperative variables assessed included age, sex, race, weight, body mass index, hematocrit, platelet count, white blood cell count, partial thrombin time, international normalized ratio, blood urea nitrogen, creatinine, albumin, aspartate aminotransferase, alkaline phosphatase, bilirubin, independent function, American Society of Anesthesiologists (ASA) class, chronic obstructive pulmonary disease (COPD), smoking, pneumonia, sepsis, disseminated cancer, diabetes, ascites, previous operation within 30 days, preoperative hospitalization, preoperative chemotherapy, and preoperative radiation therapy.

Intraoperative variables included extent of hepatectomy, operative time, concurrent major operation, and radiofrequency ablation. Concurrent major operations included gastrointestinal resection/anastomosis, biliary resection/reconstruction, thoracic operation, and ventral hernia repair. Concurrent major operations excluded cholecystectomy, lymphadenectomy, vena cava repair, diaphragm repair, and diagnostic laparoscopy.[2]

Postoperative variables included any venous thromboembolism (VTE, deep vein thrombosis and/or pulmonary embolus),[25,26] renal insufficiency/failure, respiratory failure, return to operating room (ROR), cardiac arrest, stroke, coma, myocardial infarction, postoperative sepsis/septic shock, pneumonia, surgical site infection, organ space infection (OSI), fascial dehiscence, length of stay, and 30-day mortality (or death during first hospitalization if longer than 30 days).

Definitions

"Borderline operable" patients were defined as those with any of the following preoperative conditions: age ≥75 years, lack of functional independence (as defined by NSQIP), chronic obstructive pulmonary disease, ascites/varices, myocardial infarction in last 6 months, stroke or TIA history, steroid use in last 30 days, weight loss >10% in last 6 months, and preoperative sepsis or systemic inflammatory response syndrome. These variables (with exception of age) were chosen because they have the potential to be optimized, based on previous work in the preoperative assessment of patients undergoing pancreatic surgery.[24,27] The age cutoff was based on past NSQIP studies on older cancer surgery patients.[2,28,29] Post-hepatectomy severe complications included the following NSQIP occurrences: OSI, ROR, dehiscence, re-intubation, ventilator dependence or failure to wean >48 hours, acute renal insufficiency or failure, stroke or coma, cardiac arrest or myocardial infarction, VTE, sepsis or septic shock, and pneumonia. In accordance with the NSQIP definition, postoperative mortality was defined as death within 30 days of surgery or death during first hospitalization if longer than 30 days.

Statistical analysis

The association between pre- and intra-operative risk factors (BL operability, comorbidities, and extent of resection) and morbidity/mortality were compared. Mann-Whitney U-tests were used for comparison of nonparametric continuous data. Chi-squared test or Fisher's exact test were used for comparison of nonparametric categorical data. After univariate analysis, significant risk factors (p<0.05 and >1% of all patients) were entered into a multivariate logistic regression model to determine independent associations with morbidity/mortality. Statistical analyses were performed using SPSS Statistics 21 (IBM, Armonk, NY). All tests were two-sided. Multivariate statistical significance was defined as p<0.05.

RESULTS

Patients, age distribution, comorbidities, and extent of hepatectomy

BL operable patients represented 22.5% (n=3574) of the 15,920 patients who met inclusion criteria. This population was more likely to have the following comorbidities: diabetes, medical hypertension, elevated bilirubin, elevated INR, elevated white blood cell count, dyspnea on exertion, cardiac disease, hypoalbuminemia, hematocrit < 39%, uremia, elevated creatinine, thrombocytopenia, and ASA class ≥3 (Table 1). Across all extents of hepatectomy, there was no statistical difference in the proportions of non-BL vs. BL patients undergoing resection. From 2005–2013, there was no statistical difference in the proportion of patients who met BL criteria (2010=22.5%, 2011=21.4%, 2012=22.8%, and 2013=20.8%; p=0.078).

Post-hepatectomy major morbidity

Despite undergoing hepatectomies of similar anatomic magnitude, BL patients more frequently experienced severe complications across all extents of hepatectomy (Figure 1A). Severe complication rates were strongly associated with the magnitude of hepatectomy in BL patients [33.9% (113/333) for extended, 32.2% (217/674) for right, 24.7% (99/401) for left, and 18.6% (402/2166) for partial hepatectomies, Figure 1A]. The univariate analysis of risk factors associated with severe complications among BL patients is detailed in Table 2. In multivariate analysis, risk factors independently associated with severe complications included both preoperative and intraoperative risk factors: ASA class >3 (odds ratio, OR, 1.30, 95% confidence interval, CI, 1.03–1.63, p=0.026), smoking (OR 1.41, 95% CI 1.14–1.75, p=0.002), albumin <3.5g/dL (OR 1.36, 95% CI 1.11–1.67, p=0.003), operative time >240 min (OR 1.58, 95% CI 1.33–1.89, p=0.001), concurrent colorectal procedure (OR 1.78, 95% CI 1.10–2.87, p=0.019), and major concurrent abdominal operation (OR 1.73, 1.25–2.39, p<0.001).

Post-hepatectomy mortality

The overall (both BL and non-BL) post-hepatectomy mortality rate was 1.8%, which correlated with the magnitude of hepatectomy (extended, 4.2%, 62/1,467; right, 3.0%, 93/3,052; left, 1.1%, 19/1,673; and partial, 1.1%, 106/9,728; p<0.001). BL patients experienced a higher overall 30-day mortality rate (3.7%, 132/3,574 vs. 1.2%, 148/12,346 in non-BL, p<0.001, Figure 1B) and worse mortality rates at each extent of hepatectomy. The mortality rate difference was most pronounced after extended (7.5%, 25/333, vs. 3.3%, 37/1,134) and right (6.8%, 46/674, vs. 2.0%, 47/2,378) hepatectomies (p<0.001, Figure 1B). The univariate analysis of risk factors associated with mortality among BL patients is listed in Table 3. Independently associated risk factors for mortality among BL patients identified in multivariate analysis included the following preoperative and intraoperative variables (all potentially modifiable): albumin <3.5 g/dL (OR 1.94, 95% CI 1.31–2.86, p=0.001), platelets <150,000/μL (OR 1.95, 95% CI 1.25–3.42, p=0.003), bilirubin >1.0 mg/dL (OR 2.21, 95% CI 1.47–3.34,p<0.001), ASA ≥4 (OR 1.84, 95% CI 1.10–3.08, p=0.02), disseminated cancer (OR 0.44, 95% CI 0.28–0.70, p<0.001), and magnitude of anatomic resection (extended/right vs. left/partial, OR 2.81, 95% CI 1.93–4.08, p<0.001).

Failure to rescue: mortality after severe complications

Having at least one severe complication was associated with a 14.1% (117/831) mortality rate in BL patients vs. 7.3% (137/1884) in non-BL patients (p<0.001, Figure 2). Of the 831 BL patients who suffered at least one severe complication, 51.9% (431/831) experienced a second and 27.3% (227/831) experienced a third. Those who experienced this cascade were least likely to be rescued. To emphasize the downward spiral that often led to death, the mortality rate for 1 SC= 14.1% (117/831), 2 SC=24.6% (106/431), and ≥3 SC=34.4% (78/227) in BL patients (Figure 2). Mortality rates were at least 7 absolute percentage points greater in BL vs. non-BL patients at each level of SC (e.g. 34.4% (78/227) vs. 23.4% (93/398), with ≥3 severe complications, p=0.004).

DISCUSSION

This analysis of a multi-institutional sample of hepatectomy patients was able to define a cohort of patients who were considered to have BL operability, irrespective of their anatomic tumor resectability. The finding that 22.4% of patients met the BL operability definition indicates that a substantial number of patients can be identified as high-risk prior to surgery. The study also defined the magnitude of risk engendered by the BL status. The results determined that BL patients experienced significantly more SC at each magnitude of hepatectomy and triple the 30-day mortality rate of non-BL patients, indicating that an inability to rescue these patients after a severe complication was responsible for the significantly higher mortality rate.

When reviewing overall outcomes that group all types of patients and all extents of resection, the “safety” of liver surgery can be overestimated. While it is true that 30-day mortality rates have been reduced to 1% or less at major academic centers and 1.8% among the 2005–2013 NSQIP patients, this national database analysis reveals that mortality rates remain high for a right hepatectomy (3.0%) and for extended hepatectomy (4.2%). In BL patients undergoing a major hepatectomy, the mortality rates double those of the whole population at 6.8% for right hepatectomy and 7.5% for extended hepatectomy.

The finding that there was no difference in surgical magnitude between BL and healthier patients, despite the availability of the BL criteria data in the preoperative setting, suggests that surgeons are not currently using these data to modify operative planning. Given that the BL patients were older and had a greater number of baseline comorbidities, it appears that there is an opportunity to improve outcomes with better patient selection, more specific preoperative optimization, and modulation of surgical approach and extent.[2] With regard to prehabilitation, the positive impact of these programs has been well demonstrated in pancreatic cancer surgery patients receiving multi-modality therapy.[24,27] Prehabilitation programs can address advanced ASA class, smoking, and hypoalbuminemia with smoking cessation, nutritional support, and physiologic conditioning. With over 85% of elective liver resections in the NSQIP sample being done for malignancies,[2] most cancer surgeons will acknowledge that a short delay to optimize comorbidities is unlikely to affect long-term oncologic outcomes. The greater risk comes from rushing into surgery and having severe complications which hinder *return to intended oncologic therapy* (RIOT).[31] Either through an inability to RIOT, or other immunologic mechanisms, postoperative complications have clearly been shown to decrease survival after abdominal cancer resections.[32–34] Based on this paradigm, to the extent that the disease process allows, preoperative outpatient nutritional support and medical optimization are likely to reduce complications and prolong cancer-specific survivals.[35,36]

Severe complication and mortality rates have been correlated with the magnitude of operation and its covariates including transfusions, longer operations, combination procedures, and major anatomic resections. The data from this study suggest that longer and more complex (including combination) procedures raise the risk of severe complications and death for BL patients. For example, BL patients who underwent combination liver/colorectal operations had a 44.4% (55/124) rate of severe complications. These data offer a “reality check” in regard to the significantly increased risk of severe complications and failure to rescue faced by BL patients, particularly those undergoing extensive hepatic resections. By using creative treatment sequencing,[16,18,19,37] avoiding synchronous gastrointestinal tract resections,[17,38] limiting chemotherapy-associated liver injury,[5,39] maximizing future liver remnant,[40–42] and performing parenchyma-sparing resections,[7,8] surgeons can limit the anatomic magnitude and physiologic sequelae of hepatectomy in BL patients, potentially improving on an otherwise unacceptable risk/benefit ratio for a particular patient needing a hepatectomy.

The last point to emphasize is the alarmingly high rate of failure to rescue in BL patients. The rate of failure to rescue rose steeply with the additive burden of severe complications, with mortality rates of 14.1%, 24.6%, and 34.4%, after ≥1, ≥2, and ≥3 severe complications, respectively. When evaluating patients with increasing number of severe complications, BL patients’ rates of failure to rescue were equivalent to that of non-BL patients with one less complication (Figure 2). In other words, BL patients enter the operating room with one strike against them and, therefore, have less clinical reserve to recover from physiologic insults. Furthermore, they are more susceptible to having adverse events postoperatively. This emphasizes the significance of preoperative patient selection (and identification of who is medically BL), medical optimization, and choosing operations of lesser magnitude when oncologically appropriate. Vigilance in the postoperative course should be aimed at preventing severe complications and watching for any early signs to mitigate the complication cascade once a severe complication develops.[43]

The intent of this study is not to discourage surgeons from operating on patients who meet this study's BL operability definition. With the population aging, BL patients will constitute an increasingly larger proportion of patients being referred for hepatectomy.[23],[44] Preventive strategies to identify and remedy the comorbid conditions that define the BL criteria are needed to address this increasing demand for complex procedures.[40]

Basing this analysis on the NSQIP database has both strengths and weaknesses.[45] Although not tailored for liver surgery, NSQIP-recorded variables were effective for this study's extensive analysis of morbidity/mortality in BL hepatectomy patients. Due to its large scale and inclusion of the most recent available data (n=15,920 patients) this dataset facilitated a detailed analysis of morbidity/mortality predictors unavailable in single-institution studies.[46–48] While single-institution studies have more granular data, their results are biased toward well-published academic medical centers, which may not be applicable to national practice. Additionally, NSQIP data does not record occurrences after 30 days. Evidence in cancer surgery literature indicates that 90-day morbidity/mortality is more reflective of the true sequelae after oncologic resections. For example, as many as one-third of deaths from postoperative hepatic insufficiency occur after 30 days.[39] In addition, NSQIP does not record data on cancer-specific or overall survival, making an analysis of the potential overall benefit to patients from hepatectomy as an oncologic treatment impossible. Nonetheless, the NSQIP database facilitated a realistic view of nationwide trends, including the fact that BL patients comprise greater than one-fifth of hepatectomy patients.

In conclusion, BL operable patients have an overall post-hepatectomy mortality rate that is triple that of non-BL patients. With less clinical reserve, BL patients who suffer severe complications are at greater risk of post-hepatectomy death, reflecting their low tolerance for physiologic insults. To improve surgical outcomes, hepatobiliary surgeons should emphasize the preoperative identification of BL operable patients in order to optimize modifiable medical risk factors and to choose appropriate magnitude operations.

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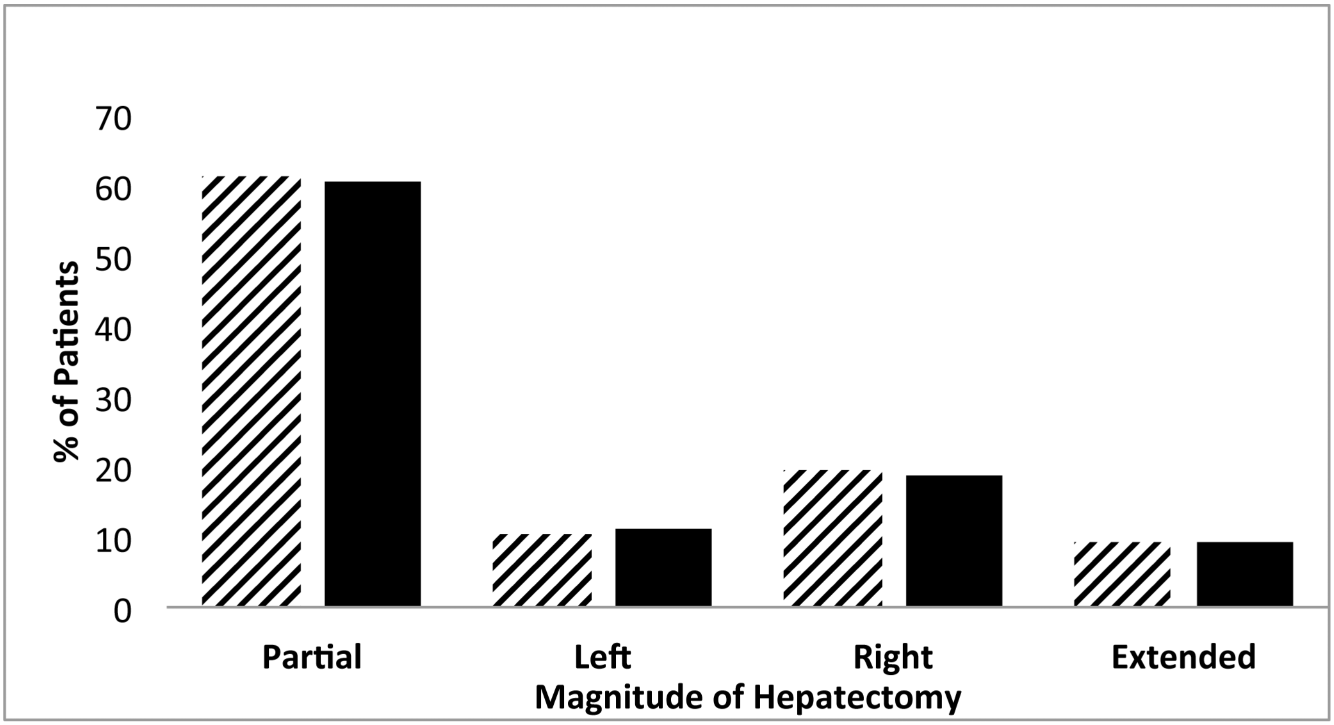

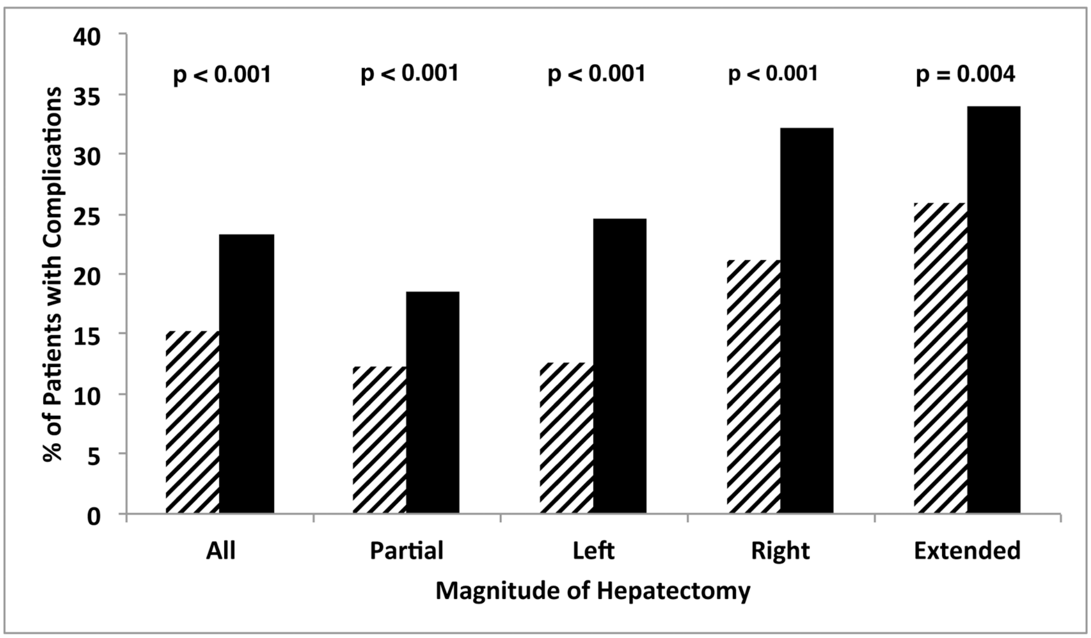

Figure 1.

Comparison of magnitude of hepatectomy, borderline status, morbidity (A) and mortality (B) demonstrates that rates of severe complications and death increased with magnitude of hepatectomy and were significantly worse in borderline patients for each extent of hepatectomy.

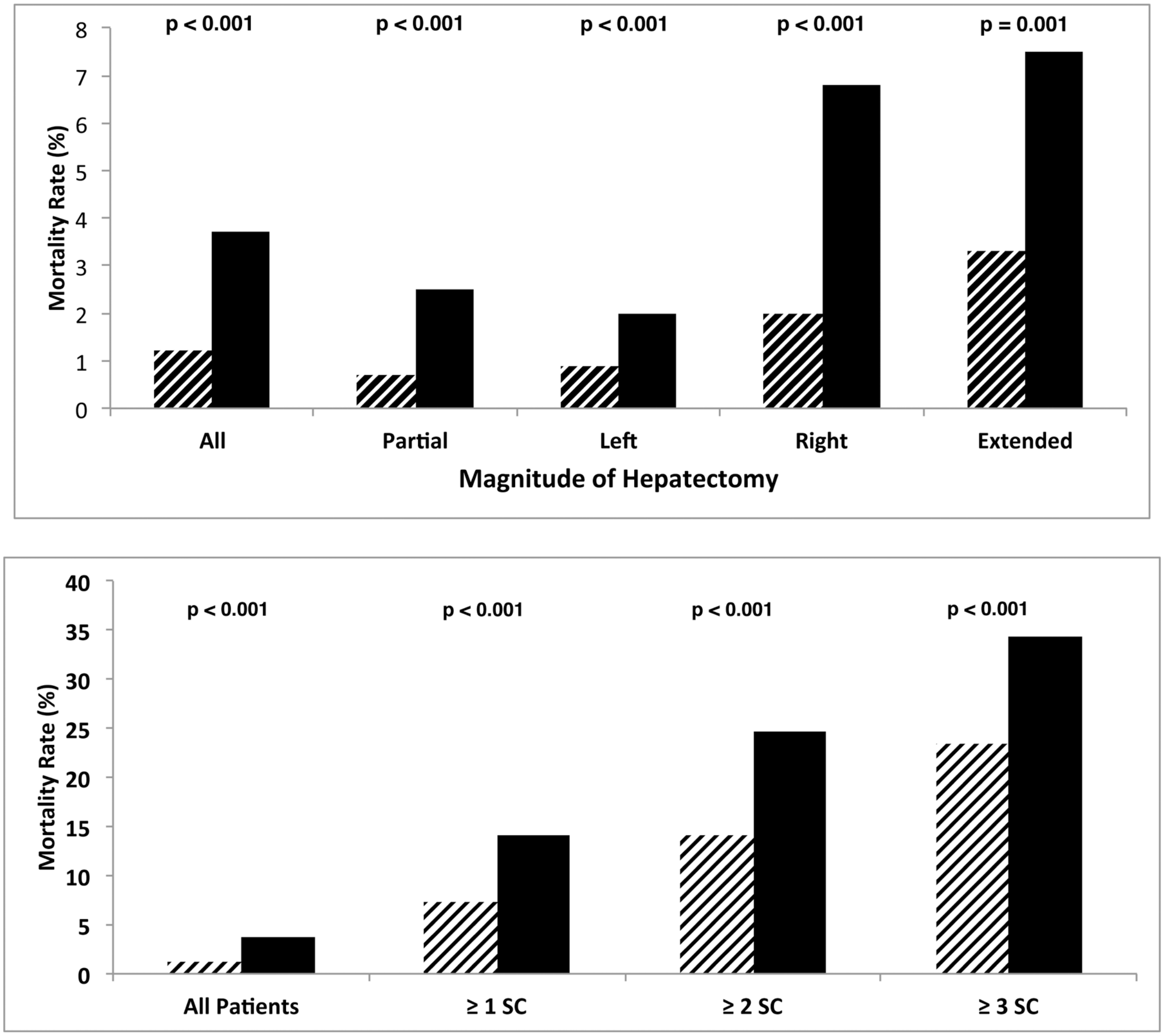

Figure 2.

Comparison of number of severe complications, mortality and borderline status demonstrates that rates of failure to rescue worsen with increasing cascade (number) of severe complications. At each extent of hepatectomy, borderline patients were more susceptible to postoperative death after severe complication(s).

Table 1.

Differences Between Borderline and Non-Borderline Operable Patients

	All Patients (n=15920)		Non-Borderline Operable		Borderline Operable		
Clinical Characteristic	**n or median**	**% or range**	**n or median**	**% or range**	**n or median**	**% or range**	***P***
n	15920	100%	12346	77.6 %	3574	22.4%	
Preoperative factors							
Age	60	17–90	57	18–74	74	17–90	**<0.001**
Gender, male	7582	47.6%	5677	46.0%	1905	53.3%	**<0.001**
BMI ≥30 kg/m^2	5057	31.8%	4110	33.3%	947	26.5%	**<0.001**
Diabetes	2470	15.5%	1718	13.9%	752	21.0%	**<0.001**
Dyspnea on exertion	1095	6.9%	659	5.3%	436	12.2%	**<0.001**
Previous coronary stent	333	2.1%	187	1.5%	146	4.1%	**<0.001**
Previous cardiac surgery	289	1.8%	153	1.2%	136	3.8%	**<0.001**
Medical hypertension	7352	46.2%	5165	41.8%	2187	61.2%	**<0.001**
Albumin <3.5 g/dL	1910	12.0%	1166	9.4%	744	20.8%	**<0.001**
Alkaline phosphatase >93IU/L	6814	42.8%	5128	41.5%	1686	47.2%	**<0.001**
AST ≥30 IU/L	6039	37.9%	4617	37.4%	1422	39.8%	**0.009**
Bilirubin >1 mg/dL	1734	10.9%	1249	10.1%	485	13.6%	**<0.001**
Sodium <135 mEq/L	1403	8.8%	986	8.0%	417	11.7%	**<0.001**
White blood cells >11,000/µL	862	5.4%	564	4.6%	298	8.3%	**<0.001**
INR >1	5627	35.3%	4050	32.8%	1577	44.1%	**<0.001**
PTT >29 sec	5342	33.6%	4078	33.0%	1264	35.4%	**0.009**
Hematocrit<39	7601	47.7%	5628	45.6%	1973	55.2%	**<0.001**
BUN ≥20 mg/dL	2404	15.1%	1535	12.4%	869	24.3%	**<0.001**
Creatinine >1.3mg/dL	779	4.9%	462	3.7%	317	8.9%	**<0.001**
Platelets <150,000/µL	1968	12.4%	1466	11.9%	502	14.0%	**0.001**
Chemotherapy within 30d	934	5.9%	762	6.2%	172	4.8%	**0.002**
ASA class ≥3	10888	68.4%	7993	64.7%	2895	81.0%	**<0.001**
ASA class ≥4	692	4.3%	409	3.3%	283	7.9%	**<0.001**
Admitted ≥1day before operation	1154	7.2%	705	5.7%	449	12.6%	**<0.001**
Intraoperative							
Operative time, min	222	7–1045	223	7–1045	217	19–1029	0.178
Operative time >240 min	6910	43.4%	5405	43.8%	1505	42.1%	0.076
Extent of hepatectomy							0.441
Partial	9728	61.1%	7562	61.3%	2166	60.6%	
Left	1673	10.5%	1272	10.3%	401	11.2%	
Right	3052	19.2%	2378	19.3%	674	18.9%	
Extended	1467	9.2%	1134	9.2%	333	9.3%	
Partial vs. Left/Right/Extended	9728	61.1%	7562	61.3%	2166	60.6%	
Right/Extended vs. Left/Partial							0.752
Right/Extended	4159	28.4%	3512	28.4%	1007	28.2%	
Left/Partial	11401	71.6%	8834	71.6%	2567	71.8%	

	All Patients (n=15920)		**Non-Borderline Operable**		**Borderline Operable**		
Clinical Characteristic	**n or median**	**% or range**	**n or median**	**% or range**	**n or median**	**% or range**	***P***
Biliary repair/reconstruction	772	4.8%	531	4.3%	241	6.7%	**<0.001**
Another abdominal organ	2073	13.0%	1515	12.3%	558	15.6%	**<0.001**
Postoperative							
Postoperative pneumonia	448	2.8%	277	2.2%	171	4.8%	**<0.001**
Reintubation	477	3.0%	278	2.3%	199	5.6%	**<0.001**
Ventilator >48hrs	489	3.1%	289	2.3%	202	5.7%	**<0.001**
Stroke	50	0.3%	30	0.2%	20	0.6%	**0.003**
Renal insufficiency/Failure	305	1.9%	211	1.7%	94	2.6%	**<0.001**
Urinary tract infection	516	3.2%	368	3.0%	148	4.1%	**0.001**
Cardiac arrest	125	0.8%	74	0.6%	51	1.4%	**<0.001**
Myocardial infarction	75	0.5%	36	0.3%	39	1.1%	**<0.001**
Sepsis	805	5.1%	572	4.6%	233	6.5%	**<0.001**
Septic shock	292	1.8%	168	1.4%	124	3.5%	**<0.001**
Return to OR (ROR)	603	3.8%	419	3.4%	184	5.1%	**<0.001**
Deep SSI or dehiscence	269	1.7%	184	1.5%	85	2.4%	**0.079**
Dehiscence	125	0.8%	86	0.7%	39	1.1%	**0.019**
VTE (DVT and/or PE)	421	2.6%	306	2.5%	115	3.2%	**0.015**
Any severe complication	**2715**	**17.1%**	**1884**	**15.3%**	**831**	**23.3%**	**<0.001**
Postop LOS, days (IQ Range)	6	(4–8)	6	(4–7)	6	(5–9)	**<0.001**
Death within 30 days	280	1.8%	148	1.2%	132	3.7%	**<0.001**

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; OR, operating room; SSI, surgical site infection; LOS, length of stay; PVD peripheral vascular disease

Not significant: race, smoker, alcohol use, radiation or operation in preceding 30 days, chief resident involvement; simultaneous colorectal operation, additional RFA, any SSI or wound disruption, organ space infection

Not analyzed in the univariate analysis because <0.9% total cases: preoperative open wound, postoperative coma

Table 2.

Factors Associated with Severe Complications in Borderline Operable Patients

	All Borderline Patients		No Severe Complications		Severe Complications		
Clinical Characteristic	**n or median**	**% or range**	**n or median**	**% or range**	**n or median**	**% or range**	***P***
n	3574	100%	2743	76.7%	831	23.3%	
Preoperative factors							
Gender, male	1905	53.3%	1416	50.7%	489	58.8%	**<0.001**
Diabetes	752	21.0%	559	20.0%	193	24.7%	**0.078**
Smoker	574	16.1%	409	14.6%	165	21.1%	**0.001**
Previous cardiac surgery	136	3.8%	94	3.4%	42	5.4%	**0.087**
Albumin <3.5 g/dL	744	20.8%	490	17.5%	254	32.5%	**<0.001**
Alkaline phosphatase >93 IU/L	1686	47.2%	1207	43.2%	479	61.3%	**<0.001**
AST ≥30 IU/L	1422	39.8%	1038	37.2%	384	49.2%	**<0.001**
Bilirubin >1 mg/dL	485	13.6%	328	11.7%	157	20.1%	**<0.001**
INR >1	1577	44.1%	1144	41.0%	433	55.4%	**<0.001**
PTT >29 sec	1264	35.4%	906	32.4%	358	45.8%	**<0.001**
Hematocrit <39%	1973	55.2%	1455	52.1%	518	66.3%	**<0.001**
Open wound	49	1.4%	29	1.0%	20	2.6%	**0.003**
ASA class ≥3	2895	81.0%	2187	78.3%	708	90.7%	**<0.001**
Admitted ≥1day before operation	449	12.6%	292	10.5%	157	20.1%	**<0.001**
Intraoperative							
Operative time, min	217	19–1029	205	19–869	270	25–1029	**<0.001**
Operative time >240 min	1505	42.1%	1022	36.6%	483	61.8%	**<0.001**
Extent of hepatectomy							**<0.001**
Partial	2166	60.6%	1764	63.2%	402	51.5%	
Left	401	11.2%	302	10.8%	99	12.7%	
Right	674	18.9%	457	16.4%	217	27.8%	
Extended	333	9.3%	220	7.9%	113	14.5%	
Partial vs. Left/Right/Extended	2166	60.6%	1764	63.2%	402	51.5%	**<0.001**
Right/Extended vs. Left/Partial							**<0.001**
Right/Extended	1007	28.2%	677	24.2%	330	42.3%	
Left/Partial	2567	71.8%	2066	74.0%	501	64.1%	
Biliary repair/reconstruction	241	6.7%	119	4.3%	122	15.6%	**<0.001**
Colorectal operation	124	3.5%	69	2.5%	55	7.0%	**<0.001**
Another major abdominal operation	558	15.6%	317	11.3%	241	29.0%	**<0.001**
Postoperative							
Postoperative LOS, days (IQ Range)	6	(5–9)	6	(4–9)	11	(7–19)	**<0.001**
Death within 30 days	**132**	**3.7%**	**15**	**0.5%**	**117**	**15.0%**	**<0.001**

Abbreviations: AST, aspartate aminotransferase; INR, international normalized ratio; PTT, partial thrombin time; ASA, American Society of Anesthesiologists; LOS, length of stay

Not significant: age, race, year of operation, body mass index, alcohol use, previous coronary stent/angioplasty, medical hypertension, disseminated cancer, chemotherapy within 30 days, radiation therapy within 90 days, sodium, blood urea nitrogen, creatinine, platelets, white blood cells, operation in preceding 30 days

Table 3.

Factors Associated with Post-Hepatectomy Death in Borderline Patients

	All Borderline Patients		No Death in 30 days		Postoperative Death (30 days)		
Clinical Characteristic	**n or median**	**% or range**	**n or median**	**%**	**n or median**	**% or range**	***P***
n	3574	100%	3442	96.3%	132	3.7%	
Preoperative factors							
Age	74	17–90	74	17–90	76	29–90	**0.830**
Previous cardiac surgery	136	3.8%	122	3.5%	14	10.6%	**<0.001**
Sodium <135 mEq/L	417	11.7%	391	11.4%	26	19.7%	**0.003**
Albumin <3.5 g/dL	744	20.8%	687	20.0%	57	43.2%	**<0.001**
Alkaline phosphatase >93 IU/L	1686	47.2%	1601	46.5%	85	64.4%	**<0.001**
AST ≥30 IU/L	1422	39.8%	1346	39.1%	76	57.6%	**<0.001**
Bilirubin >1 mg/dL	485	13.6%	438	12.7%	47	35.6%	**<0.001**
WBC >11,000/μL	298	8.3%	283	8.2%	15	11.4%	**0.200**
INR >1	1577	44.1%	1501	43.6%	76	57.6%	**0.002**
Platelets <150,000/μL	502	14.0%	473	13.7%	29	22.0%	**0.008**
ASA class ≥3	2895	81.0%	2779	80.7%	116	87.9%	**0.040**
Disseminated cancer	1297	36.3%	1272	37.0%	25	18.9%	**<0.001**
Admitted ≥1day before operation	449	12.6%	417	12.1%	32	24.2%	**<0.001**
Intraoperative							
Operative time, min	217	19–1029	222	7–1045	268	67–891	**<0.001**
Operative time >240 min	1505	42.1%	1428	41.5%	77	58.3%	**<0.001**
Extent of hepatectomy							**<0.001**
Partial	2166	60.6%	2113	61.4%	53	40.2%	
Left	401	11.2%	393	11.4%	8	6.1%	
Right	674	18.9%	628	18.2%	46	34.8%	
Extended	333	9.3%	308	8.9%	25	18.9%	
Partial vs. Left/Right/Extended	2166	60.6%	2113	61.4%	53	40.2%	**<0.001**
Right/Extended vs. Left/Partial							**<0.001**
Right/Extended	1007	28.2%	936	27.2%	71	53.8%	
Left/Partial	2567	71.8%	2506	72.8%	61	46.2%	
Biliary repair/reconstruction	241	6.7%	219	6.4%	22	16.7%	**<0.001**
Another major abdominal operation	558	15.6	527	15.3%	31	23.5%	**0.011**
Postoperative							
Any severe complication	831	23.3%	710	20.6%	114	86.4%	**<0.001**
≥2 severe complications	431	12.1%	325	9.4%	106	80.3%	**<0.001**
≥3 severe complications	227	6.4%	149	4.3%	78	59.1%	**<0.001**
Postoperative LOS, days (IQ Range)	6	(5–9)	6	(5–9)	9	(5–16.8)	**<0.001**

Abbreviations: AST, aspartate aminotransferase; WBC, white blood cells; INR, international normalized ratio; ASA, American Society of Anesthesiologists; LOS, length of stay

Not significant: gender, race, year of operation, body mass index, diabetes, smoker, alcohol use, dyspnea on exertion, previous coronary stent/angioplasty, medical hypertension, chemotherapy within 30 days, radiation therapy within 90 days, blood urea nitrogen, creatinine, hematocrit, partial thrombin time, chief resident involvement, operation in preceding 30 days, open wound