Original Article

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Regression analysis of the risk factors for postoperative nosocomial infection in patients with abdominal tumors: experience from a large cancer centre in China

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Summary **Nosocomial infection is a common complication after abdominal oncology surgery. Aimed at finding its independent risk factors for prevention, all the patients who underwent abdominal oncology surgery were summarized from March 1st, 2010 to March 1st, 2013 from the oncology surgery department, Beijing Shijitan Hospital. The investigated variances were patients' information including admission number, sex, age, diabetes, diagnosis, length of stay, American society of anesthesiologists (ASA) grade, surgery time, number of drainage tubes. Comparisons were taken between the infected cases and non-infected cases for retrospective logistic regression analysis. 4 variances including diabetes, preoperative hospitalization time ≥ 6 days, surgery time ≥ 230 minutes, ASA grade ≥ III were found out to be related to nosocomial infection after surgery. The 4 variances mentioned above were risk factors for nosocomial infection after surgery.**

Keywords: Nosocomial infection, regression analysis, oncology surgery

1. Introduction

In patients who underwent surgical procedures, the natural barrier against bacteria was broken by surgical trauma or invasive procedures such as tracheal intubation under general anesthesia, central venous cannulation, urethral catheterization and gastrointestinal decompression (*1-4*). Long-term postoperative application of broad-spectrum antibiotics also increased the possibility of dysbacteriosis (*5,6*). Some scholars investigated the mortality in patients experiencing postoperative nosocomial infection in the departments of general surgery. The results showed 7.5% mortality in patients with single-pathogen nosocomial infection and a mortality of 17.1% in patients with multiple-pathogen mixed infection, which is higher than the average postoperative mortality of 0.53% (*7*).

The patients who underwent surgical operations were a high-risk population for nosocomial infection. Based on analysis of post-surgery patients in 30 countries by International Nosocomial Infection Control Consortium, the nosocomial infection rate was 2.88% (*8*). Some analyses of risk factors have been reported to reduce and control the occurrence of such complications previously (*9,10*). The primary objective of our study was to identify the independent risk factors of postoperative nosocomial infection. Subsequently we can manage patients by different postoperative infection risk levels, and establish a set of effective protocols for the prevention and control of infections in high-risk populations.

2. Materials and Methods

2.1. *Patients*

All postoperative patients with abdominal digestive tumors underwent surgical procedures in Capital Medical Cancer Centre, Beijing Shijitan Hospital between March 1st, 2010 and March 1st, 2013 were included. The analytical contents included the gender, age, diabetes mellitus, diagnosis, preoperative hospitalization days, American society of anesthesiologists (ASA) grade, type

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Table 1. Percentiles of continuous variables in presumptive risk factors

Risk factor	5%	10%	25%	50%	75%	90%	95%
Age	38.85	43.00	51.00	58.00	68.00	74.00	78.00
Preoperative hospitalization days	2.00	2.00	3.00	4.00	6.00	10.00	12.00
Operation time	65.00	90.00	120.00	170.00	230.00	280.00	315.00
Number of drainage tubes	1.00	2.00	2.00	2.00	2.00	3.00	3.00
Postoperative hospitalization days	5.00	8.00	9.00	11.00	15.00	20.00	27.30

In order to take the logistic regression analysis, all continuous variables were divided into binomial variables using 75% as the cut-off point. Accordingly, age ≥ 68 years, preoperative hospitalization stay≥ 6 days, operation time ≥ 230 minutes, drainage tubes ≥ 3, ASA ≥ class III were the presumptive risk factors.

of surgery, number of drainage tubes, and central venous catheters to identify the independent risk factors. The presumptive risk factors referred to the article published by "National Nosocomial Infection Surveillance" of the U.S. Center for Disease Control in 2003 (*1*).

2.2. *Inclusion and grouping criteria*

The included patients were randomized into the observation group or the control group. The diagnosis of patients with nosocomial infection was based on the diagnostic criteria for nosocomial infection issued by the ministry of health in 2001 (*2*). The patients who suffered from nosocomial infection after surgery were included in the observation group. The patients who underwent surgical procedures during the same period without nosocomial infection were included in the control group.

2.3. *Collection and identification of microbe samples*

The collection of pathogenic microbe samples complied with "Good Laboratory Practice". The identification employed VITEK-2 automated microbial identification system made by French bioMérieux; the drug sensitivity test followed National Committee for Clinical Laboratory Standard.

2.4. *Determination of the statistical indexes*

With reference to the statistical index processing method reported by Daniel N Nan (*5*), the means of all variables were calculated and all variables were divided into binomial variables using 75% as the cut-off point. Accordingly, age ≥ 68 years, preoperative hospitalization stay ≥ 6 days, operation time ≥ 230 minutes, drainage tubes ≥ 3, ASA ≥ class III and diabetes mellitus were the presumptive risk factors (Table 1). Their presence and absence were regarded as binomial variables.

2.5. *Statistical analysis*

These cases were calculated by a retrospective logistic regression analysis method. SPSS (version 19.0.2; SAS Institute Inc., Cary, NC) software was employed for statistical analysis.

Table 2. Diagnostic frequency of the included patients

Diagnosis	Frequency	Percent	Valid Percent
Carcinoma of the distal bile duct	71	5.9	5.9
Carcinoma of the gallbladder	12	1.0	1.0
Hepatocellular carcinoma	69	5.8	5.8
Hilar cholangiocarcinoma	15	1.3	1.3
Periampullary carcinoma	8	0.7	0.7
Colon cancer	251	21.0	21.0
Malignant lymphoma of the colon	1	0.1	0.1
Duodenal cancer	33	2.8	2.8
Gastric cancer	401	33.5	33.5
Carcinoma of pancreatic body and tail	4	0.3	0.3
Carcinoma of pancreatic head	61	5.1	5.1
Sigmoid colon cancer	40	3.3	3.3
Colorectal cancer	230	19.2	19.2
Total	1196	100.0	100.0

Table 3. Diagnostic frequency of the infected patients

Diagnosis	Frequency	Percent	Valid Percent
Cholangiocarcinoma	7	5.9	5.9
Hepatocellular carcinoma	6	5.1	5.1
Hilar cholangiocarcinoma	2	1.7	1.7
Colon cancer	19	16.1	16.1
Duodenal cancer	7	5.9	5.9
Gastric cancer	25	21.2	21.2
Carcinoma of pancreatic head	3	2.5	2.5
Pancreatic cancer	9	7.6	7.6
Colorectal cancer	9	7.6	7.6
Total	118	100.0	100.0

3. Results

During the study period, 1,196 consecutive patients underwent surgeries for abdominal digestive system malignancies (Table 2). There were 87 patients who suffered from infections including 22 cases of mixed infections. The infection person-times were 118 (Table 3).

The overall postoperative infection rate was 7.3%. In all patients who suffered from postoperative nosocomial infection, the major infection sites were distributed as follows: 38.1% pulmonary infection, 12.7% biliary tract infections, and 11.9% surgical site infection (Table 4).

Nosocomial infection was mainly caused by Gram-negative bacteria which accounted for 45.8% of

Table 4. Sampling sites of nosocomial infection pathogens

Sample	Frequency	Percent	Valid Percent
Stool culture	1	0.8	0.8
Bile	15	12.7	12.7
Catheter	4	3.4	3.4
Feces	4	3.4	3.4
Ascites	7	5.9	5.9
Urine	3	2.5	2.5
Pus	1	0.8	0.8
Incision	1	0.8	0.8
Sputum	45	38.1	38.1
Pleural fluid	3	2.5	2.5
Blood culture	8	6.8	6.8
Pharyngeal swabs	12	10.2	10.2
Drainage fluid	14	11.9	11.9
Total	118	100.0	100.0

Table 5. Type of nosocomial infection pathogens

Pathogen	Frequency	Percent
Gram-positive	36	30.5
Gram-negative	54	45.8
Fungus	28	23.7
Total	118	100.0

Table 6. Strains of nosocomial infection pathogens

Pathogen	Frequency	Percent
MRSA	21	17.8
Candida albicans	13	11.0
Acinetobacter baumannii	10	8.5
Acinetobacter	1	0.8
Enterococcus gallinarum	1	0.8
Rough-type bacteria	1	0.8
Escherichia coli	22	18.6
Klebsiella pneumoniae	7	5.9
Enterococcus faecalis	6	5.1
Citrobacter freundii	1	0.8
Gram-positive bacteria	1	0.8
Gram-positive coccus	2	1.7
Candida glabrata	4	3.4
Saccharomyces	1	0.8
Raoultella ornithinolytica	1	0.8
Enterobacter agglomerans	1	0.8
Monilia krusei	4	3.4
Candida	1	0.8
Enterococcus casselifavus	1	0.8
Staphylococcus haemolyticus	1	0.8
Stenotrophomonas maltophilia	5	4.2
Pseudomonas aeruginosa	3	2.5
Aeromonas veronii	1	0.8
Enterobacter cloacae	2	1.7
Enterococci cloacae	3	2.5
Fungal spores	4	3.4
Total	118	100.0

nosocomial infection (Table 5). Among them *Escherichia coli* accounted for (22/54) 40.7% of these Gram-negative bacteria; and these pathogens were resistant to the fourth-generation cephalosporins and sensitive to imipenem. *Acinetobacter baumannii* accounted for 20.5% (11/54) of the Gram-negative bacteria; the drug resistant spectrum and sensitivity were identical to *Escherichia coli*; and some strains were highly sensitive to amikacin. The Gram-negative bacteria mainly came from peritoneal drainage fluid, bile, *etc*.

Gram-positive bacteria accounted for 30.5% of nosocomial infection. Among them methicillin-resistant staphylococcus aureus (MRSA) accounted for 58.3% (21/36) of the Gram-positive bacteria. They were all sensitive to vancomycin; and no vancomycin resistant staphylococcus aureus was identified. The bacteria were mainly from sputum and blood cultures. Fungi accounted for 23.7% and mainly came from pharyngeal swabs and sputum culture (Table 6).

The results of binomial logistic regression analysis of the variables are shown as follows (Table 7). The four variables of significance were diabetes mellitus, operation time $\geq$ 230 minutes, preoperative hospitalization time $\geq$ 6 days, and ASA classification $\geq$ class III. However, male gender, $p = 0.968$; drainage tubes ≥ 3, $p = 0.763$ and age $\geq$ 68 years, $p = 0.120$ didn't show statistical significance at $p = 0.05$ level.

Multivariate analysis of the relative risk of these four independent risk factors showed that all the odds ratios were greater than 1 within a 95% confidence interval. The results once again demonstrated the reliability of these 4 variables as the nosocomial infection risk factors (Table 8).

The average hospitalization time was 11 days after operation of abdominal malignancies. The 75 percentile days were 15 days (Table 1). Based on the linear regression results for infection and postoperative hospitalization time $\geq$ 15 days, the correlation between these two indexes had statistical significance. The analysis confirmed that postoperative nosocomial infection increased the hospitalization stay and the medical costs.

The 4 variables including diabetes mellitus, operation time $\geq$ 230 minutes, preoperative hospitalization stay $\geq$ 6 days, ASA classification $\geq$ class III are the risk factors for postoperative nosocomial infection in patients with tumors. Postoperative nosocomial infection increases the postoperative stay in the hospital.

4. Discussion

Our study and the other reports stressed the prevention and control of abdominal postoperative nosocomial infection. Surgical operation of abdominal tumors has a high fatality (*11*). In our study, 7.3% of the patients experienced postoperative nosocomial infection. Although the mortality was not calculated, the postoperative hospitalization stay $\geq$ 15 days was certainly correlated with nosocomial infection. Identification of the risk factors is a prerequisite for better preventive methods and to develop prospective plans for infection control and treatment.

Long-term metabolic disturbance in diabetes

Table 7. The results of binomial logistic regression analysis of each variable

Step	B	S.E.	Wald	Sig.	Exp.
Step 1					
SEX	-0.122	0.251	0.234	0.628	0.886
DIABETES	1.028	0.299	11.857	0.001	2.796
AGE	0.431	0.268	2.587	0.108	1.539
SURTIME	1.268	0.279	20.604	0.000	3.555
DRAIN	-0.116	0.322	0.129	0.719	0.890
ASA	0.727	0.246	8.754	0.003	2.068
POSTSTAY	0.645	0.260	6.165	0.013	1.907
PRESURG	1.328	0.251	27.916	0.000	3.773
Constant	-4.274	0.457	87.309	0.000	0.014
Step 2					
SEX	-0.123	0.251	0.239	0.625	0.884
DIABETES	1.042	0.296	12.375	0.000	2.835
AGE	0.430	0.268	2.571	0.109	1.537
SURTIME	1.231	0.261	22.272	0.000	3.425
ASA	0.728	0.246	8.788	0.003	2.071
POSTSTAY	0.626	0.255	6.038	0.014	1.871
PRESURG	1.330	0.251	27.987	0.000	3.783
Constant	-4.276	0.457	87.489	0.000	0.014
Step 3					
DIABETES	1.025	0.294	12.127	0.000	2.786
AGE	0.416	0.266	2.433	0.119	1.515
SURTIME	1.228	0.261	22.159	0.000	3.415
ASA	0.733	0.245	8.942	0.003	2.082
POSTSTAY	0.619	0.254	5.923	0.015	1.857
PRESURG	1.352	0.248	29.822	0.000	3.867
Constant	-4.451	0.292	232.094	0.000	0.012
Step 4					
DIABETES	1.081	0.291	13.770	0.000	2.946
SURTIME	1.130	0.252	20.175	0.000	3.097
ASA	0.789	0.242	10.619	0.001	2.202
POSTSTAY	0.699	0.249	7.884	0.005	2.012
PRESURG	1.319	0.246	28.867	0.000	3.740
Constant	-4.325	0.275	246.518	0.000	0.013

SEX, DIABETES, AGE, SURTIME, DRAIN, ASA, POSTSTAY, PRESURG stood for "male", "diabetes", "age ≥ 68 years old", "operation time ≥ 230 minutes", "drain ≥ 3", "ASA grade ≥ 3", "hospital stay post-surgery ≥ 15days", "hospital stay pre-surgery≥ 6 days". Binomial logistic regression analysis of multiple variables was taken. The result showed that the four variables including diabetes mellitus, operation time ≥ 230 minutes, hospital stay pre-surgery ≥ 6 days, and ASA classification ≥ class III had statistical significance.

Table 8. Odds Ratio of the nosocomial infection risk factors at 95% confidence interval

Iterm of Odds Ratio for infection	Mean Value	Lower Value	Higher Value
For cohort with operation time > 230 minutes = 1	3.481	2.236	3.481
For cohort with ASA > 2 = 1	1.901	1.225	1.901
For cohort with preoperative hospitalization time > 6 days = 1	8.407	5.017	8.407
For cohort with diabetes mellitus = 1	3.453	2.041	3.453

mellitus caused multi-system and multi-organ impairments and undermines the immune function. Diabetic patients became the susceptible and an absolutely high-risk population for nosocomial infection (*12-14*). Generally, the interactions among multiple factors including metabolic disturbance, vasculopathy, and neuropathy effects were considered to be the main mechanisms of diabetes-complicated nosocomial infection (*15*).

The longer operation time and wound exposure time were likely to result in a higher possibility of contamination and higher probability of postoperative infection (*16*). Non-standardized surgical procedures, contamination of the surgical incision, surgeon's rough maneuvers, severe intraoperative bleeding and local tissue injuries could turn the surgical wounds into media for growth and multiplication of bacteria (*17*). Contamination in the operating room is closely related to surgical site contamination and postoperative nosocomial infection. It was reported that medical staff cell phones were severely contaminated with a strain detection rate of 95.5% and a HBsAg detection rate of

13.6% (*18*). The average microbial content conformity rate in the indoor air of the operating room was 78.57% for the first operation each day, 95.74% for successive operations, and 93.75% for successive operations following ventilation, wet cleaning and disinfection after the first operation (*19*).

It can be concluded from the statistical analysis results in this study that the extended hospitalization days are correlated with postoperative nosocomial infection. It can also be inferentially interpreted as increasing abdominal operation-related mortality.

The pathogen's drug resistance shows an ascending trend annually. It was reported that: the fungal resistance rate to fluconazole and itraconazole were 19% and 28% respectively in 2006; and 18% and 19%, respectively in 2007 (*20*). Drug resistance of G+ cocci, especially coagulase-negative staphylococcus, to penicillin was up to 84%~89%; the 2-year drug resistance of G+ cocci to cefotaxime, cefepime, ciprofloxacin, erythromycin, azithromycin and other antibiotics was up to ≥ 92%. The 2-year drug resistance of G- bacilli to ampicillin was up to ≥ 90% (*21*). The results of this study have confirmed this viewpoint. Therefore, the prophylactic application of antibiotics should be strictly standardized by the guidelines in order to reduce the overall induction of resistant bacteria at the nation wide level.

The 4 risk factors obtained from our research by binomial logistic regression analysis method has indicative significance. The 3 risk factors including diabetes mellitus, preoperative hospitalization stay ≥ 6 days and ASA grade ≥ III can easily be identified preoperatively. This can provide the basis not only for the management of high-risk patients but also for the formulation of measures to reduce infection complications. For the risk factor of operation time > 230 minutes, it is necessary to carry out serious surgery discussion, formulate the operation plan, and estimate all possible situations preoperatively in order to shorten the operation time as much as possible under the premise of quality assurance.

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