

# Surgical mortality in patients with malignant obstructive jaundice: a multivariate discriminant analysis

Xi-Chun Han, Jin-Long Li and Gang Han

Changchun, China

**OBJECTIVE:** To estimate the operative mortality in patients with malignant obstructive jaundice.

**METHODS:** Twelve risk factors were analyzed using multivariate discriminant analysis in 90 patients who had been operated on.

**RESULTS:** Operative mortality was significantly related to the following factors: age, duration of jaundice, packed RBC volume, white blood cell count and concentration of blood urine nitrogen; it was not significantly related to diseases and types of operation. The following formula was obtained: packed RBC volume  $\times 0.09954$  - age  $\times 0.04018$  - blood urine nitrogen  $\times 0.23693$  - duration of jaundice  $\times 2.07388$  - WBC count  $\times 0.21118 + 5.26593$ . With this formula, an operative mortality of 77.8% was predicted.

**CONCLUSION:** With a positive value from the formula, the patient should be operated on; otherwise non-operative treatment is advocated.

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**Key words:** malignant obstructive jaundice; postoperative mortality; multivariate discriminant analysis

## Introduction

In patients with obstructive jaundice, formidable mortality is frequent after surgery. Patients with malignant biliary tract disease involve a high operative risk as noted by Dixon et al.<sup>[1]</sup> Even in the recently reported series, postoperative death would occur in 20% to 28.6% of the patients.<sup>[1-3]</sup> The aim of this study was to evaluate prognostic factors affecting operative mortality in patients with malignant obstruction jaundice based on the results of multivariate analysis.

## Methods

Ninety consecutive patients were operated on from October 1994 to October 1999 at the Second Hospital of Jilin University, Changchun, China. Included patients were at age of 18 years or more, with a serum bilirubin concentration of more than 50  $\mu\text{mol/L}$ , as a result of obstructive carcinoma of the biliary duct, pancreas or liver. Patients with a serum bilirubin concentration of less than 50  $\mu\text{mol/L}$  or whose jaundice was caused by benign diseases were excluded.

Histopathological proof of malignancy was obtained only in 24 patients. Because of the inherent risks, biopsy specimens were not regarded essential for patients who were to undergo palliative treatment, so the malignant causes of jaundice was diagnosed in the remaining 66 patients by clinical, operative, or follow up criteria. There were 58 patients with carcinoma of the pancreas, 8 with ampullary carcinoma, 19 with carcinoma of the bile

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From the Department of Surgery, Second Hospital, Jilin University, Changchun 130041, China (Han XC, Li JL and Han G)

Correspondence: Xi-Chun Han, MD, Department of Surgery, Second Hospital, Jilin University, Changchun 130041, China (Tel: 86-431-8974617 ext6552; Fax: 86-431-8934741; Email: hanchun601@sohu.com)

**Table 1.** Diagnosis, operation and deaths (in paranthese)

Tumors	Operations						Total
	Hepatico-jejunostomy	Choledocho-jejunostomy	Cholecysto-jejunostomy	Resection + bypass	Pancreato-duodenectomy	Exploratory laparotomy	
Cancer of pancreas	0	4(1)	43(6)	0	8(2)	3(1)	58(10)
Carcinoma of ampulla	0	0	4(1)	0	3(1)	1	8(2)
Cholangiocarcinoma	4(1)	0	3	6(1)	0	1	14(2)
Carcinoma of gallbladder	2	0	0	2	0	1(1)	5(1)
Carcinoma of porta hepatis	3(1)	0	0	0	0	0	3(1)
Metastasized carcinoma	0	0	0	0	0	2(1)	2(1)
Total	9(2)	4(1)	50(7)	8(1)	11(3)	8(3)	90(17)

duct (including 5 with carcinoma of the gallbladder), and 5 with other malignant tumors (hepatic or lymph nodes metastasis). Of these 90 patients, 9 had peritoneal carcinomatosis, and 5, ascites. In this study, operative mortality was defined as death within 30 days after operation.

Clinical and laboratory data were collected at the time of admission. Clinical factors recorded included age and duration of jaundice before operation. Blood tests included packed red blood cell volume, white blood cell count, serum concentrations of bilirubin, albumin, and blood urine nitrogen, activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase. Two factors were also considered: the type of operation (excision or bypass) and the cause of jaundice (periampulla or biliary carcinoma). All the 90 patients were operated on: exploratory laparotomy (8 patients), biliary bypass (71), and Whipple procedures (11) (Table 1).

## Results

In this group, 48 were men and 42 women, with a mean age of 66.58 (12.13). The mean values and percentages of two clinical and eight biochemical variables are listed in Table 2. The overall mortality was 19% ( $n = 17$ ) and the causes of death are listed in Table 3. Univariate analysis showed that survival was highly correlated with age, packed red blood cell volume, white blood cell count, concentrations of bilirubin, albumin, blood urine nitrogen and duration of jaundice, but not with the type of operation or the type of adenocarcinoma (Table 4).

Discriminant analysis allowed 70 patients (77.8%) to be classified correctly. Factors that were significantly related to death were packed cell volume, age, blood urine nitrogen, duration of jaundice, and white cell count. Based on these data we calculated a mortality index: Packed RBC volume  $\times 0.09954$  - Age  $\times 0.04018$  - Blood urine nitrogen  $\times 0.23693$  - Duration of jaundice  $\times 2.07388$  - WBC count  $\times 0.21118 + 5.26593$ .

Patients with negative values had a high probability to death, whereas those with positive values had a high probability to survive after the operation.

**Table 2.** Ten clinical and lab variables

Variables	Average value (SD)
Age	66.58(12.13)
Duration of jaundice (month)	1.15(0.61)
Packed RBC volumn (%)	38.50(4.80)
White cell count ( $\times 10^9$ )	8.35(3.16)
Serum bilirubin ( $\mu\text{mol/L}$ )	261.36(125.51)
Serum albumin (g/L)	36.87(5.63)
AST (U/L)	86.48(47.68)
ALT (U/L)	90.56(49.65)
Alkaline phosphatase (U/L)	557.10(203.75)
Blood urine nitrogen ( $\mu\text{mol/L}$ )	5.52(2.91)

**Table 3.** Death cause of patients

Causes of death	Number
Cachexia	3
Acute renal failure	2
Pulmonary infection	1
Upper alimentary canal hemorrhage	1
Abdominal abscess	2
MOSF	8
Total	17

**Table 4.** Operative mortality: univariate analysis of 12 variables (SD)

Variables	Survivors (n = 73)	Deaths (n = 17)	P value
Age	64.8(11.8)	74.1(10.2)	0.0045
Duration of jaundice (month)	1.02(0.51)	1.70(0.72)	0.0001
Packed RBC volume (%)	39.2(4.5)	35.5(4.8)	0.0031
White cell count ( × 10 <sup>9</sup> /L)	7.92(2.71)	10.2(4.26)	0.0080
Serum bilirubin ( μmol/L)	248.4(126.2)	317.1(109.2)	0.0417
Albumin (g/L)	37.86(5.30)	32.62(5.11)	0.0004
AST (U/L)	84.26(46.72)	96.05(52.11)	0.3639
ALT (U/L)	86.03(43.7)	110.5(68.2)	0.0728
Alkaline phosphatase ( μmol/L)	540.22(178.75)	634.25(271.32)	0.0970
Blood urine nitrogen ( μmol/L)	4.87(2.66)	6.78(3.27)	0.0322
Operation (%)			
Resection	15(28.94)	4(5.56)	0.4771
Bypass or drainage	53(31.07)	10(7.43)	0.9833
Exploratory laparotomy alone	5(14.59)	3(5.64)	0.3730
Diagnosis (%)			
Periampullary carcinoma	54(32.78)	12(8.37)	0.5230
Carcinoma of bile duct	16(31.21)	3(7.98)	0.6016
Other malignant tumors	3(2.92)	2(2.00)	0.7527

**Table 5.** Complications and their relationship to mortality

Complication	Morbidity		Mortality	
	n	%	n	%
Renal failure	15	16.67	9	60.00 *
Infection of incisional wound	11	12.22	6	54.55 **
Upper alimentary tract haemorrhage	2	2.22	1	50.00
Urinary infection	4	4.44	1	25.00
Abdominal infection	4	4.44	2	50.00
Pulmonary infection	6	6.67	4	66.67 *
Pancreatitis	1	1.11	0	0
Others	4	4.44	0	0

\* P < 0.01; \*\* P < 0.05; patients with complications compared with those without complications.

**Table 6.** Complications significantly related to mortality and their relationship to risk factors

Risk factors	Complications		
	Renal failure	Wound infection	Pulmonary infection
WBC count ( × 10 <sup>9</sup> )	10.41(4.22) *	9.56(4.51) **	10.80(3.29) *
Packed RBC volume (%)	39.5(5.3)	37.9(4.1)	38.2(5.1)
Urine nitrogen ( μmol/L)	6.91(3.21) *	5.61(4.36)	5.57(3.75)
Age (years)	72.3(13.1) *	68.7(15.2)	69.4(17.1)
Duration of jaundice (month)	1.40(0.81) **	1.15(0.73)	1.22(0.65)

\* P < 0.01; \*\* P < 0.05; patients with complications compared with those without complications.

operative period. Discriminant analysis also showed that diseases did not influence the outcome.

Complications and their relations to mortality are shown in Table 5. The most common complications included acute renal failure (15 patients) and wound infection (11). Acute renal failure, wound infection, and pulmonary infection were significantly related to mortality among all complications and they were related to five independent risk factors, suggesting that postoperative renal failure is related to white blood cell count, age, and duration of jaundice, but wound infection and pulmonary infection are only related to white blood cell count (Table 6).

## Discussion

Utilizing discriminant analysis and five factors enabled us to classify correctly more than 75% of the patients with respect to the probability of postoperative death. These factors included packed cell volume, age, blood urine nitrogen, duration of jaundice, and white cell count. Concentrations of bilirubin and albumin, which were significantly related to survival in the univariate analysis, lost their significance in the multivariate analysis (discriminant analysis).

Our population was defined to include consecutive patients with malignant obstructive jaundice. This encompassed patients with jaundice of various causes from intrahepatic obstruction to periampullary cancer. Whether in univariate analysis or multivariate analysis, there was no significant correlation between survival and the type of operation or the type of cancer.<sup>[4]</sup>

Mortality is related to the duration of jaundice in univariate analysis, the longer the duration, and the worse the prognosis. In these previous studies, some have not studied the relationship between mortality and the duration of jaundice,<sup>[2-5]</sup> and some have not got any evidence for jaundice-related mortality.<sup>[6,7]</sup> The result of the present study suggested that early diagnosis and treatment plays an important role in the prognosis of patients with malignant obstructive jaundice.

Although activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase can determine whether there is hypofunction of the liver, they are not significantly correlated with the survival either in univariate analysis or in multivariate analysis. Dixon and Bonnel et al<sup>[1,5]</sup> shared a same conclusion with us; whereas Pitt et al<sup>[2]</sup> and Little et al<sup>[8]</sup> thought that the mortality is related to the activity of alkaline phosphatase and aminotransferase respectively. Fraser and Nakayama et al<sup>[9,10]</sup> considered that mitochondrion respiratory controlling rate (MRCR) is more sensitive than aminotransferase and alkaline phosphatase as an index of liver damage, and that MRCR seems to be independent of these liver enzymes, but does relate to the duration of jaundice. The MRCR is decreased a little bit in short-term jaundice patients and recovered quickly after the repassing of the obstructive bile duct; but in long-term jaundice patients, opposite result would be obtained. This conclusion also supports that the mortality is related well to the duration of jaundice.

The concentration of bilirubin is related to the survival in univariate analysis but not in multivariate analysis. A retrospective study<sup>[10]</sup> indicated that the patients prepared preoperatively with percutaneous transhepatic decompression had a lower mortality than those undergoing biliary surgery

without preoperative decompression (8% to 28%). But the following prospective studies haven't obtained the same conclusion. A percutaneous transhepatic decompression decreased the concentration of bilirubin about 40% in 10 to 20 days, but not the mortality.<sup>[11,12]</sup> McPerson et al<sup>[13-15]</sup> observed 65 patients suffering from malignant obstructive jaundice and found a mortality of 32% for the patients prepared preoperatively with percutaneous transhepatic decompression, and a mortality of 19% for the patients without percutaneous transhepatic decompression. Zou et al<sup>[16]</sup> got the similar result. Others<sup>[17]</sup> found that preoperative biliary drainage may improve cytokine and acute-phase response derangements in 24 patients with obstructive jaundice so that cause an increased operative mortality. Aly and Johnson<sup>[18]</sup> reviewed all papers about experimental or clinical observations of preoperative biliary drainage and found that there is no evidence to support the view that routine preoperative biliary drainage improves postoperative mortality in patients with obstructive jaundice. Carios<sup>[19]</sup> considered a high concentration of bilirubin is usually associated with old age in operative patients, which couldn't be excluded. His patients prepared preoperatively with percutaneous transhepatic decompression did not get a lower mortality. The preoperative concentration of bilirubin is not one of the independent factors which determine mortality, but it is related to the duration of jaundice. Hutun et al<sup>[20]</sup> found that the longer the duration of jaundice the worse the prognosis.

White cell count has a significant correlation with operative mortality both in univariate analysis and multivariate analysis. An increasing white cell count usually suggests a patient with a biliary infection.<sup>[18]</sup> There is a significant correlation between an increased white cell count and postoperative complications such as acute renal failure, wound infection and pulmonary infection. These complications will result in an increasing mortality.

Packed RBC volume is also related to mortality in multivariate analysis, whereas serum albumin is only related to mortality in univariate analysis. Satisfied serum albumin indicates a good nutrition, vice versa. These factors are related to operative mortality, indicating poor nutrition goes with bad

prognosis. We still consider anemia and hypoproteinemia the risk factors for operative mortality.

Acute renal failure proves to be a common complication in patients with malignant obstructive jaundice (about 9%–36%). Once it occurs, operative mortality can reach to 76%.<sup>[21,22]</sup> There is an obviously lower mortality in patients without jaundice signs than in those with jaundice signs when they have received biliary operation. Obstructive jaundiced patients are usually accompanied with impaired renal function because of concurrent endotoxemia.<sup>[21]</sup> Our study indicated that increased level of blood urine nitrogen does have a relationship with postoperative acute renal failure, which can obviously increase the operative mortality. Hence, improving renal function will help decrease operative mortality.

There is no significant correlation between the type of operation and the cause of jaundice.<sup>[16]</sup> In developing countries, although exploratory laparotomy and palliative surgery (when possible) are the only option since sophisticated instruments and expertise are limited there,<sup>[23]</sup> active operative procedure should be performed by experienced surgeons to improve the survival and life quality of patients. When palliative treatment of malignant jaundice has to be selected, bile duct bypass should be chosen rather than gallbladder bypass because the latter produces more complications or more additional surgical procedures.<sup>[24]</sup>

## Competing interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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