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**CLINICAL RESEARCH** 

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# Prophylactic Use of Antibiotics for Fever After Drainage Removal Following a Dural Tear During Lumbar Spinal Surgery: A Retrospective Study

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Bacl	(ground:	Dural tear and subsequent cerebrospinal fluid leakage are frequent complications during lumbar spine su						
			This retrospective study aimed to investigate the risk factors and the use of prophylactic antibiotics in patients					
		with fever after drainage removal (FDR) following lumbar dural tear during lumbar spinal surgery.						
Material/M	Aethods:	The authors retrospectively analyzed 2812 patients who underwent different spinal surgical procedures from						
		January 2015 to December 2017. The basic information of patients was obtained to analyze the risk factors of						
		dural tear and FDR. The patients were divided into 5 groups according to their antibiotic strategies for FD						
		antibiotics, ceftriaxone, vancomycin, ceftriaxone+vancomycin, other antibiotics). Body temperature, labo	orato-					
	Results:	ry test results, and pathogen profiles were collected for analysis.						
	Results:	There were 326 cases diagnosed as dural tear, including 198 cases of FDR. Sex, age, type of disease, and pre-						
		vious lumbar surgery played significant roles in the dural tear rate ( $P<0.05$ ). Patients older than 60 years old had a higher insidence of EDP after dural tear ( $P<0.05$ ). There was no significant difference in the insidence of						
		had a higher incidence of FDR after dural tear ( $P$ <0.05). There was no significant difference in the incider surgical site infection among the various treatment groups ( $P$ >0.05).						
Con	clusions:	surgical site infection among the various treatment groups (P>0.05). Age has obvious effect on dural tear and FDR, whereas sex, revision surgery, primary diagnosis, and procedure						
Con	LIUSIONS.	type only affect the rate of dural tear. The prophylactic use of antibiotics has no effect on the incidence						
		gical site infection when fever after drainage removal occurred in patients with dural tear.	'i sui-					
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## Background

Low back pain is a common, costly, and disabling health problem, the incidence of which was estimated to be as high as 60-70% [1]. Lumbar spine surgery is the last treatment for low back pain if conservative treatments fail [2]. Dural tear and subsequent cerebrospinal fluid (CSF) leakage are undesirable but frequent complications during lumbar spine surgery, with an incidence ranging from less than 1% to 17% [3,4]. The reported risk factors for incidental durotomy include older age, sex, BMI, smoking status, revision surgery, primary diagnosis, and type of surgery [5-11]. If not treated properly, it can cause several adverse complications, such as intracranial hypotension syndrome (headache, nausea, and vomiting), hematoma, and a higher surgical site infection rate (SSI) [12-17]. Various management strategies have been used to treat dural tear, including watertight closure, dural substitutes, minimally invasive techniques, fat grafts, and adhesive glues [18-21]. Among them, spinal drainage associated with bed rest for 4-7 days has been widely used, with good clinical effect [3].

However, fever is frequently observed within 2 days after the spinal drainage was removed in clinical practice. The body temperature of patients was usually higher than 38°C, accompanied by increased white blood cell count, neutrophils count and percentage, and erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Considering that postoperative fever is often closely related to surgical site infection (SSI), which is a common and critical complication after lumbar spine surgery [22], clinicians often use antibiotics prophylaxis as a routine preventive treatment strategy for patients undergoing lumbar spine surgery. However, there is no unified and clear view of whether and how to use antibiotics to treat FDR. Therefore, this retrospective study from a single center aimed to investigate the effect of prophylactic antibiotics on the rate of surgical site infection when a fever occurs after drainage removal in patients who had a dural tear during lumbar spinal surgery.

### **Material and Methods**

This study was approved by the local ethics committee (the Medical Ethics Committee of the Second Affiliated Hospital of Xian Jiaotong University; approved on February 3, 2016, Approval No. 2016016). The research data we collected did not have any identifiers, so individual participation was anonymous and the data collected cannot be linked to these people. Given that this was a retrospective study, the requirement for informed consent was waived. In this single-center study, we retrospectively analyzed 2812 patients who underwent various surgical procedures due to diseases located in the lumbar spine in these 4 hospitals from January 2015 to December 2017. Information on sex, age, BMI, smoking status, previous

surgery history, primary diagnosis, operation type, and antibiotics prophylaxis was obtained to analyze the risk factors for dural tear and FDR. The primary purpose of this study was to investigate fever after CSF leakage followed by dural tears. Thus, we defined a dural tear as including incidental dural tears found during and after lumbar surgery [23] and intended durotomies such as intradural tumors, diastematomyelia, and tethered cord syndrome. FDR was defined as patients who (1) had a dural tear in the lumbar spine surgery, with or without CSF leakage; (2) underwent intraoperative drainage placement and had it removed 5-7 days after the operation; (3) had normal body temperature (<37.5°C) before drainage removal and fever (>38°C) within 2 days after drainage removal; (4) received prophylactic antibiotics or not before drainage removal; (5) had an abnormal rise in white blood cell count, neutrophil count and percentage, and CRP after drainage removal. The exclusion criteria were patients with (1) solid vertebral tumor, metastatic tumor, or if the tumor originated from other sites (eg, solid tumor, malignant lymphoma, leukemia); (2) definite infections located in the spine or other sites; (3) connective tissue disease like rheumatic fever; (4) tuberculosis; (5) parasitic diseases (eg, brucellosis, malaria); (6) definite viral diseases; (7) other definite diseases that can cause fever (eg, blood transfusion reaction); (8) cerebrospinal fluid leak before surgery; (9) who died during surgery or were lost to follow-up.

The antibiotics used after FDR was diagnosed were recorded as prophylaxis antibiotics, regardless of whether they were supported by the bacterial culture results. The following clinical parameters were collected for analysis: body temperature, laboratory tests (white cells count, neutrophil cells count and percentage, CRP), and pathogen profiles. To observe the effect of various antibiotics on the FDR, Ceftriaxone and Vancomycin were selected, as they all can penetrate the blood-brain barrier and cover the gram-positive cocci and gram-negative bacilli, respectively [24]. Other first/second-generation cephalosporin and clindamycin were selected as controls. The FDR patients were divided into 5 groups according to their antibiotics strategies after FDR: (1) NA group (No antibiotics); (2) CTRX group (Ceftriaxone); (3) VA group (Vancomycin); (4) CTRX+VA group (Ceftriaxone+Vancomycin); (5) OTHERS group (Other antibiotics: the first/second-generation cephalosporin and clindamycin). The selected antibiotics covered all the gram-positive cocci and gram-negative bacilli. Then, changes in body temperature and laboratory test results, and the rates of SSI of all the antibiotics subgroups were compared with each other.

The body temperatures were collected 3 times a day after drainage was removed. The highest body temperature on each day was recorded for analysis. The blood test results were collected every 3-5 days after surgery in 4 different hospitals. The white blood cell count (WBC), neutrophil percentage (NEUT%), and neutrophil count (NEUT#) were recorded in every laboratory

Parameter	No DT (n=2486)	DT (n=326)	Р	No FDR (n=128)	FDR (n=198)	Р
Sex (n)						
Male	1188	139	0.03	50	89	0.29
Female	1298	187		78	109	
Age (year)						
<60	613	35	<0.001	22	13	0.003
60-70	1214	138		44	94	
>70	659	153		62	91	
BMI						
<25	729	87	0.40	38	49	0.58
25-30	1026	147		54	93	
>30	731	92		36	56	
Smoking						
Yes	782	107	0.62	39	68	0.47
No	1704	219		89	130	
Previous lumbar spine surgery						
Yes	641	198	<0.001	80	118	0.60
No	1845	128		48	80	

Table 1. Correlation between patient clinical characteristics and the incidence of dural tear and fever after drainage removal (FDR).

test. The percentages of patients with abnormal WBC (>10<sup>9</sup>/L), NEUT% (>70%), and NEUT# (>10<sup>9</sup>/L) in FDR patients were recorded for analysis. Because the normal values of CRP used in each hospital were different, we normalized CRP by the maximum normal value of each involved hospital to analyze the trend of CRP change [25].

The SPSS Statistics 22.0 was used for the analysis of these clinical statistical data. Categorical variables were compared by Pearson's chi-square test. Continuous variables were compared using a one-way ANOVA and summarized with means $\pm$ standard deviations. *P*<0.05 indicated a significant difference.

# Results

### The Risk Factors for Dural Tear and FDR

We reviewed 2812 patients who underwent lumbar surgery; 326 cases were diagnosed as dural tear, among which 198 patients had FDR. The correlations between the patient clinical characteristics and the incidence of dural tear and FDR are shown in **Table 1**. Sex, age, and previous lumbar surgery

were significantly associated with the dural tear rate (P < 0.05). Women, patients older than age 60, and those who had previous lumbar spine surgery had higher rates of dural tear. BMI and smoking history did not affect the incidence of dural tear (P>0.05). For patients with FDR, a significant difference only existed in different age groups (P<0.05) (Table 1). The incidence rate of dural tear increased significantly when the patient was older than 60 years old. The incidence of dural tear varied significantly among diseases (Table 2) (P<0.05). The degenerative group had the lowest incidence of dural tear (6.8%), which was close to the spinal stenosis group (8.4%) and significantly lower than the other 4 groups. The patients diagnosed with primary intraspinal tumor had the highest dural tear rate (46.2%). No significant difference in the rate of FDR was found between each disease (P>0.05) (Table 2). Various surgical procedures were associated with significantly different dural tear rates (P<0.05). As shown in Table 3, the other surgery group, in which the intended durotomy for the intraspinal tumor was included, had the highest dural tear rate (39.3%), while the microscopic discectomy had the lowest dural tear rate. There was no significant difference in FDR rate among the various surgical procedure groups (P>0.05) (Table 3). Various preoperative antibiotics such as the first/second/third cephalosporins, 
 Table 2. The rate of dural tear and fever after drainage removal (FDR) of patients with various initial diagnoses.

	Diagnosis	Rate of DT	Rate of FDR
1	Spinal stenosis	8.4% <sup>#,+</sup>	60.4%
2	Degenerative disc disease	6.8% <sup>*,\$,#,+</sup>	61.8%
3	Spondylolysis	11.7%#	64.5%
4	Deformity	12.1%#	63.4%
5	Primary intraspinal tumor	46.2%+	59.5%
6	Other disease	15.4%	47.8%
	Р	<0.001	0.822

<sup>®</sup> Means compare with 1; <sup>&</sup> means compare with 2; <sup>\*</sup> means compare with 3; <sup>s</sup> means compare with 4; <sup>#</sup> means compare with 5; <sup>+</sup> means compare with 6. <sup>@</sup>, <sup>&</sup>, <sup>\*</sup>, <sup>5</sup>, <sup>#</sup>, <sup>+</sup> means statistical significance.

Table 3. Rate of dural tear and fever after drainage removal (FDR) of patients treated with various surgeries.

	Diagnosis	Rate of DT	Rate of FDR
1	Microscopic discectomy	4.8% <sup>*,#</sup>	33.3%
2	Post discectomy	7.6%#	64.7%
3	Decompression±fusion	10.9%#	61.4%
4	Anterior procedures	6.4%#	57.1%
5	Other surgeries	39.3%	64.6%
	Р	<0.001	0.108

\* Means compare with 3; # means compare with 5. \*, # means statistical significance.

Table 4. Effect of preoperative antibiotics on the incidence of fever after drainage removal (FDR).

	No antibiotics		Second generation cephalosporins		Clindamycin	Other antibiotics
Rate of FDR	61.3%	63.0%	61.0%	39.1%	65.6%	60.0%
	<i>P</i> >0.05					

clindamycin, and levofloxacin were used in some of the patients. The third-generation cephalosporins were associated with a lower FDR rate than other antibiotics, but with no statistical significance (P>0.05) (**Table 4**).

# The Effect of Prophylactic Antibiotics on Temperature and Laboratory Tests

Once FDR was diagnosed, the patients were treated with ceftriaxone, vancomycin, ceftriaxone combined with vancomycin, other antibiotics (first/second-generation cephalosporin, clindamycin), or no antibiotics. **Table 5** shows the clinical characteristics of patients who had FDR. No obvious difference was found in sex, age, BMI, smoking, accompanying disease, previous surgery, or initial diagnosis among the various treatment groups (*P*>0.05). FDR was defined as a body temperature of more than 38°C after the drainage tube was removed. None of the patients had a fever on the day when the drainage was removed. **Figure 1** shows the changes in body temperature and laboratory test results of FDR patients in all treatment groups. The CTRX and CTRX+VA reduced the patients' body temperature, WBC counts, neutrophil count and percentage, and normalized CRP faster than in the other 3 groups. No difference was found in body temperature and laboratory test results between CRTX and CTRX+VA (*P*>0.05).

# The Effect of Prophylactic Antibiotics on the Rate of Surgical Site Infection

Although antibiotic regimens changed the recovery curve of the patients with FDR, they seemed to have no effect on the morbidity of SSI. As shown in **Table 6**, the incidence of SSI was not associated with the use of antibiotics or the type of antibiotics used (*P*>0.05). For all the patients with SSI, experimental

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Parameters	No antibiotics	Ceftriaxone	Vancomycin	Ceftriaxone plus Vancomycin	Other antibiotics	P
Sex (M/F)	9/12	20/22	11/14	14/18	35/43	0.9962
Age (Yrs, Mean±Sd)	66.4±10.2	70.5±9.6	68.3±11.3	70.1±8.4	72.5±11.2	0.123
Age groups (Yrs)						
<60	2	2	3	4	2	0.545
60-70	10	21	12	16	35	
>70	9	19	10	12	41	
Body weight (Kg)	75.5±10.8	71.7±9.6	68.4±12.7	72.6±11.9	69.7±11.3	0.163
BMI groups (Kg/m <sup>2</sup> )						
<25	5	11	4	7	22	0.478
25-30	9	21	13	20	30	
>30	7	10		5	26	
Smoking	8/21	14/42	9/25	10/32	27/78	0.988
Other disease						
Hypertension	8	14	9	11	29	1.0
Diabetes	3	7	4	5	12	
Osteoporosis	2	5	3	4	9	
Previous surgery	9	25	13	23	48	0.27
Diagnosis						
Spinal stenosis	3	7	4	4	14	1.0
Degenerative disc disease	6	8	5	5	18	
Spondylolysis	3	9	5	6	17	
Deformity	2	6	3	5	10	
Primary intraspinal tumor	5	10	7	10	15	
Others	2	2	1	2	4	

### Table 5. Characteristics of fever after drainage removal (FDR) patients receiving various treatments.

antibiotics were used until the bacteria were detected. Among them, 4 cases were treated with abscess incision and drainage. The other cases are cured by conservative treatment (such as debridement, lavage, and drainage). None of these infective cases required the removal of spinal implants.

### Discussion

Dural tear and cerebrospinal fluid (CSF) leak is one of the most common complications of spinal surgery. Spinal drainage is a widely used treatment for CSF leak. In clinical practice, the authors observed a fever after drainage removal (FDR) phenomenon. To better prevent the occurrence of dural tear and address the possible surgical site infection (SSI), the present study investigated the risk factors associated with dural tear and the effect of preventive antibiotics on SSI when a fever occurs after drainage removal. The results suggest that among all the risk factors for dural tear and FDR, sex, age, previous surgery, and primary diagnosis were significantly associated with the occurrence of dural tear, and age exerted a significant influence on the rate of FDR. For patients with FDR, our study found that the use of CTRX or CTRX+VA can exert a positive effect in reducing the body temperature and laboratory test results like WBC counts, neutrophils percent, neutrophils count, and CRP. The temperature of the patients undergoing

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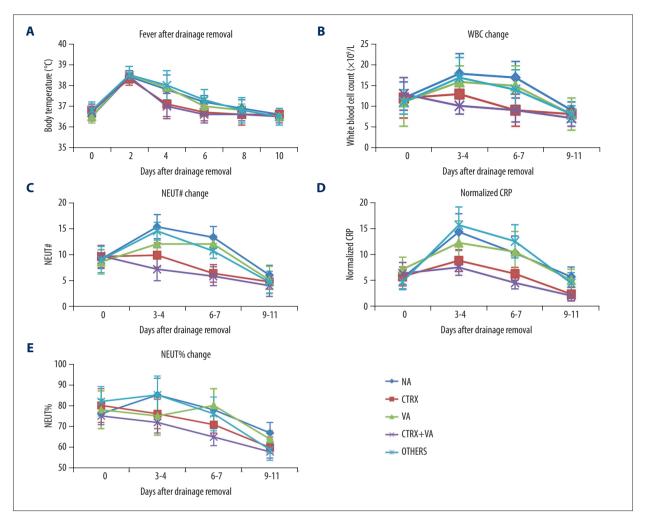


Figure 1. The effect of antibiotics on the change of fever (A), white blood cell count (WBC) (B), neutrophil count (NEUT#) (C), C-reactive protein (CRP) (D), and neutrophil percentage (NEUT%) (E) in patients with fever after drainage removal (FDR). NA – no antibiotics (NA group); CTRX – Ceftriaxone (CTRX group); VA – Vancomycin (VA group); CTRX+VA – Ceftriaxone+Vancomycin (CTRX+VA group); OTHERS – Other antibiotics (OTHERS group) – the first-/second-generation cephalosporin and clindamycin. The figure was created using GraphPad Prism 9.1.1 (223) for Mac, GraphPad Software, San Diego, California, USA, www.graphpad.com.

Group	SSI	Pathogen
No antibiotics	1 (4.8%)	Staphylococcus aureus
Ceftriaxone	2 (4.8%)	Klebsiella Pneumoniae (–)
Vancomycin	1 (4.0%)	Proteus mirabilis
Ceftriaxone/Vancomycin	1 (3.1%)	Escherichia Coli
Other antibiotics	3 (3.8%)	Escherichia Coli/Klebsiella Pneumoniae Acinetobacter baumannii (–)
Ρ	0.997	

this treatment strategy also dropped to the normal level faster. However, no obvious difference in the rate of surgical site infection (SSI) was found to be caused by the efficacy of the various antibiotics.

Dural tear has been proved to be a complication following all spinal surgeries and has been reported to have a variable incidence ranging from 1% to 17% [3,4]. If not effectively treated, the dural tear can induce serious consequences like pseudomeningocele, headache, postoperative meningitis, and intracranial hemorrhage [12-15]. Thus, it is necessary to estimate the risk of intro-operative dural tear in various groups of patients to prepare for it in advance. The possible risk factors reported being associated with dural tear include sex, age, obesity, smoking status, revision surgery, primary diagnosis, and procedure type [6,7,9,26]. Women tended to have a higher incidence of dural tear than men in this study, probably because of the finer and thinner dural sac in women. Takahashi et al [27,28] alsohave described sex as a risk factor for dural tear, which is consistent with the present study. With the increase of age, the incidence of dural tear gradually increased in the present study. A significantly higher dural tear rate was found in patients older than 60 years (P<0.05), mainly because patients' diseases get worse with the increase of age, and the comorbidities associated with aging increased the difficulty of surgeries [29]. Furthermore, more revision surgeries occurred among the older patients. All these could lead to higher rates of dural tear in older patients than in younger ones. In contrast to some previous experiments, our study found no significant correlation between BMI or smoking status and the incidence of dural tear, but the rate of dural tear was higher when BMI was >30 Kg/m<sup>2</sup>, which is consistent with the study conducted by Baker et al [4]. This might be caused by the increasing difficulty in surgical exposure because of thicker soft tissues and deeper wounds [9]. The level of smoking may be the reason for the non-correlation between smoking and dural tear.

In the present study, we found that patients undergoing revision surgery had a significantly higher incidence of dural tear (P<0.05), similar to the results reported by many previous studies [5,6,10], probably due to the dural adhesions caused by previous surgeries. Furthermore, the existence of abnormal anatomic structures can lead to loss of landmarks during surgery, which may cause an increased risk of dural tear [30]. The rates of dural tear among various primary diagnosis subgroups were significantly different (P<0.05). Patients with intraspinal tumors tend to have significantly higher rates of dural tear, due to the characteristics of the spinal cord tumor itself needing intentional durotomy (which we included in dural tear in this study). Owing to this inevitable characteristic, more attention should be paid to this kind of patient. In contrast with others, the degenerative disc disease group showed a significantly lower incidence of dural tear (P<0.05). This may be because more microscopic discectomy surgeries were carried out in this group. Among the various surgical procedure subgroups, the other surgery group had a significantly higher rate of dural tear (P<0.05). This may be because the surgical procedure for diseases included in this group, like intradural tumors or tethered cord syndrome, needs durotomy, which was also included in our study if a dural tear occurred.

Concerning the complications following lumbar spine surgery, surgical site infection (SSI) should not be ignored during the early postoperative stage, the rates of which have been reported to be 0.7-12.0% [16,17]. Normally, fever is a precursor of infection, and sometimes is the most common presenting symptom. In the clinical setting, we found that patients with dural tear often had FDR within 2 days. In the current study, we observed that 60.73% of patients went through FDR and increased laboratory parameters - body temperature, white cell count, neutrophil count and percentage, and C-reactive protein. In addition, the present study analyzed the aforementioned factors thought to be associated with dural tears to find out whether they affect the incidence of FDR. No significant relationships among sex, BMI, smoking, and fever after drainage removal were found, but the patients age 60 and younger had a much lower rate of FDR than the groups over 60 years old (P<0.05). The reason may be: (1) patients age 60 and under were less susceptible to tissue damage caused by surgical procedures [29]; (2) more patients in this group underwent microscopic discectomy surgery; (3) homeostasis was easier to maintain in younger patients. These results suggested that dural tear and age are the risk factors of FDR, not sex, obesity, smoking status, revision surgery, primary diagnosis, and procedure type. This strongly indicates that surgeons need be cautious when a dural tear occurs in older patients.

The primary diagnosis exerts no significant influence on the rate of FDR, with the spondylolysis group being the highest and the other diseases group being the lowest. In terms of the surgical procedure, the microscopic discectomy group has the lowest rate of FDR (almost half the rate of other groups), probably because the minimally invasive surgical procedure caused less inflammatory response due to less tissue damage [31]. But the variability of the rates of FDR among the groups was not statistically significant. The application of antibiotics before the operation was often used by the clinician to prevent SSI [32]. However, in the current study, whether to use antibiotics before the operation and the kind of antibiotic used had no effect on the incidence of FDR. This indicates that administration of antibiotics before surgery should be carefully considered due to the low efficacy in preventing SSI and the risk of producing resistant bacteria.

Once fever occurs, the possibility of infection and necessary treatments should be considered and appropriate steps taken.

Most previous literature suggested using preoperative antibiotic prophylaxis to prevent infections in spinal surgery. William and Erwin gave some important evidence-based clinical guidelines for antibiotic prophylaxis in spine surgery [33,34]. However, few studies have discussed whether and how prophylactic antibiotics should be used in patients with dural tear, especially when fever occurred after drainage removal. In the current study, the patients received different treatments when fever after drainage removal occurred: no antibiotics, ceftriaxone, vancomycin, ceftriaxone+vancomycin, and other antibiotics. The result showed that the body temperature of all the patients with FDR increased to the peak level on day 2 after drainage removal and then started to steadily decline to the normal level. The laboratory parameters in the CTRX and CTRX+VA subgroups tended to decline faster than in the other 3 groups. However, there was no significant difference in the surgical site infection rate among all the 5 groups, which were 4.8%, 4.8%, 4%, 3.1%, and 3.8%, respectively. The utility of antibiotics did not reduce the rate of SSI, which is not consistent with some previous studies [35]. In the study by Barker et al [6], the row pooled infection rates were reduced from 5.9% to 2.2% by antibiotics. This discrepancy may be caused by the different numerical calculations used. In most previous studies, the SSI rate was calculated by dividing the number of infected patients by the total number of surgical patients. However, in the current study, the SSI rate was defined as the number of infected patients divided by the number of patients with FDR. This result may indicate that antibiotic prophylaxis should be started earlier in dural tear patients, immediately after surgery instead of after the fever appears. We speculate that in the event of fever, the role of antibiotics is more to treat than to prevent.

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There are some limitations in the current study. The first one is that the present study is limited by its retrospective nature. There was a relatively high probability of incomplete data, especially in the patient's personal history and antibiotic intake history; thus, more randomized prospective studies are needed. Secondly, our study covered only 4 hospitals, making its generalizability limited. Our results need to be confirmed over a longer period in a larger group of patients. Thirdly, the antibiotics used in this study included only a few kinds, which means the effectiveness of the other antibiotics is uncertain. Given these limitations, more rigorous prospective randomized controlled trials and multicenter studies are needed in the future.

### Conclusions

For patients undergoing lumbar surgeries, sex, revision surgery, primary diagnosis, and procedure type are statistically important factors associated with the rate of dural tear. Age exerts a statistically important influence on the rates of dural tear and FDR. The findings from this study show that the use of prophylactic antibiotics did not affect the incidence of surgical site infection following lumbar dural tear as a complication of lumbar spinal surgery.

#### **Declaration of Figures' Authenticity**

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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