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ORIGINAL ARTICLE

Predicting poor outcome following hepatectomy: analysis of 2313 hepatectomies in the NSQIP database

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Abstract

Background: For the past two decades multiple series have documented that liver resection has become safer. The purpose of this study was to determine the current status of hepatic resection in the USA by analysing the multi-institutional experience within the National Surgical Quality Improvement Program (NSQIP) dataset.

Methods: Of the 363 897 cases in the 2005–2007 NSQIP Participant Use File, 2313 elective open hepatectomy cases were identified (1344 partial, 230 left, 510 right and 229 extended hepatectomies). A total of 57 perioperative risk factors and 28 postoperative complications were compared. To determine the applicability of NSQIP general risk models to hepatic surgery, the prognostic value of standard multivariate analysis was compared with the NSQIP general surgery aggregate risk indices (expected probability of morbidity [morbprob], expected probability of mortality [mortprob]).

Results: The median age of patients listed in the database was 60 years; sex distributions were equivalent; 78% were White; 65% of patients had an ASA score of 3 or 4, and the most prevalent co-morbidity was hypertension (46%). A total of 41% of patients had disseminated cancer, 19% of whom had received chemotherapy within 30 days of surgery. The overall 30-day mortality rate was 2.5% (57/2313) and the 30-day major morbidity rate was 19.6% (453/2313). Multivariate analysis identified nine risk factors associated with major morbidity and two risk factors associated with mortality. In contrast, the morbprob and mortprob statistics did not predict outcomes accurately. For those patients who developed major morbidity, the median length of stay was longer (10 vs. 6 days; $P = 0.001$) and the mortality rate was higher (11.3% vs. 0.3%; $P = 0.001$).

Conclusions: Analysis of the NSQIP experience with hepatectomy indicates that the current mortality and major morbidity rate benchmarks are 2.5% and 19.6%, respectively. Poor outcomes were associated with nutritional status, liver function and the extent of hepatectomy. The NSQIP general surgery morbprob and mortprob values were relatively poor predictors of post-hepatectomy observed morbidity, indicating the need for specialty-specific NSQIP modelling.

Keywords

surgical quality, liver resection, morbidity, mortality

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Introduction

For the past two decades multiple series have documented that liver resection has become safer.[1] Several relatively large, single-institution experiences have been reported documenting overall morbidity and mortality rates for hepatectomy.[2–10] In addition, these studies have identified several perioperative clinical factors associated with poor post-hepatectomy outcomes. However, these data are weakened by the fact that they are derived from mainly institutional experiences that may not be applicable to general hepatic surgery practices and few of them represent a modern experience.

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To address these weaknesses and to update the morbidity and mortality rates that should be expected following hepatectomy, we examined the National Surgical Quality Improvement Program (NSQIP) public use file (PUF) dataset. The recently released 2005–2007 PUF dataset includes 363 897 cases contributed by over 120 member institutions of variable size and type of practice.

The NSQIP, recently described by the Institute of Medicine as the 'best in the nation' for measuring and reporting surgical quality and outcomes, is based on three important quality measurement principles.[11] Firstly, specially trained nurse reviewers collect and enter all NSQIP risk factor and outcomes data independently of the possible bias inherent in the traditional 'surgical databases' used in clinical research. Secondly, 30-day follow-up is obtained in all cases regardless of postoperative admission status. In other words, NSQIP nurses will account for postoperative morbidity and mortality at 30 days from operation, even if the patient is discharged from the operative admission, thereby significantly increasing the accuracy and thoroughness of reporting. Thirdly, cases are categorized by current procedural terminology (CPT) code, leading to the standardization of reporting and analysis across member institutions.

From these data, the NSQIP has been able to develop robust predictive models across broad categories, such as general and vascular surgery.[12] Given the rapid increase in patients in the dataset, the NSQIP is examining the applicability of the NSQIP models in assessing specialty-specific outcomes. One area of emphasis is hepatopancreatobiliary (HPB) surgery. Currently, HPB-specific outcomes (e.g. pancreatic fistula following pancreatectomy) are not recorded in the NSQIP dataset, but over 25 detailed surgical outcomes are collected. Combined, these factors predict that the NSQIP dataset will be an extremely valuable instrument with which to determine the true and current incidence of morbidity and mortality following major hepatic surgery in America. These data have value not only for surgeons, but also for patients and for the oncologists and gastroenterologists who refer patients for surgical evaluation.

Materials and methods

Of the 363 897 cases in the 2005–2007 NSQIP PUF, 2313 elective open hepatectomy cases were identified.[13,14] Emergency cases were excluded from analysis. Included in this subset were 1344 partial hepatectomies (58%), 230 left hepatectomies (10%), 510 right hepatectomies (22%) and 229 extended hepatectomies (10%). The clinical characteristics of these patients are detailed in Table 1.

For each patient, 43 preoperative risk factors, 13 preoperative laboratory values, 14 perioperative risk factors and 28 postoperative complications (also termed 'occurrences') were assessed. In addition to traditional prognostic clinical variables, the NSQIP-derived 'mortprob' and 'morbprob' estimates were statistically assessed to determine their applicability to liver resection patients. The mortprob and morbprob are calculated values that assess the expected mortality and morbidity rates for each patient based on complex risk models created from the entire NSQIP dataset. To date, the mortprob and morbprob statistics have been derived from an analysis of outcomes for all patients in the NSQIP dataset. In this general setting, they have strong predictive value. However, the applicability of these measures to patients undergoing hepatectomy has not previously been assessed. To determine the applicability of NSQIP general risk models (as measured by morbprob and mortprob statistics) to hepatic surgery, the 75th percentile morbprob and mortprob values were compared with observed rates of major complications and mortality in the hepatectomy patients.

Major morbidity was defined by the occurrence of at least one of the following complications: organ space infection; pneumonia; unplanned intubation; pulmonary embolism; ventilator requirement for >48 h; progressive renal insufficiency; acute renal failure; cerebrovascular accident; coma; cardiac arrest; myocardial infarction; deep venous thrombosis; sepsis; septic shock, and return to operating room.

To identify clinical variables associated with 30-day major morbidity and 30-day mortality following hepatectomy, univariate analysis with chi-squared tests for categorical data and Mann–Whitney *U*-tests for continuous data were used. Clinical variables with univariate association with these two outcome endpoints at a significance level of $P < 0.05$ were entered into Cox proportional hazards models to determine independent associations with outcomes. A *P*-value <0.05 in multivariate analysis was used to determine final significance. All statistical calculations were performed using SPSS Version 14.0 (SPSS, Inc., Chicago, IL, USA).

Results

The median age of the 2313 hepatectomy patients in the dataset was 60 years (range 18–90 years), their sex distributions were equivalent and 78% were White. With regard to preoperative risk factors, 65% of patients had an ASA (American Society of Anesthesiologists) score of 3 or 4. No hepatectomy patients were classified as ASA 5. The most prevalent co-morbidity was hypertension (46%). Overall, 15% of patients were smokers and 14% had diabetes mellitus. A total of 10% of patients complained of dyspnoea on exertion, but only 3% carried a diagnosis of chronic lung disease. Only 4% had been treated with a coronary artery intervention. A total of 41% of patients underwent hepatectomy for disseminated cancer, 19% of whom had received chemotherapy within 30 days of surgery (Table 1).

The 30-day major morbidity rate was 19.6% (453/2313). Major morbidity rates correlated with the extent of hepatic resection (Table 2). The 30-day major morbidity rates for patients treated with partial, left, right and extended hepatectomy were 16.8%, 15.7%, 25.9% and 31.9%, respectively. With regard to major morbidity, multivariate analysis identified five independent preoperative risk factors (Table 3). Operative factors associated with major morbidity included extent of hepatectomy operative time, intraoperative red blood cell transfusion, and early postoperative transfusion (Table 3).

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Table 1 Clinical characteristics of 2313 hepatectomy patients in the National Surgical Quality Improvement Program (NSQIP) dataset. Values are *n* (%) unless otherwise stated

Strata	Variable	Subset	Descriptor
Preoperative	Median age (range)		60 years (17–90 years)
	Gender	Male	1141 (49%)
		Female	1172 (51%)
	Race	White	1799 (78%)
		Other	514 (22%)
	ASA score	1–2	821 (35%)
		3–4	1492 (65%)
	Median BMI (range)		27 m/kg^2 (10–81 m/kg^2)
	Diabetes	None	1976 (85%)
		NIDDM	239 (10%)
		IDDM	98 (5%)
	Smoking	No	1959 (85%)
		Yes	354 (15%)
	Functional status	Independent	2273 (98%)
		Partially dependent	33 (1%)
		Totally dependent	7 (1%)
	Dyspnoea on exertion	No	2082 (90%)
		Yes	231 (10%)
	Previous coronary intervention	No	2224 (96%)
		Yes	89 (4%)
	Hypertension	No	1260 (55%)
		Yes	1053 (45%)
	Cancer	No	1357 (59%)
		Yes	956 (41%)
	Preoperative chemotherapy	No	2115 (91%)
		Yes	198 (9%)
	BMI loss >10%	No	2187 (95%)
		Yes	126 (5%)
Biochemistry	Median creatinine (range)		1 mg/dl (1–10 mg/dl)
	Median albumin (range)		4 mg/dl (2–6 mg/dl)
	Median bilirubin (range)		0 mg/dl (0–15 mg/dl)
	Median glutamic oxaloacetic transaminase (range)		96 mg/dl (8–837 mg/dl)
	Median alkaline phosphatase (range)		101 mg/dl (32–1000 mg/dl)
	Median prothrombin time (range)		12 s (8–40 s)
	Median partial thromboplastin time (range)		28 s (11–85 s)
	Median morbprob (range)		0.36 (0.04–0.90)
	Median mortprob (range)		0.01 (0.0005–0.60)
Perioperative	Extent of resection	Partial hepatectomy	1344 (58%)
		Hemi-hepatectomy	740 (32%)
		Extended hepatectomy	229 (10%)
	Median operative time (range)		232 min (18–1029 min)
	Intraoperative red cell transfusion	No	1646 (73%)
		Yes	662 (27%)
Postoperative	Postoperative red cell transfusion	No	2292 (99%)
		Yes	21 (1%)
	Median postoperative length of stay (range)		8 days (0–138 days)

ASA, American Society of Anesthesiologists; BMI, body mass index; NIDDM, non-insulin dependent diabetes mellitus; IDDM, insulin dependent diabetes mellitus

The 30-day mortality rate for all hepatectomy patients was 2.5% (57/2313). As with major morbidity, mortality rates paralleled the extent of hepatic resection. The 30-day mortality rates for patients treated with partial, left, right and extended hepatectomy were 1.8%, 0.9%, 3.7% and 5.2%, respectively. Univariate and multivariate analyses were examined to determine associations with perioperative risk factors and postoperative 30-day mortality. This analysis determined that the two risk variables that

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Table 2 Incidence of major complications by type of hepatic resection

	All hepatectomy, *n* (%)	Partial hepatectomy, *n* (%)	Left hepatectomy, *n* (%)	Right hepatectomy, *n* (%)	Extended hepatectomy, *n* (%)	*P*-value
Total	2313 (100)	1344 (58)	230 (10)	510 (22)	229 (10)	
Organ space infection	138 (6.0)	61 (4.5)	12 (5.2)	40 (7.8)	25 (10.9)	0.0001
Pneumonia	93 (4.0)	41 (3.1)	8 (3.5)	28 (5.5)	16 (7.0)	0.009
Unplanned intubation	85 (3.7)	39 (2.9)	6 (2.6)	24 (4.7)	16 (7.0)	0.009
Pulmonary embolism	38 (1.6)	16 (1.2)	1 (0.4)	13 (2.5)	8 (3.5)	0.011
Ventilator requirement for >48 h	101 (4.4)	43 (3.2)	7 (3.0)	34 (6.7)	17 (7.4)	0.001
Progressive renal insufficiency	15 (0.6)	5 (0.4)	1 (0.4)	7 (1.4)	2 (0.9)	0.107
Acute renal failure	35 (1.5)	13 (1.0)	1 (0.4)	16 (3.1)	5 (2.2)	0.003
Cerebrovascular accident	11 (0.5)	4 (0.3)	1 (0.4)	3 (0.6)	3 (1.3)	0.220
Coma	0 (0.3)	4 (0.3)	0 (0)	1 (0.2)	1 (0.4)	0.794
Cardiac arrest	25 (1.1)	10 (0.7)	1 (0.4)	10 (2.0)	4 (1.7)	0.073
Myocardial infarction	8 (0.3)	5 (0.4)	0 (0)	2 (0.4)	1 (0.4)	0.823
Deep venous thrombosis	47 (2.0)	17 (1.3)	4 (1.7)	14 (2.7)	12 (5.2)	0.001
Sepsis	154 (6.7)	77 (5.7)	12 (5.2)	43 (8.4)	22 (9.6)	0.038
Septic shock	86 (3.7)	36 (2.7)	5 (2.2)	26 (5.1)	19 (8.3)	0.000
Return to operating room	112 (4.8)	46 (3.4)	11 (4.8)	37 (7.3)	18 (7.9)	0.001

Table 3 Analysis of clinical factors in the National Surgical Quality Improvement Program database associated with major morbidity following hepatectomy

Strata	Risk factor	MV *P*-value	Odds ratio
Preoperative	ASA score	0.001	1.4
	Smoking	0.0001	1.7
Biochemistries	Elevated alkaline phosphatase	0.0001	4.9
	Low albumin	0.006	2.8
	Elevated partial thromboplastin time	0.047	2.0
Perioperative	Extent of hepatectomy	0.0001	1.8
	Intraoperative red cell transfusion	0.0001	2.2
	Prolonged operative time	0.011	1.6
	Postoperative red cell transfusion	0.001	1.4

MV, multivariate; ASA, American Society of Anesthesiologists

strongly correlated with death in the 57 patients who died following hepatectomy were elevated serum bilirubin prior to surgery (P = 0.002, odds ratio [OR] 5.98, 95% confidence interval [CI] 1.091–18.860) and the need for intraoperative red cell transfusion (P = 0.037, OR 2.5, 95% CI 1.055–5.947).

In addition, morbprob and mortprob statistics were examined to determine their prognostic potential. A 75th percentile morbprob (0.40) was associated with a major complication positive predictive value of only 29.8%, with a sensitivity of 50.8% and a specificity of 70.9%. A 75th percentile mortprob (0.0315) was associated with a major complication positive predictive value of only 6.1%, with a sensitivity of 61.4% and a specificity of 75.9%.

One of the most important factors for mortality following hepatectomy was the development of major morbidity. Patients with minor morbidities were far less likely to experience a catastrophic event. By contrast, patients who developed major morbidityexperienced a longer median length of stay (10 vs. 6 days; P = 0.001) and a higher mortality rate (11.3% vs. 0.3%; P = 0.001).

Discussion

The purpose of this study was to determine the current status of hepatic resection in the USA by analysing the NSQIP dataset. Analysis of this multi-institutional experience with hepatectomy indicates that the current mortality and major morbidity rate benchmarks are 2.5% and 19.6%, respectively. The examined dataset represents a broad analysis of hepatectomy types, practice environments and patient risk factors. The results of this analysis are supported by the strengths of the NSQIP structure, including independent nurse data recording and mandatory 30-day follow

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up. These tenets insure the most accurate reporting of surgical risk factors and outcomes compared with previously analysed multi-institutional datasets.

Analysis of the hepatectomy subset of cases in the NSQIP determined that poor outcomes were not associated with age or body mass index. Instead, poor outcomes were most dependent on nutritional status, liver function at the time of hepatectomy, and the extent of resection. In fact, major morbidity rates closely correlated with the extent of resection. Only 17% of patients with partial hepatectomy experienced a major complication, whereas hemihepatectomy patients experienced a 23% major morbidity rate and extended hepatectomy patients experienced the highest major morbidity rate at 32%. Likewise, mortality rates correlated with the extent of hepatectomy, with the highest mortality rates experienced by patients undergoing right hepatectomy (3.7%) and extended hepatectomy (5.2%).

In comparison with recently published mortality rates for hepatectomy, the mortality rates in the NSQIP dataset may appear alarmingly elevated. In fact, several specialty centres have reported large-volume experiences with minimal to no operative mortality.[2–6,8–10,15–17] However, the NSQIP hepatectomy mortality rates closely correlate with two recent analyses of the National Inpatient Sample.[1,18] One of these analyses included 11 429 hepatectomy patients and found an overall mortality rate of 5.6%, 1.6 times higher than an aggregate of recently published mortality rates.[18] Combined, these data suggest that a broader, and more objective, analysis of morbidity and mortality may result in a realistic assessment of the current risk associated with hepatectomy, facilitating comparison between programmes and the development of institution-specific quality improvement initiatives.

The data points in the NSQIP PUF allowed for a detailed analysis of risk and outcome in a large cohort of patients. The NSQIP was not, however, specifically designed to comment on this subset of surgical patients. Therefore, several data points of interest are not included in this analysis. Firstly, the categorization of anaesthesia type in the NSQIP does not differentiate general anaesthesia from epidural anaesthesia when both modalities are utilized. Based on the lack of detail in this area, no specific comments can be made regarding the ongoing discussion of the use of epidural anaesthesia in hepatic surgery and its possible association with poor outcomes, including elevated transfusion rates.[19,20] Secondly, data collection ends at 30 postoperative days. Given that recent reports suggest that delayed hepatic regeneration may lead to elevated 90-day mortality rates following hepatectomy,[7,21] this may be viewed as a weakness of this dataset. However, late mortality (from 31–90 postoperative days) remains a rare occurrence and should not detract from the mortality risk analysis included here.

In addition, the PUF database does not allow for the tracking of cases to specific institutions or surgeons and therefore we cannot verify the contribution of programme experience, hospital size and surgeon-specific experience to these results. Further experience with data analysis from the PUF and the formation of working groups to allow extraction and evaluation of site-specific data may allow more detailed appraisal of outcomes associated with these relevant factors.

The secondary goal of this analysis was to determine the ability of the general NSQIP dataset to comment on a specialty-specific area in HPB surgery, such as hepatectomy. The large number of patients and variables contained in the NSQIP PUF clearly facilitated one of the most detailed multicentre examinations of morbidity and mortality in hepatectomy patients, identifying multiple independent prognostic factors. However, the analysis determined that the general surgical risk models created from the entire NSQIP database, as reflected in the general surgical morbprob and mortprob statistics, are relatively inaccurate at predicting actual morbidity and mortality in hepatectomy patients. Further study will be needed to determine if similar discrepancies apply toother complex elective or emergency operations. Reappraisal of risk modelling methods for this cohort of procedures may be warranted.

This finding indicates that patients undergoing hepatectomy have a unique risk to outcome relationship that differs from that in a general population of surgical patients. For the NSQIP to accurately comment on this relationship requires that two issues are addressed. Firstly, the NSQIP might use its robust statistical core to validate the findings of this study and to create a hepatectomy-specific mortprob and morbprob statistic from the variables currently recorded in the NSQIP database. Based on our analysis of the current version of variables included in NSQIP data collection, adding the prognostic risk factors we identified to the risk modelling would result in a hepatobiliary-specific morbprob and mortprob with significantly more predictive strength.

Table 4 Suggested hepatobiliary-specific additions to the current list of recorded National Surgical Quality Improvement Program preoperative risk factors, perioperative data points and outcome measures

• Preoperative variables/risk factors
○ Presence of biliary obstruction
○ Presence of indwelling biliary drainage catheters
○ Portal vein embolization
○ Neoadjuvant chemotherapy details (drugs, cycles, duration)
○ Preoperative Model for End-stage Liver Disease (MELD) score
• Perioperative variables/risk factors
○ Use of epidural anaesthesia
○ Liver transection technique
○ Combined resection/ablation procedure
○ Bilio-enteric reconstruction
○ Use of perihepatic drains
○ Histology of tumour(s)
○ Histologic condition of the non-tumoral liver
• Postoperative occurrences (complications)
○ Deep surgical space infection with vs. without biloma
○ Peak postoperative bilirubin

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Secondly, the hepatobiliary-specific models might be further strengthened by the addition of hepatectomy patient-specific preoperative and perioperative risk variables. For example, the NSQIP might add the presence of biliary drainage catheters and the need for biliary reconstruction at the time of hepatectomy to the list of preoperative and perioperative variables collected in NSQIP hepatectomy patients. Likewise, the risk model might be strengthened by the addition of hepatectomy-specific outcomes measures, such as bile leak. It is likely that this outcome is captured in the 'organ space infection' category; however, further refinement to clarify the presence of bile leak vs. other organ space infection would add specificity to the data collection. A detailed listing of suggested hepatobiliary-specific additions to the current list of recorded NSQIP risk factors, perioperative data points and outcomes measures is included in Table 4.

This study reveals that the American College of Surgeons (ACS) NSQIP risk models currently in use do not accurately predict outcomes for patients undergoing hepatectomy. A major strength of the ACS-NSQIP PUF is that this multi-institutional verified database produces a more generalizable view of outcomes and risk stratification of patients undergoing hepatectomy. In order to optimize programmatic and surgeon-specific comparisons, ongoing reappraisal of risk models and the development of analytic tools and metrics for specific high-risk procedures will be needed. The deficiencies of the NSQIP in predicting post-hepatectomy outcomes highlighted in this discussion should not, however, detract from the power of this dataset. The NSQIP, even in its current state, is the most robust and comprehensive multi-institutional database available to assess surgical risk in these patients. Our analysis of the current NSQIP hepatectomy dataset identified multiple significant and independent variables that can be used by hepatobiliary surgeons, their patients and referring physicians to estimate the morbidity and mortality risks of major hepatic resection.

ACS-NSQIP data disclaimer

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

Conflict disclosure

TAA is a member of the Sanofi Aventis Speakers Bureau.

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