Further, in regard to the perioperative outcomes between the well-matched groups, the LLR patients had less blood loss, shorter hospital stay, and less morbidity than the OLR patients as shown in Table 3. These results are consistent with the recommendations in the 2nd International Consensus Conference on LLR held in Morioka, Japan, from 4 to 6 October 2014 [28]. However, in the subgroup analysis, major LLR failed to show less blood loss, although it still had shorter hospital stay and less morbidity (Table S1). These significances cannot be blindly accepted as the patient number of each matched group was small. It is also likely that major LLR was in an introduction phase and the learning curve must have an impact during our study period.

With respect to the contents of the complications, the frequency of the liver failure after LLR was lower than after OLR. This result might be explained by less destruction of the collateral blood/lymphatic flow by LLR during mobilization of the liver. Reduction of surgery-induced injury with LLR may lower the risk of liver failure after LLR for HCC patients with severe cirrhosis [29, 30].

In conclusion, compared with OLR, LLR in selected patients with HCC showed similar long-term outcomes, associated with less blood loss, shorter hospital stay, and fewer postoperative complications. Especially, the minor LLR in selected patients is confirmed to be one good option as a standard practice for the treatment of HCC.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1 Comparison of perioperative outcomes according to the surgical procedure.
Fig. S1 Receiver operating characteristics (ROC) curve.
Fig. S2 Histogram of propensity score before and after PSM.
Fig. S3 Standardized differences before and after PSM.

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ORIGINAL ARTICLE

Clinical practice guidelines for the management of biliary tract cancers 2015: the 2nd English edition

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Abstract

Background The Japanese Society of Hepato-Biliary-Pancreatic Surgery launched the clinical practice guidelines for the management of biliary tract and ampullary carcinomas in 2008. Novel treatment modalities and handling of clinical issues have been proposed after the publication. New approaches for editing clinical guidelines, such as the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system, also have been introduced for better and clearer grading of recommendations.

Methods Clinical questions (CQs) were proposed in seven topics. Recommendation, grade of recommendation and statement for each CQ were discussed and finalized by evidence-based approach. Recommendation was graded to grade 1 (strong) and 2 (weak) according to the concept of GRADE system.

Results The 29 CQs covered seven topics: (1) prophylactic treatment, (2) diagnosis, (3) biliary drainage, (4) surgical treatment, (5) chemotherapy, (6) radiation therapy, and (7) pathology. In 27 CQs, 19 recommendations were rated strong and 11 recommendations weak. Each CQ included the statement of how the recommendation was graded.

Conclusions This guideline provides recommendation for important clinical aspects based on evidence. Future collaboration with cancer registry will be a key for assessment of the guidelines and establishment of new evidence. Free full-text articles and a mobile application of this guideline are available via http://www.jshbps.jp/en/guideline/biliary-tract2.html.

Keywords Ampullary carcinoma · Bile duct carcinoma · Biliary tract cancer · Gallbladder carcinoma

Introduction

The prognosis of biliary tract cancers, including bile duct carcinoma, gallbladder carcinoma, and ampullary carcinoma, still remains poor. However, due to the paucity of high-level evidence for diagnosis and treatment of these diseases, there are wide disparities in the levels of patients' care among different institutions. These backgrounds indicate that the clinical guidelines for the management of biliary tract cancers edited by the specialists in these fields are very useful for physicians involved in the care of these diseases. It also helps to eliminate cancer care disparities among the institutions.

The Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS) published the clinical practice guidelines for the management of biliary tract and ampullary carcinomas in 2008 [1–10]. This was the only clinical guidelines focused on these complicated diseases

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ORIGINAL ARTICLE

Classification of biliary tract cancers established by the Japanese Society of Hepato-Biliary-Pancreatic Surgery: 3rd English edition

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Abstract The 3rd English edition of the Japanese classification of biliary tract cancers was released approximately 10 years after the 5th Japanese edition and the 2nd English edition. Since the first Japanese edition was published in 1981, the Japanese classification has been in extensive use, particularly among Japanese surgeons and pathologists, because the cancer status and clinical outcomes in surgically resected cases have been the main objects of interest. However, recent advances in the diagnosis, management and research of the disease prompted the revision of the classification that can be used by not only surgeons and pathologists but also by all clinicians and researchers, for the evaluation of current disease status, the determination of current appropriate treatment, and the future development of medical practice for biliary tract cancers. Furthermore, during the past 10 years, globalization has advanced rapidly, and therefore, internationalization of the classification was an important issue to revise the Japanese original staging system, which would facilitate to compare the disease information among institutions worldwide. In order to achieve these objectives, the new Japanese classification of the biliary tract cancers principally adopted the 7th edition of staging system developed by the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC). However, because there are some points pending in these systems, several distinctive points were also included for the purpose of collection of information for the future optimization of the staging system. Free mobile application of the new Japanese classification of the biliary tract cancers is available via http://www.jshbps.jp/en/classification/cbt15.html.

Keywords Biliary tract cancers · Internationalization · Japanese classification · UICC/AJCC staging system

Introduction

In 2013, the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS) published a new version of the Japanese classification of biliary tract cancers [1]. On the basis of the new version, an English-language version is now available here.

General principles

JSHBPS classification of biliary tract cancers is only applied to primary carcinomas of the extrahepatic biliary tract, although anatomical biliary tract includes the bile ductule and intrahepatic bile ducts. In consideration of anatomical and functional characteristics, primary carcinomas of the ampullary region can be classified in this manual.

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ORIGINAL ARTICLE

Revision concepts and distinctive points of the new Japanese classification for biliary tract cancers in comparison with the 7th edition of the Union for International Cancer Control and the American Joint Committee on Cancer staging system

Masayuki Ohtsuka · Shuichi Miyakawa · Masato Nagino · Tadahiro Takada · Masaru Miyazaki

Published online: 26 January 2015

Abstract
Background The 3rd English edition of the Japanese classification of the biliary tract cancers (JC) is now available in this journal. The primary aim of this revision is to provide all clinicians and researchers with a common language of cancer staging at an international level. On the other hand, there are several important issues that should be solved for the optimization of the staging system.
Methods Revision concepts and major revision points of the 3rd English edition of the JC were reviewed. Furthermore, comparing with the 7th edition of staging system developed by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC), distinctive points in the JC was discussed.
Results In this edition of the JC, the same stage groupings as those in the UICC/AJCC staging system were basically adopted. T, N, and M categories were also identical in principle with those in the UICC/AJCC staging system, although slight modifications were proposed as the "Japanese rules". As distinctive points, perihilar cholangiocarcinomas and ampullary region carcinomas were clearly defined. Intraepithelial tumor was discriminated from invasive carcinoma at ductal resection margins. Classifications of site-specific surgical margin status remained in this edition. Histological classification was based on that in the former editions of the JC, but adopted some parts of the World Health Organization classification.
Conclusions The JC now share its staging system of the biliary tact carcinomas with the UICC/AJCC staging system. Future validation of the "Japanese rules" could provide important evidence to make globally standardized staging system.

Keywords Biliary tract cancers · Japanese classification · Staging system · UICC/AJCC staging system

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Introduction

The first edition of the Japanese classification of the biliary tract cancers (JC) (named "General Rules for Surgical and Pathological Studies on Cancer of the Biliary Tract"), organized by the Japanese Society of Biliary Surgery (JSBS), was published in 1981. Since then, the JSBS has revised the classification four times, and the English editions were published based on the fourth and fifth Japanese editions in 2001 and 2004, respectively. These editions have provided the Japanese rules to describe the cancer status and to evaluate the outcome, only in patients undergoing surgery.

In 2013, the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS) that merged with JSBS published a new version of the JC [1], and English edition based on this new version is now available in this journal [2]. The primary aim of the revision is to provide not only surgeons and pathologists but also all clinicians treating the biliary tract cancers

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ORIGINAL ARTICLE

Updated clinical practice guidelines for the management of biliary tract cancers: revision concepts and major revised points

Hideyuki Yoshitomi · Shuichi Miyakawa · Masato Nagino · Tadahiro Takada · Masaru Miyazaki

Published online: 18 March 2015

Abstract
Background In 2008, the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS) launched the clinical practice guideline for the management of biliary tract cancers. JSHBPS decided to revise these guidelines for distribution of updated points concerning the treatment of biliary tract cancers.
Methods To make clearer recommendations, we introduced the concepts of Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach, in which the strength of recommendations are decided considering not only quality of evidence, but also balance of benefits and harms/burdens, patients' preferences, and cost benefits.
Results We emphasize the importance of the dynamic contrast enhanced multiple row detector CT (MDCT) in the diagnosis of biliary tract and gallbladder carcinomas. For biliary drainage, we suggest to perform endoscopic approaches instead of percutaneous approach to avoid complications. Regarding the surgical treatments, we included new clinical questions about the importance of combined vascular resection, intraoperative histological examination of the bile duct resection margin, and the combined extrahepatic bile duct resection for the gallbladder carcinoma. We also discussed details about premalignant lesions and non-neoplastic lesions in pathology section.
Conclusion With this major revision, we expect that the Japanese standards of treatments of these diseases are recorded and reported in the universal language.

Keywords Ampullary carcinoma · Bile duct carcinoma · Biliary tract cancer · Clinical guidelines · Gallbladder carcinoma

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Introduction

The rapid progress of recent medical technology has contributed to improvements in diagnosis and treatment, resulting in better treatment outcomes in many diseases. Recent advances in information technology also enable rapid distribution of new medical information. However, it is impossible for an individual health professional to manage all of this new information and provide updated treatment for each patient. Under these circumstances, the clinical guidelines edited by specialists in each field have been published to organize this information and provide updated evidence-based medicine.

In 2008 (2007 in Japanese), the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS) launched the first edition of the clinical practice guidelines for the management of biliary tract cancers [1–10]. This was the only clinical guideline focused on biliary tract cancers (including hilar cholangiocarcinoma, extrahepatic biliary tract carcinoma, gallbladder carcinoma, and ampullary region carcinoma). It has greatly contributed to providing general as well as specialized clinicians with knowledge on standard treatments based on evidence and consensus, not only in Japan but also worldwide. Many novel treatment modalities and handling of clinical issues have been proposed after its publication. In 2010, the board members of JSHBPS decided to revise these clinical

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REVIEW ARTICLE

National Clinical Database feedback implementation for quality improvement of cancer treatment in Japan: from good to great through transparency

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Abstract The National Clinical Database (NCD) of Japan was established in April, 2010 with ten surgical subspecialty societies on the platform of the Japan Surgical Society. Registrations began in 2011 and over 4,000,000 cases from more than 4100 facilities were registered over a 3-year period. The gastroenterological section of the NCD collaborates with the American College of Surgeons' National Surgical Quality Improvement Program, which shares a similar goal of developing a standardized surgical database for surgical quality improvement, with similar variables for risk adjustment. Risk models of mortality for eight procedures; namely, esophagectomy, partial/total gastrectomy, right hemicolectomy, low anterior resection, hepatectomy, pancreaticoduodenectomy, and surgery for acute diffuse peritonitis, have been established, and feedback reports to participants will be implemented. The outcome measures of this study were 30-day mortality and operative mortality. In this review, we examine the eight risk models, compare the procedural outcomes, outline the feedback reporting, and discuss the future evolution of the NCD.

Keywords Gastrointestinal surgery · National Clinical Database · Nationwide web-based database · Mortality · Risk model

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Abbreviations

NCD	National Clinical Database
ACS NSQIP	The American College of Surgeons National Surgical Quality Improvement Program
ASA	American Society of Anesthesiologists
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
DIC	Disseminated intravascular coagulation
JSS	The Japan Surgical Society
JSGS	The Japanese Society of Gastroenterological Surgery
ROC	Receiver operating characteristic
SIRS	Systemic inflammatory response syndrome
SSI	Surgical site infection

Introduction

Until recently, no nationwide data on cancer were available in the field of gastroenterological surgery in Japan. In 2006, the Japanese Society of Gastroenterological Surgery (JSGS) formed a committee to devise a database to track surgical patients treated in Japan over the 3 years from 2006 to 2008, and reported relatively low mortality rates for the major surgical procedures [1, 2]. The JSGS acknowledged the importance of risk-adjusted surgical outcomes for accurate comparisons and quality improvement; thus, in April, 2010, it created the database as a subset of the National Clinical Database (NCD) of Japan with major support from the Japan Surgical Society (JSS). Eight other surgical professional societies, including the Japanese Society for Cardiovascular Surgery, the Japanese Society for Vascular Surgery, the Japanese Association for Thoracic Surgery, the Japanese Association for Chest Surgery, the Japanese Society of Pediatric Surgeons, the Japanese Breast Cancer

Society, the Japan Association of Endocrine Surgeons, and the Japanese Society of Thyroid Surgery, joined the NCD. Registrations began in 2011, since when more than 4100 facilities have enrolled and over 4,000,000 cases have been registered over a 3-year period.

The gastroenterological section of the NCD collaborates with the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) [3], which shares a similar goal of developing a standardized surgical database for quality improvement. The NSQIP was originally developed in the 1990s by the United States Veterans' Health Administration and led to marked improvement in surgical quality [4]. The American College of Surgeons (ACS) initiated the ACS-NSQIP in 2006 and demonstrated improved surgical outcomes across all participating hospitals in the private sector [5]. The core members of the NCD joined the meetings and seminars of the ACS-NSQIP and debated various aspects of clinical databases, such as data collection methods and public relations [3]. In addition, the NCD implemented the same items as those of the ACS-NSQIP to conduct international cooperative studies. Reliable 30-day outcomes, including mortality and morbidity, serve as a quality improvement catalyst for ACS-NSQIP-participating institutions. Risk adjustment is a key component of the ACS-NSQIP and most variables included in risk adjustment models focus on patient factors and comorbidities. In this article, we focused on the gastrointestinal surgery subset of the NCD. All cases are input with items representing the surgical performance in each specialty for the following eight procedures: esophagectomy (Eso), total/distal gastrectomy (TG/DG), right hemicolectomy (RHC), low anterior resection (LAR), hepatectomy performed for more than one segment apart from the lateral segment (Hx), pancreaticoduodenectomy (PD), and surgery for acute diffuse peritonitis (ADP). Risk models of mortality for each procedure were created using approximately 120,000 cases registered in 2011, and each model has been accepted and published in peer-reviewed journals [6–13]. We review the results and discuss the future evolution of the NCD using these risk models in terms of the surgical quality improvement program in Japan.

NCD data entry system

Submitting cases to the NCD is a prerequisite for all member institutions of the JSS and JSGS, and only registered cases can be used for board certification [3]. To assure the traceability of data, the NCD continuously tracks persons who approve data, persons in departments who are in charge of annual cases, and persons responsible for data entry, through its web-based data management system. The NCD also continuously validates data consistency through random site visits.

The NCD variables are almost identical to those applied in the ACS-NSQIP (http://www.site.acsnsqip.org/wp-content/uploads/2013/10/ACSNSQIP.PUF_.UserGuide.2012.pdf#search='user+guide+for+the+2012+ACS+NSQIP). The potential independent variables include patient demographics, pre-existing comorbidities, preoperative laboratory values, and perioperative data. The demographic variables include age, sex, smoking status, and drinking status. Patients were categorized according to whether they were brought to hospital directly, by ambulance. General factors such as the patient's body mass index (BMI) and preoperative functional status, defined as independent, partially dependent, or totally dependent, according to their ability to perform activities of daily living (ADL) in the 30 days prior to surgery and immediately before surgery, were also considered. We evaluated the physical status classification by the American Society of Anesthesiologists (ASA) and considered pre-existing comorbidities, including the cardiovascular status, respiratory status, renal status, hematological status, oncological status, preoperative blood transfusion, chronic steroid use, ascites, sepsis, diabetes, open wound, and pregnancy. The laboratory parameters included in the analysis were the white blood cell count, hemoglobin level, hematocrit, platelet count, prothrombin time, and activated partial thromboplastin time, as well as the serum levels of albumin, total bilirubin, aspartate amino transferase, alanine aminotransferase, alkaline phosphatase, urea nitrogen, creatinine, sodium, hemoglobin A1c, and C-reactive protein. The length of surgery, intraoperative blood loss, amount of transfusion, and any accident during the operation were also considered.

Postoperative outcomes evaluated 30 days after surgery were categorized according to the Clavien and Dindo classification [14]. The outcomes included relaparotomy within 30 days after surgery, wound events, anastomotic leak, respiratory events, urinary tract events, central nervous system events, cardiac events, other events, systemic sepsis, sepsis, systemic inflammatory response syndrome, and 24 other complications added by the NCD. For Hx procedures, the indications for surgery and resected subsegments (S1–S8) were included as preoperative variables to create risk models [9].

Outcome measures and statistical analysis

The outcome measures of this study were 30-day mortality and operative mortality. The former was defined as death within 30 days of surgery, regardless of the patient's geographical location, even if the patient had been discharged from hospital. The latter was defined as death within the index hospitalization period, regardless of the length of hospital stay (up to 90 days), as well as any death after discharge, up to 30 days after surgery. Data were randomly

Table 1 Registered cases used to create risk models for 8 surgical procedures [6–13]

	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
Registered cases	5354	20,011	33,917	19,070	16,695	7732	8575	8482
Participating hospitals	713	1623	1737	1689	1620	987	1167	1285
(%)	34.9	79.4	84.9	82.6	79.2	48.3	57.1	62.8
30-day mortality (%)	1.2	0.9	0.5	1.1	0.4	2.0	1.2	9.0
Operative mortality (%)	3.4	2.3	1.2	2.3	0.9	4.0	2.8	14.1
Cancer surgery (%)	98.4	98.5	99.9	92.6	98.5	94.5	91.4	10.8
Emergent case (%)	0.8	2.0	0.9	8.4	1.1	0.8	0.9	92.9

Esophagectomy (Eso), total/distal gastrectomy (TG/DG), right hemicolectomy (RHC), low anterior resection (LAR), hepatectomy performed for >1 segment except for the lateral segment (Hx), pancreaticoduodenectomy (PD), and operation for acute diffuse peritonitis (ADP)

assigned into two subsets that were split 80/20: the first, for model development, and the second, for validation. The two sets of logistic models (30-day mortality and operative mortality) were constructed for dataset development using step-wise selection of the predictors with a probability (p) value for inclusion of 0.05. A "goodness-of-fit" test was performed to assess how well the model could discriminate between patient survival and death. The receiver operating characteristic (ROC) curves for the 30-day and operative mortalities were created for the validation dataset. An ROC curve is a plot of a test's true-positive rate (sensitivity) versus its false-positive rate (1—specificity). Model calibration, being the degree to which the observed outcomes matched the predicted outcomes from the model across a group of patients, was examined by comparing the observed and predicted averages with each of 10 equally sized subgroups, arranged in the order of increasing patient risk.

Case number and participating hospitals for each procedure and mortality rates

The NCD is a nationwide project in cooperation with Japan's board certification system in surgery, for which more than 1,200,000 surgical cases from over 3500 hospitals were collected in 2011. The number of participating hospitals in the gastroenterological section was 2045 at the time of the analysis (July, 2012). Among these cases, approximately 120,000 were used to create the risk models. Table 1 lists the number of cases for each procedure and the number of hospitals performing the respective procedure with its ratio to the total number of hospitals (%). Most procedures, except for ADP, were performed for cancer. Emergency surgery was most common for ADP (93 %). The 30-day mortality and operative mortality rates for the eight procedures were as follows: Eso, 1.2/3.4; TG, 0.9/2.3; DG, 0.5/1.2; RHC, 1.1/2.3; LAR, 0.4/0.9; HX, 2.0/4.0; PD, 1.2/2.8; and ADP, 9.0/14.1 %, respectively (Table 1). The operative mortality for each procedure, apart from ADP, was more than twice that of the 30-day mortality.

Risk models in the eight procedures

The 30-day mortality and operative mortality risk models for the eight procedures were created, and the C-index for those in the validation data sets was as follows: Eso, 0.767/0.742; TG, 0.811/0.824; DG, 0.785/0.798; RHC, 0.836/0.854; LAR, 0.75/0.766; HX, 0.714/0.761; PD, 0.675/0.725; and ADP, 0.851/0.852, respectively (Tables 2, 3). The final logistic models for the 30-day mortality with odds ratios for the eight procedures are listed in Table 2. Age; sex; emergency surgery; ADL; ASA class; BMI; cardiovascular, pulmonary, and renal comorbidities; and other patient conditions such as disseminated cancer, ascites, preoperative transfusion, bleeding disorder, diabetes, weight loss, sepsis, and chronic steroid use, including 121 variables, were found to be risk factors for certain procedures. Age, ADL ASA, BMI, disseminated cancer, bleeding disorder, and weight loss appeared to be common risk factors in most of the procedures. Table 3 lists the final logistic models for the operative mortality with odds ratios for the eight procedures, including 159 variables. New and additional 38 variables were captured for these models.

Feedback implementation (risk calculator)

A risk-adjusted analysis based on nationwide data allows personnel to establish and provide feedback on the risks that patients face before undergoing a procedure. On the basis of these objective data, healthcare professionals can then determine the treatment indicators and obtain informed consent. The risk calculator for all eight procedures will be available soon, on the websites of the hospitals that are a part of NCD, although the calculators for TG, PD, Hx, Eso, RHC, and LAR are currently available (February, 2015). The real-time feedback system gives the predicted mortality of patients simultaneously with data input. Standardized information on patient risk and predicted mortality can be reformulated as case reports and shared at conferences.

Table 2 Risk models for 30-day mortality after 8 gastrointestinal procedures (refs 6–13)

Variables	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
Age category	1.5	1.2	1.2		1.3	1.4	1.3	1.2
Male sex						1.6	2.0	
Ambulance transport								1.4
Emergent surgery				1.9		3.8	4.3	
ADL within 30 days before surgery								
Any assistance	4.2					2.1		
Total			3.0					
ADL immediately before surgery								
Any assistance		2.1		2.8				
Total								1.4
ASA								
Class 3				2.3				2.7
Class 4								4.3
Class 5								8.7
Class 3, 4, 5			2.0			2.0	2.2	
Class 4, 5		9.4		4.0				
BMI								
>25 kg/m^2							2.4	
>30 kg/m^2					7.0			
Congestive heart failure				2.3				
Previous cardiac surgery		2.3						
Myocardial infarction			3.1					
Previous PCI								2.0
Previous PVD surgery					6.2			2.5
Cerebrovascular disease			2.1					
COPD							2.4	
Preoperative pneumonia			2.8					
Respiratory distress								1.6
Acute renal failure				3.2				
Preoperative dialysis		3.9						
Cancer with multiple metastases				2.2				
Disseminated cancer		2.6			4.9			2.2
Preoperative transfusion		1.9			5.4			1.6
Bleeding disorder without treatment			3.2		5.2			1.6
Bleeding disorder							4.4	
Diabetes		2.2						
Smoking within 1 year	2.6							
Ascites		2.0				2.1		
Without control			3.0					
Chronic steroid use								1.7
Weight loss	2.4		2.3					
Sepsis				2.0				
Habitual alcohol consumption			1.6					
WBC								
>12,000/μl	3.7		3.7					
>9000/μl				1.5				
<4000/μl	2.8							1.4

Table 2 continued

Variables	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
Hemoglobin								
M < 13.5 g/dl, F < 12.5 g/dl		1.7	1.8					
<10.0 g/dl								1.3
Platelet								
>400,000/μl	2.5							
<150,000/μl								1.5
<120,000/μl				1.9	5.0	1.7		
<80,000/μl		3.1						1.5
<50,000/μl				5.6				
Albumin								
<4.0 g/dl				2.0	3.4			
<3.5 g/dl		1.7	1.5			2.0		
<2.0 g/dl								1.7
Total bilirubin								
>3.0 mg/dl				3.1				1.7
>2.0 mg/dl		2.9						
AST								
>35 U/l		2.3		3.1		2.3		1.4
ALP								
>600 U/l		2.5						1.7
>340 U/l		1.7	2.2					
BUN								
>25 mg/dl		1.9			2.5			1.4
>20 mg/dl								1.8
<8.0 mg/dl							2.3	
Creatinine								
>2.0 mg/dl						3.9		
>1.2 mg/dl			1.8					
Serum Na								
>145 mEq/l								1.7
<138 mEq/l				2.1	3.6			
<135 mEq/l	3.6		2.5					
<130 mEq/l								1.7
CRP								
<10.0 mg/dl								1.5
APTT								
>40 s							3.2	
PT-INR								
>1.25		2.2	2.0					
>1.1	2.0			1.5		1.7		
Non-tumor bearing								0.6
Surgical procedures						#1		
Indication for surgery						#2		

#1 Hepatectomy with S8 (2.2), hepatectomy with revascularization (3.8)

#2 Hilar bile duct carcinoma (2.5), gallbladder cancer (4.1)

ADL, Activities of daily living, PT-INR Prothrombin time-international normalized ratio, *WBC* white blood cells, *ASA* American society of anesthesiologists, *ADL* activities of daily living, *PCI* percutaneous coronary intervention, *COPD* chronic obstructive pulmonary disease, *AST* aspartate amino transferase, *ALP* alkaline phosphatase, *APTT* activated partial thromboplastin time

Table 3 Risk models for operative mortality after 8 gastrointestinal procedures [6–13]

Variables	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
Age category	1.4	1.3	1.3	1.1	1.4	1.4	1.3	1.3
Male sex	2.3				1.9	1.5		
Emergent surgery		1.7	1.9	1.9		2.8		
ADL within 30 days before surgery								
Any assistance	4.7					2.8	2.5	
Total								1.6
ADL immediately before surgery								
Any assistance		2.0		2.5	2.5			1.4
Total			3.0		2.9			
ASA								
Class 3		1.8		1.6				2.3
Class 4								4.7
Class 5								6.5
Class 3, 4, 5			1.9			2.0	2.1	
Class 4, 5		5.2		2.9				
BMI								
>25 kg/m^2							1.9	
>30 kg/m^2					4.6			
Congestive heart failure				2.2				
Angina							2.6	
Previous PVD surgery				3.1	5.8			
Cerebrovascular disease			1.8					
Cerebrovascular accident		1.9						
Respiratory distress								
Any		1.7	2.4		2.9		2.4	
COPD	2.1					2.0		
Preoperative pneumonia						3.8		1.4
Preoperative dialysis		2.6		2.1				
Cancer metastasis/relapse	4.5			1.6				
Disseminated cancer		3.5	2.9	3.1	2.8			2.1
Preoperative transfusion					2.6			1.8
Bleeding disorder without therapy								1.6
Brinkman index							1.6	
Ascites								
Any		1.8		1.6	4.0	1.9		
Without control			2.8					
Chronic steroid use			2.8	2.0				1.9
Weight loss	2.0	1.6	2.2	1.6			2.1	1.4
Sepsis				1.7				
WBC								
>11,000/μl		2.0	2.5				3.1	
>9000/μl				1.6				
<4500/μl	1.8							1.5
<3500/μl		1.6						
Hemoglobin								
M < 13.5 g/dl, F < 12.5 g/dl					2.6			1.3
<10 g/dl						1.8		
Hematocrit								
M > 48 %, F > 42 %					3.6			

Table 3 continued

Variables	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
M < 37 %, F < 32 %			1.4	1.4				
<30 %		1.3						1.2
Platelet								
<120,000/μl	2.0		2.0	1.7	3.4	1.6	2.1	1.4
<80,000/μl				2.6		2.1		
Albumin								
<3.8 g/dl			1.7					
<3.5 g/dl	2.2	1.4				1.6		
<3.0 g/dl		1.4		1.5		1.7		1.4
<2.5 g/dl					2.7			
<2.0 g/dl								1.5
Total bilirubin								
>3.0 mg/dl								2.0
>2.0 mg/dl		2.8	2.6					
>1.0 mg/dl				1.6				
AST								
>40 U/l			1.5	2.7	1.9	1.7		
>35 U/l		1.7						1.4
ALP								
>600 U/l		3.1						1.6
>340 U/l			1.6					
BUN								
>60 mg/dl				2.4				
>25 mg/dl								1.3
>20 mg/dl								1.8
<8 mg/dl	2.6			1.6				
Creatinine								
>2.0 mg/dl								1.5
>1.2 mg/dl			1.8					
Serum Na								
>145 mEq/l				1.9				
<138 mEq/l	2.1	1.4		1.9	2.5			
<135 mEq/l			2.3					
<130 mEq/l								1.8
CRP								
<10.0 mg/dl								1.5
APTT								
>40 s			1.6				2.0	
PT-INR								
>1.25	3.0	1.9						
>1.1			1.5	1.4		1.4	1.5	
Non-tumor bearing								0.5
Surgical procedure		#1				#2		
indication for surgery						#3		

#1 Pancreatico splenectomy (2.2)

#2 Hepatectomy with S1 (1.6), S7 (1.6), S8 (2.0), left tri-segmentectomy with S1 resection (3.9), hepatectomy with revascularization (3.0)

#3 Intrahepatic cholangiocarcinoma (1.8), hilar bile duct carcinoma (2.0), gallbladder cancer (3.2)

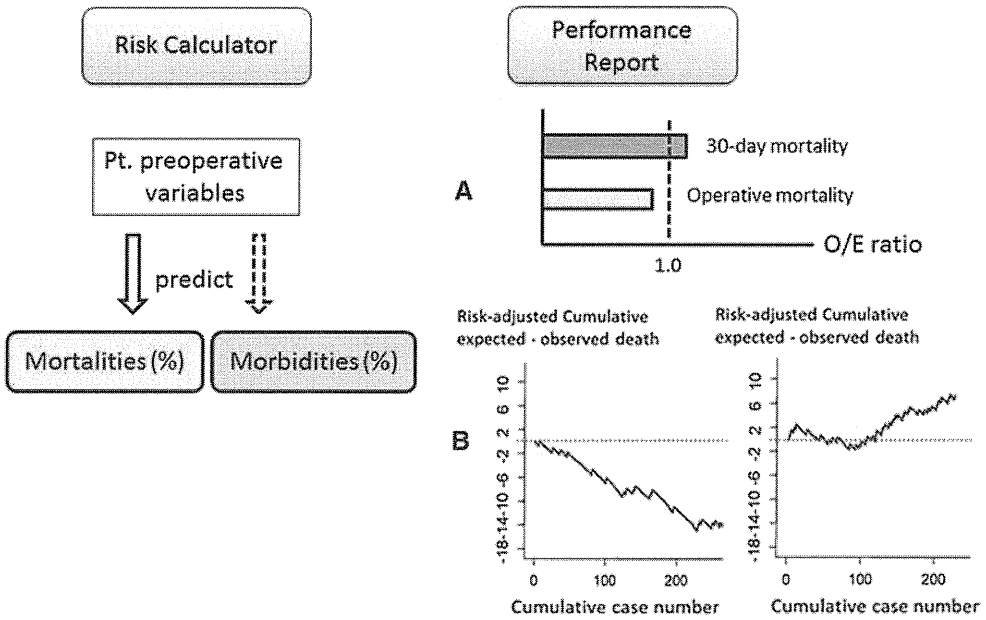

Fig. 1 The National Cancer Database feedback system includes a risk calculator for the mortality and morbidity of pre-operative patients (*left schema*) and performance reports of each participating hospital (*right schema*). The latter includes each facility's severity-adjusted clinical performance (*benchmark*) in comparison with the national data (**a**) and the risk-adjusted cumulative expected–observed death (**b**). Better (*right*) or worse (*left*) outcomes can be detected by the monitoring report

The NCD will soon be able to provide data on each facility's severity-adjusted clinical performance (benchmark), which can be compared with national data (Fig. 1a). Cumulative observed–expected mortality can be traced periodically after each operation and used to detect special cause variations showing better (right) and worse (left) outcomes (Fig. 1b).

Future evolution of NCD

A complete data acquisition system link to board certification

More than 4,000,000 cases were retrieved from the NCD during the 3 years before April 2013. The number of esophagectomy and pneumonectomy cases registered in the NCD accounted for approximately 95 % of all cases registered in the Regional Bureau of Health and Welfare. Thus, most cases in Japan appear to be captured by the NCD system. This NCD project started with support from Health and Labor Sciences Research Grants by the Ministry of Health Labour and Welfare (Principal Investigators; MG, T.I.) and considerable funding from the JSGS and JSS. Participating institutions can now use the database system at no cost; however, it is mandatory for the institutions to participate in the benchmarking project when applying for the board certification system. Currently, the board certification system is operating adequately on the web for surgical society members and allows members to obtain information on their cases being used to assess a member's qualifications for certification during a certain period. Any applicant who has a sufficient number of cases for application no longer needs to write case reports. All participating healthcare professionals use information acquired from the NCD. Moreover, the board certification system itself can be revalidated using the surgical improvement program of the NCD.

Share benefits and costs of the NCD with relevant stakeholders

A previous study by Hall et al. [5] showed that participation in the benchmark reporting system of the ACS-NSQIP improved surgical outcomes across all participating hospitals in the private sector. Improvement is reflected for both poor- and well-performing facilities. They speculated in the model using 183 participating hospitals that each institution may have avoided 200–500 complications and 12–36 deaths. Participation in the ACS-NSQIP benefits patients, surgeons, and hospitals and costs 10,000–29,000 (US$) depending on the ACS-NSQIP options [15.]

In the gastroenterological section, risk models of mortality for the eight procedures were created to enable feedback. Simultaneously, risk models of morbidities for the eight procedures are being created to enable feedback for the next year. Currently, the database system is built up to enable efficient provision of benchmark reports to each institute. The benefits and costs can now be shared with the relevant stakeholders. A participation fee depending on the number of cases for retrieval is expected to be charged by the NCD to each hospital. Research grants from various sources are also expected to support clinical investigations using the NCD data.

Eliminating burden on physicians and maintaining data accuracy

To avoid burdening physicians, the NCD allows data entry by other medical staff members. The NCD data entry privileges allow people other than physicians to enter the data. An appropriate educational system for data managers would be mandatory to maintain the accuracy of data and reduce the burden on physicians. This could be achieved by holding an annual data manager educational meeting and eventually introducing an e-learning system. The JSGS is planning to create an audit committee separately from the NCD, with the goal of achieving accurate data inputs and of educating data managers.

Quality improvement of surgical care for cancer patients

The NCD generalizes site-specific cancer registries by taking advantage of their excellent organizing ability. Some site-specific cancer registries have already been combined with the NCD [16]. Cooperation between the NCD and site-specific cancer registries can establish a valuable platform upon which a cancer care plan can be developed in Japan. Furthermore, information on the prognosis of cancer patients gathered using population- and hospital-based cancer registries can enable efficient data accumulation into the NCD.

Currently, quality assessment of hospitals is being carried out using the Diagnosis Procedure Combination (DPC) data from the participating hospitals [17, 18]. The DPC data include variables for preoperative morbidities, cancer variables, and postoperative complications, but they are based mainly on administrative claim data. A low participation rate by very small hospitals in the DPC system covers 50% of institutions conducting surgical services [17] and hampers complete enumeration. The NCD is a quality assessment and improvement program in which clinical data are used with a high collection rate (95 %). Site-specific cancer registries in the NCD would not only be more accurate and suitable for perioperative assessment, but also for long-term outcomes of cancer patients.

Further improvements through transparency

Public reporting and transparency are being demanded by multiple stakeholders [19, 20]. Although it has been shown that performance data released to the public promote quality improvement activity at the hospital level [21, 22], opponents counter that public reporting induces gaming and other unintended consequences such as "cherry picking" (hospitals selecting lower-risk patients to avoid poorer outcomes) or losing patients to better-performing hospitals [23]. With the consent of participating surgical societies, the NCD stated that the performance of each institute would be fed back only to respective institutes but not to the general public. This practice is similar to that of the ACS-NSQIP, from which a report is prepared for administrators and surgical services staff to compare their risk-adjusted surgical outcomes with those of participating sites that are blinded to data other than their own.

In 2012, the ACS-NSQIP partnered with the Centers for Medicare and Medicaid Services (CMS) to promote public reporting and transparency of surgical outcomes [24]. Although there were few measurable differences between CMS-NSQIP-participating and CMS-NSQIP-nonparticipating hospitals, it was found that of all possible hospital structural characteristics, only the teaching hospital status predicted participation in the CMS-NSQIP public reporting initiative. It may be a challenge for participating hospitals to show their performance to the general public. There is an interesting study by Sherman et al. [25, who investigated surgeons' perceptions of public reporting of hospital and individual surgeon quality. They stated that surgeons recommended patient education, simplified data presentation, and continued risk-adjustment refinement, and conducted an internal review before public reporting to make public reporting more acceptable for them. Linkage between hospital information systems and the NCD registry system may improve data accuracy and save costs. Presentation of care quality is increasingly regarded as imperative to support patients' choice and efficiency of care provision. We want medical professionals to realize that good to great performance can be achieved only through transparency for providers and patients.

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胆道癌全国登録データより見た胆嚢癌の動向

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要約：国際的にみて，日本は胆嚢癌の多い国の一つである。本稿では，胆道癌全国登録に登録され，予後調査の終了している1998～2011年度の胆嚢癌8,631例を対象とし，疫学の分析と胆道癌取扱い規約第5版に基づいた予後の検討を行った。男女比1：1.46であり，女性の割合が多かった。診断時年齢は，男女ともに，70歳代がピークであった。合併病変は，胆嚢結石，総胆管結石，膵・胆管合流異常の順に多かった。術前に胆嚢癌と診断された症例は76.3%であり，13.6%は良性疾患として手術されたincidental gallbladder cancerであった。切除率は75.0%であり，5年生存率は，非切除例2.9%，切除例48.2%であった。切除例は，非切除例に比し有意に予後良好（$P<0.001$）であった。組織学的胆嚢周囲進展度（pT），組織学的リンパ節転移（pN），総合的進行度（fStage）は，いずれも，その程度が進むにつれ，有意（$P<0.001$）に生存率は低下していた。

Key words：胆嚢癌，胆道癌全国登録，疫学，胆道癌取扱い規約

はじめに

胆嚢癌の国別年齢調整罹患率は，女性は，チリ，インド，スロバキア，チェコ，ドイツに次いで6位，男性は，チリ，インド，韓国，チェコに次いで5位であり[1]，国際的にみて，日本は胆嚢癌の多い国の一つである。本邦の胆嚢癌の詳細な集積は，日本肝胆膵外科学会の胆道癌登録事業により行われている。

そこで本稿では，胆道癌全国登録に登録され，予後調査の終了している1998～2011年の胆嚢癌8,631例を対象とし，胆道癌取扱い規約第5版[2]に基づき検討を行った。

Recent Trend of Gallbladder Cancer in Japan：Results from The Biliary Tract Cancer Statistics Registry
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Ⅰ．患者背景

1．性別，年齢

性別は，男性3,192例，女性4,663例，男女比1：1.46であり，女性の割合が多かった。

年齢別男女比は，男性を1とした場合の女性の比率は，30歳未満1.0，30歳代1.0，40歳代0.9，50歳代1.2，60歳代1.1，70歳代1.2，80歳代1.4，90歳代2.6であった。40歳未満では，男女差は認めず，40歳代は，女性より男性が多かった。40歳代の初発症状における無症状の割合は，男性42.4%，女性29.8%であり，男性の方が，無症状で発見される割合が女性より有意（$P=0.030$）に多く，職場検診などによる影響が考えられた。

診断時年齢（図1）は，男女ともに，70歳代がピークであり，次いで60歳代，80歳代の順であった。

2．初発症状

初発症状は，症状のないものが32.8%，有症状例が62.7%であった（表1）。有症状例の内訳は，腹痛（52.5%），黄疸（15.9%），全身倦怠感（9.6%），食思不振（8.0%），発熱（7.2%）が多い症状であった。

Prognostic value of intraoperative pleural lavage cytology for non–small cell lung cancer: The influence of positive pleural lavage cytology results on T classification

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Objective: Although positive pleural lavage cytology (PLC) has been demonstrated to be closely associated with a poor prognosis for patients with lung cancer, it has not been incorporated into the TNM staging system of the Union for International Cancer Control. The aim of our study was to retrospectively examine the clinical significance of PLC status and illustrate the recommendations of the International Pleural Lavage Cytology Collaborators (IPLCC) in a large national database.

Methods: The Japanese Joint Committee of Lung Cancer Registry database included 11,073 patients with non–small cell lung cancer who underwent resections in 2004. We extracted the clinicopathologic data for 4171 patients (37.3%) who underwent PLC. These patients were staged according to the seventh edition of the Union for International Cancer Control TNM classification and by recommendations of the IPLCC, in which T was singly upgraded up to a maximum of T4 for those who were PLC-positive. Prognoses based on these 2 systems were compared.

Results: A total of 217 patients (5.2%) were PLC-positive, which was significantly associated with a higher incidence of adenocarcinoma and advanced disease. The 5-year survival for patients with positive and negative PLC results were 44.5% and 72.8%, respectively, and this difference in survival was statistically significant ($P < .001$). Multivariate analysis showed that positive PLC status was an independent factor for a poor prognosis (hazard ratio, 1.57; $P < .001$). Significant differences in survival were also found between patients with positive and negative PLC results in the same T categories and stages, including T2a, T3, stage IB, and stage IIIA. The IPLCC recommendations adjusted the prognostic differences in all T categories and stages. The significant difference in survival disappeared between the 2 groups in all T categories and stages.

Conclusions: Our results indicate that a T category upgrade is prognostically adequate for patients who are PLC-positive. (J Thorac Cardiovasc Surg 2014;148:2659-64)

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See related commentary on pages 2665-6.

For surgical cases of primary lung cancer, pleural lavage cytology (PLC) is a simple, easily done technique that provides a cytodiagnosis at the time of thoracotomy to evaluate subclinical pleural dissemination of cancer cells without pleural dissemination or pleural effusion. After a PLC result was first reported by Eagan and colleagues[1] in 1984, numerous studies have shown that PLC status is a prognostic factor for primary lung cancer.[2-22] In general, the frequency of positive results is <10% of patients who underwent PLC in the larger published series. In previous multiinstitution studies, a positive PLC result was suggested to be an independent prognostic factor and a predictor of tumor recurrence.[22-26]

However, PLC findings were not incorporated in the TNM Classification of Malignant Tumours.[27,28] In 2010, the

Abbreviations and Acronyms

IPLCC = International Pleural Lavage Cytology Collaborators
NSCLC = non–small cell lung cancer
PLC = pleural lavage cytology
UICC = Union for International Cancer Control

International Pleural Lavage Cytology Collaborators (IPLCC) reported the results of a meta-analysis and recommended that a single increase in the T category up to a maximum of T4 be assigned to patients with positive PLC results.[24]

The aim of our study was to retrospectively examine the clinical significance of PLC status and to illustrate the recommendations of the IPLCC. We used a large national database that were compiled by the Japanese Joint Committee of Lung Cancer Registry.[29,30]

PATIENTS AND METHODS

In 2010, the Japanese Joint Committee of Lung Cancer Registry performed a nationwide retrospective registry study on the prognosis and clinicopathologic profiles of resected lung neoplasms in Japan.[29,30] Only primary lung neoplasms that had been resected in 2004 at certified teaching hospitals in Japan were considered for the registry, which provided a follow-up period of at least 5 years. The committee received the registries of 11,663 patients from 253 teaching hospitals.

This registry followed the ethical guidelines for epidemiologic studies published jointly by the Japan Ministry of Science, Culture, and Education and the Japan Ministry of Health, Labor, and Welfare published June 17, 2002, which were revised August 16, 2007. In addition, it was approved by the institutional review board of Osaka University Medical Hospital, where the registry office is located, after discussions were published August 13, 2009 (approval No. 09124).

The patients in this study were 4171 patients who underwent PLC from among 11,073 patients with non–small cell lung cancer (NSCLC) (37.3%). Cases involving malignant pleural effusion were excluded. There were 2524 men and 1647 women. Adenocarcinoma was detected in 2977 patients, squamous cell carcinoma in 881 patients, large cell carcinoma in 149 patients, adenosquamous carcinoma in 81 patients, and other histologic types in 83 patients. The seventh edition of the Union for International Cancer Control (UICC) TNM classification system was used for the evaluations of TNM staging.[28] There were 1694 patients in stage IA, 1009 patients in stage IB, 378 patients in stage IIA, 262 patients in stage IIB, 703 patients in stage IIIA, 38 patients in stage IIIB, and 87 patients in stage IV. In our study, the PLC technique used had not been standardized. Induction therapy was performed in 199 patients (chemotherapy in 118 patients, radiation therapy in 6 patients, and chemoradiotherapy in 75 patients). Adjuvant chemotherapy was administered to 977 patients. These menus were not uniform.

To correct the prognoses according to the pathologic stages of patients with positive PLC results to patients with negative PLC results, pathologic stages were reevaluated based on the recommendations of the IPLCC: a single increase in the p-T category up to a maximum of T4 was assigned to patients with a positive PLC result (upstage).[24] Single increases in the T category upstaged T1a to T1b, T1b to T2a, T2a to T2b, T2b to T3, and T3 to T4. Pathologic stages were rearranged according to the upstaged T categories.

Categorical data are presented as frequency and continuous data are presented as means with standard deviations. Comparisons of categorical data between the 2 groups were made using χ^2 tests or Fisher exact tests where appropriate and continuous data were compared using 2-tailed *t* test. The survival time was measured from the date of surgery to the death date or the last follow-up date. The survival curves were estimated by using the Kaplan-Meier method. Differences in survival were assessed by the log-rank test. Multivariate analyses of prognostic factors were carried out using Cox proportional hazard regression models. A P value <.05 was considered to be significant.

RESULTS

Among 4171 patients who underwent PLC, 217 patients (5.2%) had positive PLC results (Table 1). Patients with positive PLC results had larger tumors ($P < .0001$) and more frequently adenocarcinoma in the histology ($P < .0001$), advanced stage ($P < .0001$), and pleural invasion ($P < .0001$) in comparison with those who were PLC-negative.

Sixty-five percent of patients with positive PLC and 29.2% of PLC-negative patients developed recurrence within 5 years after surgery ($P < .0001$). The 5-year survival was 44.5% for patients with positive PLC results and was 72.8% for patients with negative PLC results ($P < .0001$) (Figure 1). By multivariate analysis using a Cox proportional hazard regression model, PLC status (hazard ratio, 1.57; 95% confidence interval, 1.276-1.919; $P < .0001$) and other clinical factors (ie, gender, age, T category, N category, M category, and tumor size) were independent prognostic factors (Table 2).

Comparisons of the survival between patients with positive and negative PLC results according to T categories revealed significant differences in T2a ($P < .0001$) and T3 ($P = .0184$) (Figure 2 and Table 3). In addition, comparisons of the survival between patients with positive and negative PLC results according to pathologic stages revealed significant differences in stage IB ($P = .0062$) and stage IIIA ($P = .0115$) (Table 3). Based on the recommendations of the IPLCC, if a single increase in the T category up to a maximum of T4 was assigned to a patient with a positive PLC result, the significant difference in survival disappeared between the 2 groups in all T categories and stages. (Figure 3 and Table 4).

DISCUSSION

Body cavity fluid cytology is a simple, easily done technique that provides an intraoperative cytodiagnostic evaluation of latent dissemination of cancer cells.[31] In surgical cases of abdominal malignant tumors, PLC status is an independent prognostic factor, as reflected in the UICC TNM classification for gastric, uterine, ovarian, and fallopian tube cancers.[28] PLC status is directly involved in the treatment strategy. However, PLC findings were not incorporated in the seventh edition of the UICC TNM staging system.[28,32] It is not known to what extent the noninclusion of PLC results affects treatment strategies.

In this study, 5.2% of patients who underwent PLC had positive results. When these patients were examined by T,

TABLE 1. Clinicopathologic characteristics according to pleural lavage cytology (PLC) results

Characteristic	Positive PLC	Negative PLC	*P* value
Age (y)	66.2 ± 9.9	66.3 ± 9.8	.9040
Gender			.0640
Male	118	2406	
Female	99	1548	
Histologic type			<.0001
Adenocarcinoma	193	2784	
Squamous cell carcinoma	19	862	
Others	5	308	
Surgical procedure			.0460
Pneumonectomy	9	121	
Lobectomy	177	3239	
Segmentectomy	14	321	
Wedge resection	10	234	
Others	7	38	
T category			<.0001
T1a	14	1147	
T1b	12	771	
T2a	138	1390	
T2b	9	186	
T3	35	394	
T4	9	66	
N category			<.0001
N0	109	3040	
N1	26	318	
N2	81	584	
N3	1	12	
M category			<.0001
M0	187	3886	
M1a	27	30	
M1b	3	38	
Pathologic stage			<.0001
IA	15	1679	
IB	60	949	
IIA	23	355	
IIB	12	250	
IIIA	74	629	
IIIB	4	34	
IV	29	58	
Tumor size (cm)	3.40 ± 1.63	2.99 ± 1.80	
Pleural factor			<.0001
pl 0	47	2759	
pl 1	56	669	
pl 2	85	229	
pl 3	25	279	
Not evaluated	4	18	
Total	217	3954	

PLC, Pleural lavage cytology.

N, and M categories and by pathologic stages, significantly higher percentages of advanced cases were seen among patients with positive PLC results compared with patients with negative PLC results. Patients with positive PLC results also had significantly larger tumors than those who were PLC-negative. A significantly higher percentage of

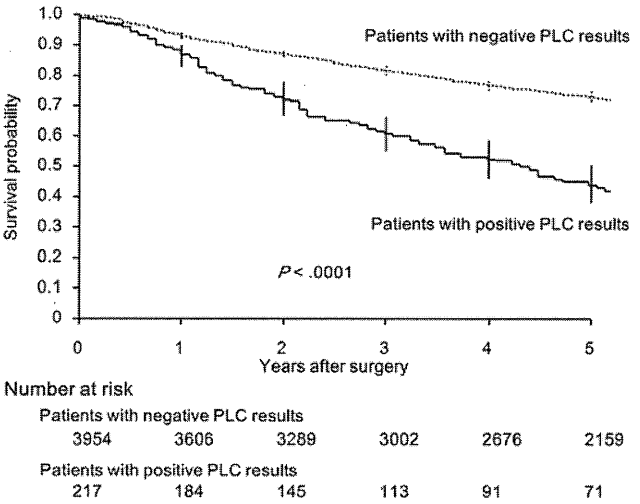

FIGURE 1. Postoperative survival curves based on pleural lavage cytology (*PLC*) status. There was a significant difference between patients with positive and negative PLC results ($P < .0001$). The *solid line* indicates patients with positive PLC results and the *dashed line* indicates patients with negative PLC results. The *vertical bars* indicate 95% confidence intervals.

pleural invasion was evident among patients with positive PLC results compared with those who were PLC-negative. These characteristics are consistent with those described in previous reports.[1,9,10,12,14,19] In our study, the 5-year survival was 44.5% for patients with positive PLC results and 72.8% for patients with negative PLC results, which indicated a significantly worse prognosis for patients with positive PLC results. A multivariate analysis revealed that PLC finding is an independent prognostic

TABLE 2. Multivariate analysis for prognostic factors

Prognostic factor	Hazard ratio	95% Confidence interval	*P* value
Positive PLC	1.57	1.276-1.919	<.0001
Male gender	1.66	1.460-1.894	<.0001
Age, per year	1.03	1.023-1.036	<.0001
T category			
T1a	1.00	—	—
T1b	1.59	1.266-1.990	<.0001
T2a	2.01	1.645-2.461	<.0001
T2b	2.79	2.048-3.794	<.0001
T3	2.94	2.271-3.807	<.0001
T4	3.87	2.692-5.564	<.0001
N category			
N0	1.00	—	—
N1	1.76	1.459-2.111	<.0001
N2	3.13	2.735-3.580	<.0001
N3	9.27	5.083-16.913	<.0001
M category			
M0	1.00	—	—
M1a	1.89	1.349-2.643	<.0001
M1b	4.02	2.601-6.206	<.0001
Tumor size (cm)	1.05	1.014-1.085	.006

PLC, Pleural lavage cytology.