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Total Parenteral Nutrition Is a Major Risk Factor for Central Venous Catheter-Related Bloodstream Infection in Colorectal Cancer Patients Receiving Postoperative Chemotherapy

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Key Words

Central venous catheter-related bloodstream infection · Total parenteral nutrition · Risk factors

Abstract

Purpose: To clarify the risk factors for central venous catheter-related bloodstream infection (CVCR-BSI) in patients receiving chemotherapy after surgery for colorectal cancer (CRC). ***Methods:*** CVCR-BSI was evaluated retrospectively from a database of patients who had received postoperative chemotherapy using central venous catheters (CVC). ***Results:*** One hundred and nine patients received 542 CVC for a total of 5,558 catheter-days. There were no significant differences in background between the patients who had CVCR-BSI and those who did not, except for the administration of total parenteral nutrition (TPN) ($p < 0.0001$). Moreover, univariate analyses (using factors including type of catheter, sex, age, troubles with insertion, kinds of disinfectant, kinds of catheter, length of inserted catheter, term of catheter insertion and administration of TPN) revealed that the administration of TPN (odds ratio, 12.74; 95% CI, 2.489–62.26; $p = 0.0023$) was the only risk factor for CVCR-BSI. ***Conclusions:*** TPN is a major risk factor for CVCR-BSI in CRC patients receiving postoperative chemotherapy.

Introduction

Recent reports of Japanese colorectal cancer (CRC) patients revealed that about 40% of patients were diagnosed as stage III or stage IV. These patients are able to prolong survival time by receiving postoperative chemotherapy. Therefore, almost half of the patients who undergo CRC surgery should receive postoperative chemotherapy, such as FOLFOX or FOLFIRI, because chemotherapy can be performed safely and correctly by using a central venous line. Nevertheless, there are still life-threatening incidents, such as catheter-related bloodstream infections. Therefore, preventing central venous catheter-related bloodstream infections (CVCR-BSI) is a most important issue to be addressed while performing postoperative chemotherapy.

Despite progress in antibiotic therapy and infection control procedures, such as a needleless infusion system, dressings and disinfectants, prevention of CVCR-BSI is difficult. Recent reports have revealed that CVCR-BSI occurs with 3–7% of catheters [1]. Moreover, once CVCR-BSI has occurred, it often becomes life-threatening [2]. However, few studies have evaluated the risk factors for CVCR-BSI in the field of CRC surgery [3]. In the present study, we investigated the risk factors for CVCR-BSI in adult CRC patients, especially those receiving postoperative chemotherapy.

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Patients and Methods

By reference to our database, we conducted a retrospective review of 109 patients, who had undergone CVC insertions for postoperative chemotherapy after surgery for advanced CRC at the Department of Gastroenterological Surgery, Dokkyo Medical University Hospital, between January 2005 and August 2007 under the care of the same trained surgical team. Informed consent was obtained from all patients before CVC insertion.

Interventions

In all cases, catheters were inserted into the veins by the single-puncture method in the patient room, using the maximal barrier precaution technique [4–6]. The insertion area was disinfected with 10% povidone-iodine [7] or 0.05% chlorhexidine and draped.

CVC were inserted via the external jugular veins (external jugular venous catheter), internal jugular veins (internal jugular venous catheter), subclavian veins (subclavian venous catheter), peripheral veins of the upper extremities (peripherally inserted central catheter) and femoral veins (femoral venous catheter).

Topical anesthetic skin infiltration with 1% lidocaine was performed, except for the insertions of external jugular venous catheters and peripherally inserted central catheters.

Accurate catheter tip placement in the superior vena cava was confirmed by chest X-ray. No procedures were performed under intravenous sedation.

Maintenance

After insertion, patients were followed up once a week with routine dressing changes until catheter removal. Routine catheter exchanges were not performed. Catheters were removed whenever fever (>38°C) occurred or if the symptoms of infection were present, such as skin redness and pus discharge at the insertion point. Blood culture and culture of the catheter tip were then performed to diagnose any CVCR-BSI [8]. Routine catheter tip cultures were not performed after removal.

Troubles with insertion were defined as malposition of the catheter tip, oozing or hematoma formation at the insertion point, pneumothorax, arterial bleeding and nerve damage. The primary endpoint of this study was the development of any CVCR-BSI, which included either bacteremia or fungemia. On the basis of CDC guidelines [9], we diagnosed CVCR-BSI by using clinical criteria. The guidelines state that CVCR-BSI is diagnosed by at least 1 of the following criteria. (1) The patient has a recognized pathogen cultured from 1 or more blood cultures, and the pathogen cultured from the blood is not related to an infection at another site. (2) The patient has at least 1 of the following signs or symptoms: fever (>38°C), chills or hypotension. Therefore, we used only blood culture positivity to determine the presence of CVCR-BSI.

Indications for Total Parenteral Nutrition

Total parenteral nutrition (TPN) was performed when the side effects of chemotherapy, such as loss of appetite due to nausea or vomiting, persisted for several days after chemotherapy. TPN was continued until the disappearance of the nausea, vomiting and diarrhea. In addition, the evaluation of each patient's nutritional level was performed on the day of admission by using laboratory data and the body mass index. Whenever a patient's condition was getting poor, we sought the advice of the nutrition support team as to whether TPN should be performed or not.

Statistical Analysis

Differences in patient characteristics were analyzed by the Mann-Whitney U test and the χ^2 test, and odds ratios with 95% CI were calculated using univariate logistic regression analyses. Statistical analyses were performed using StatView® software, version 5.0 (Abacus Concepts, Berkeley, Calif., USA) at a significance level of $p < 0.05$. The results are presented as means ± SE.

Results

During the study period, a total of 542 CVC were inserted using the single-puncture technique. One hundred and nine patients received 542 CVC for a total of 5,558 catheter-days. One hundred and eighty-one Argyle catheters (Argyle®, 16-gauge single-lumen 30-cm catheter; Nippon Sherwood, Tokyo, Japan) and 361 Groshong catheters (Groshong, 4.0-french single-lumen 60-cm catheter; Bard Access Systems, Salt Lake City, Utah, USA) were inserted.

Table 1 reveals that there were no significant differences in the frequency of the types of catheter, sex, trou-

Table 1. Comparison of patient and catheter background factors between CVCR-BSI-negative and -positive groups

Variables	CVCR-BSI negative (n = 536)	CVCR-BSI positive (n = 6)	p
Type of catheter			
PICC	28	1	0.2155
IJVC	356	3	0.3977
EJVC	132	2	0.6230
SCVC	13	0	0.6994
FVC	7	0	0.7781
Sex (male/female)	308/228	4/2	0.6501
Troubles with insertion (yes/no)	31/505	1/5	0.2607
Kinds of catheter			0.3823
Groshong catheter	356	5	
Argyle catheter	180	1	
Kinds of disinfectant			0.4084
10% povidone-iodine	430	4	
0.05% chlorhexidine	106	2	
Administration of TPN (yes/no)	39/497	3/3	<0.0001

PICC = Peripherally inserted central catheter; IJVC = internal jugular venous catheter; EJVC = external jugular venous catheter; SCVC = subclavian venous catheter; FVC = femoral venous catheter. Analyses performed with χ^2 test.

bles with insertion, types of catheter or kinds of disinfectant between the CVCR-BSI-negative and CVCR-BSI-positive patients. Only administration of TPN differed significantly between the groups ($p < 0.0001$).

Table 2 reveals that there were no significant intergroup differences in patient age, length of the inserted catheter and duration of catheter insertion. The mean age of the patients was 63.3 ± 0.4 years in the CVCR-BSI-negative group and 59.3 ± 2.9 years in the CVCR-BSI-positive group ($p = 0.1314$). The mean length of the inserted catheter was 17.0 ± 0.3 cm for the CVCR-BSI-negative group and 18.3 ± 3.4 cm for the CVCR-BSI-positive group ($p = 0.5488$). The mean duration of catheter insertion was 10.2 ± 0.4 days for the CVCR-BSI-negative group and 16.2 ± 4.7 days for the CVCR-BSI-positive group ($p = 0.0978$).

Table 3 reveals that there were no significant intergroup differences in sex, administration of TPN, CVCR-BSI, duration of catheter insertion and length of hospital stay between FOLFIRI and FOLFOX4 groups. The mean age of the patients was 65.8 ± 0.8 years in the FOLFIRI group and 62.7 ± 0.5 years in the FOLFOX4 group ($p = 0.0004$). The mean number of survival days was 317 ± 14 for the FOLFIRI group and 253 ± 10 for the FOLFOX4 group ($p = 0.0003$).

Results of univariate analyses for CVCR-BSI (using factors including the types of catheters, sex, age, troubles with insertion, kinds of disinfectant, kinds of catheters, length of the inserted catheter, term of catheter insertion and administration of TPN) are presented in table 4. Univariate analyses revealed that TPN (odds ratio, 12.74; 95% CI, 2.489–62.26; $p = 0.0023$) was the only risk factor for CVCR-BSI.

Fever occurred in 26 patients (4.68 per 1,000 catheter-days), and all the catheters in these patients were removed for diagnoses of CVCR-BSI. The results revealed blood culture positivity in 6 cases and catheter tip culture positivity in 9 cases. Three patients had both positive blood culture and positive tip culture. Thus, 6 patients were diagnosed as having CVCR-BSI (1.08 per 1,000 catheter-days).

Figure 1 shows the types of bacteria and fungus from the positive blood cultures. Infection numbers detected from blood cultures were: 1 *Staphylococcus epidermidis*, 3 *Klebsiella pneumoniae*, 1 *Escherichia coli* and 1 *Candida guilliermondii*.

Table 2. Comparison of patient and catheter background factors between CVCR-BSI-negative and -positive groups

Variables	CVCR-BSI negative (n = 536)	CVCR-BSI positive (n = 6)	p
Age, years	63.3 ± 0.4	58.5 ± 1.9	0.2080
Length of inserted catheter, cm	16.9 ± 0.3	21.3 ± 6.7	0.1461
Catheterization duration, days	10.2 ± 0.4	16.2 ± 4.7	0.0978

Analyses performed by Mann-Whitney U test.

Discussion

These results suggest that the main cause of CVCR-BSI was the use of a highly concentrated glucose solution, like that employed for TPN, rather than the period of catheter insertion [10]. In fact, Dissanaike et al. [11] demonstrated that increased parenteral caloric intake is an

Table 3. Background of chemotherapy performed

Variables	FOLFIRI (n = 160)	FOLFOX4 (n = 314)	IFL (n = 58)	Others (n = 10)	p[a]
Age, years	65.8 ± 0.8	62.7 ± 0.5	59.8 ± 1.2	57.8 ± 4.9	0.0004[c]
Sex (female/male)	62/98	138/76	28/30	2/8	0.2785[b]
Administration of TPN (yes/no)	7/153	18/296	13/45	4/6	0.5318[b]
CVC-RBSI (yes/no)	2/158	3/311	0/58	1/9	0.7666[b]
Catheterization duration, days	7.9 ± 0.4	8.7 ± 0.4	22.8 ± 1.1	21.3 ± 6.4	0.2116[c]
Term of hospital stay, days	13.4 ± 0.7	12.6 ± 0.5	27.9 ± 1.0	22.0 ± 6.5	0.2997[c]
Survival term, days	317 ± 14	253 ± 10	553 ± 40	106 ± 58	0.0003[c]

FOLFIRI = FOL: folinic acid (leucovorin), F: fluorouracil (5-Fu), IRI: irinotecan (Camptosar); FOLFOX = FOL: folinic acid (leucovorin), F: fluorouracil (5-Fu), OX: oxaliplatin (Eloxatin); IFL = I: irinotecan (Camptosar), F: fluorouracil (5-Fu), L: leucovorin.

[a] Statistical analyses were performed between FOLFIRI and FOLFOX4. [b] χ^2 test. [c] Mann-Whitney U test.

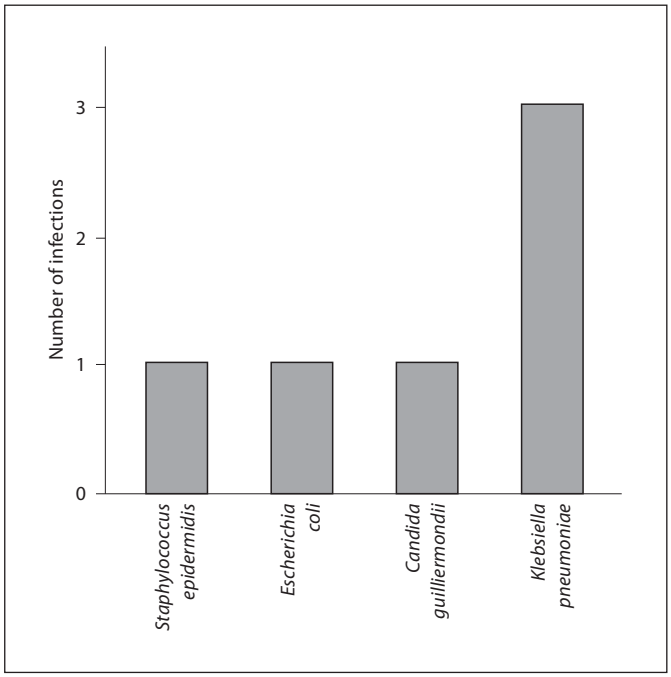

Fig. 1. Background of bacteria and fungus from the CVCR-BSI.

Table 4. Univariate logistic regression analyses in relation to CVCR-BSI

Variables	p	OR	95% CI
Types of catheter			
PICC	0.2467	3.629	0.410–32.12
IJVC	0.4065	0.506	0.101–2.531
EJVC	0.6252	1.530	0.277–8.452
SCVC	0.9769	u.p.	u.p.
FVC	0.9831	u.p.	u.p.
Sex	0.6521	1.481	0.269–8.154
Age	0.2060	0.949	0.876–1.029
Trouble with insertion	0.2877	3.258	0.369–28.75
Kinds of disinfectant (I/C)	0.4178	0.493	0.089–2.728
Kinds of catheter (G/A)	0.3988	2.528	0.293–21.81
Length of inserted catheter	0.1738	1.047	0.980–1.119
Catheterization duration	0.1204	1.042	0.989–1.097
Administration of TPN	0.0023	12.74	2.489–62.26

PICC = Peripherally inserted central catheter; IJVC = internal jugular venous catheter; EJVC = external jugular venous catheter; SCVC = subclavian venous catheter; FVC = femoral venous catheter; A = Argyle catheter; G = Groshong catheter; C = 0.05% chlorhexidine; I = 10% povidone-iodine; u.p. = unproved.

independent risk factor for bloodstream infection in patients receiving TPN.

We have found through experience that, although the FOLFIRI regimen tends to result in greater appetite loss due to drug-induced nausea, vomiting and diarrhea than FOLFOX, almost 20% of patients who receive these regimens may suffer severe appetite loss for several days (data not shown). Although there are a few effective drugs to combat these side effects of chemotherapy, some patients still suffer appetite loss. However, in most cases, this did not last for more than 1 week. Hence, most patients who have received TPN might require only additional hydration or partial parenteral nutrition, which means medium caloric fluid therapy rather than TPN.

In addition, our results revealed that the major pathogen responsible for CVCR-BSI was *Staphylococcus*. This result was compatible with recent reports [6, 12]. Therefore, bacterial contamination via line connectors or the catheter insertion point was suspected to be the chief cause of CVCR-BSI. Although this study was small and retrospective, the results suggest that avoiding temporary TPN therapy and rigorous management of CVC might decrease the incidence rate of CVCR-BSI [13].

In conclusion, administration of TPN is a major risk factor for CVCR-BSI in adult CRC patients who receive postoperative chemotherapy via CVC.

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