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## Spine immobilization and neurological outcome in Vertebral Osteomyelitis

### SPONDIMMO, a prospective multicentric cohort

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## **ABSTRACT:**

**Objective.** The aim of our study was to describe spine immobilization in a multicentric cohort of vertebral osteomyelitis (VO), and evaluate its association with neurological complications during follow-up.

**Methods.** We prospectively included patients from 2016 to 2019 in 11 centers. Immobilization, imaging, and neurological findings were specifically analyzed during a 6-month follow-up period.

**Results.** 250 patients were included, mostly men (67.2%, n=168). Mean age was  $66.7 \pm 15$  years. Diagnosis delay was 25 days. The lumbo-sacral spine was most frequently involved (56.4%). At diagnosis, 25.6% patients (n=64) had minor neurological signs and 9.2% (n=23) had major ones. Rigid bracing was prescribed for 63.5% (n=162) of patients, for a median of 6 weeks, with variability between centers ( $p < 0.001$ ). The presence of epidural inflammation and abscess on imaging was associated with higher rates of rigid bracing prescription (OR 2.33,  $p = 0.01$ ). Frailness and endocarditis were negatively associated with rigid bracing prescription (OR 0.65,  $p < 0.01$ , and OR 0.42,  $p < 0.05$ , respectively). During follow up, new minor or major neurological complications occurred in respectively 9.2% (n=23) and 6.8% (n=17) of patients, with similar distribution between immobilized and non-immobilized patients.

**Conclusion.** Spine immobilization prescription during VO remains heterogeneous and seems associated inflammatory lesions on imaging but negatively associated with frailness and presence of endocarditis. Neurological complications can occur despite rigid bracing. Our data suggest that in absence of any factor associated with neurological complication spine bracing might not be systematically indicated. We suggest that spine immobilization should be discussed for each patient after carefully evaluating their clinical signs and imaging findings.

**Keywords:** Vertebral osteomyelitis; spondylodiscitis; spinal infection; spine immobilization

## 1. INTRODUCTION

Vertebral osteomyelitis (VO) is a spine infection involving intervertebral discs and adjacent vertebral endplates. It affects 2.4/100 000 inhabitants per year in France (0.5 to 10/100 000 in Europe) [1] and 5.4/100 000 in the United States in 2013, with a mortality rate of 2.2% [2]. The incidence of VO has increased in recent decades. VO can be associated with neurological complications. In a previous study, we showed that they occurred in 40% of cases [3]. In severe cases, surgical intervention is needed: e.g. progressive neurological deficits, progressive deformity, spinal instability despite adequate antimicrobial therapy, patients with persistent or recurrent bloodstream infections, or worsening pain despite appropriate medical therapy [4].

In addition to antimicrobial therapy, spine immobilization is usually prescribed to decrease pain, reduce inflammation and prevent neurological complications [5]. However, the most recent guidelines published by the Infectious Diseases Society of America, did not mention the use of immobilization in management of VO [4]. The French Infectious Diseases Society (SPILF) recommends spine immobilization for 2 months, with 1 to 3 weeks of strict bed rest before rigid bracing [6]. Nevertheless, those recommendations are increasingly questioned because of the lack of evidence in the literature regarding the efficacy of immobilization [7] [8] and because patients frequently complain of poor tolerance of their bracing. Moreover, from a pathophysiological perspective, motor deficit is most often due to spinal cord ischemia, a septic embolism of the vertebral arteries, or a compressive abscess causing spinal stenosis [9]. The utility of spine bracing to prevent these complications still therefore needs to be investigated.

The objective of our study was to describe spine immobilization practices in a large cohort of VO patients recruited in rheumatology, infectious disease, and neurosurgery units from several hospitals. Secondary objectives were to identify factors associated with the prescription of immobilization, and to evaluate the association between immobilization and neurological complications.

## **2. METHODS**

### **2.1 Study Design and Setting:**

We conducted a prospective national observational study in 11 French Hospital centers, from February 2016 to December 2019. We prospectively included adult patients hospitalized for VO in rheumatology, infectiology, or spinal surgery units. On inclusion, patients were informed of the study, received an information letter, and gave their oral consent. The study protocol was approved by the local ethic committee and recorded in Clinical Trials (NCT04655950). The study was conducted using the format recommended by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

### **2.2 Inclusion and Exclusion Criteria:**

Patients were over the age of 18 years and hospitalized in medical or surgery units for VO occurring on a non-instrumented spine (without foreign devices from a previous spinal procedure). VO was defined on typical radiological features (Magnetic Resonance Imaging or Computed-Tomography plus radionuclear imaging) and identification of a microbiological agent (on blood cultures or vertebral biopsy). If microbiological samples were sterile, patients could be included if they had a good response to antibiotic therapy with signs of inflammation on the vertebral biopsy (Polynuclear cell infiltrate or micro-abscesses), and thus, if the clinicians in charge of the patient concluded that there was a septic cause to the spondylodiscitis.

Exclusion criteria were spinal bone device infections, VO occurring within one month of a spinal surgical procedure, or if there was no imaging available for review. Patients under the age of 18 years, under legal protection, or pregnant women were excluded. Patients with other types of spine infection were not included (e.g. isolated spondylitis, facet joint infection, or isolated epidural infection). Patients were excluded if an alternative diagnosis of spondylodiscitis was found (e.g. crystal-induced spondylodiscitis).

### 2.3 Data Collection:

Clinical information (pain scale score, neurological examination, Oswestry score for spinal function), imaging data, as well as the type (rigid or soft) and duration of spine immobilization were recorded at baseline and during the two follow-up appointments (between 6 weeks and 3 months and at 6 months). We also recorded microbiological results and modality of antibiotic therapy.

### 2.4 Definitions:

Immobilization was defined as prescription of rigid bracing. We compared immobilized patients with the others who were prescribed soft bracing or no bracing at all.

Neurological complications were defined as minor (radicular pain, reflex abolition, sensitive loss) or major (motor weakness or sphincter dysfunction). New neurological complications were defined as appearance of a new sign or worsening of neurological examination.

Imaging variables were grouped into 3 categories: structural lesion (vertebral destruction > 50%, destruction of posterior arch and sagittal angulation), inflammatory lesion (epidural inflammation and epidural abscess) and compressive lesion (spinal cord hypersignal, subarachnoid space effacement, and dural sac compression) (Figure 1).

### 2.5 Statistical Analyses:

Baseline characteristics of the overall population were expressed as frequencies (percentages) for categorical variables, as mean  $\pm$  standard deviation (SD) for continuous data and in the case of non-normal distributions as median with interquartile range (IQR; 25th–75th percentile). Risk factors for immobilization were assessed using mixed models to take center effect into account (random effect). Multivariate analyses were performed. All variables entered into the model were associated with a p value of 0.2 or lower in univariate analyses. The final set of predictors was selected via stepwise variable selection. Multiple imputations with the use of chained equations were performed to address missing data under

a missing-at-random assumption. All tests were two tailed, and p values of less than 0.05 were considered significant. Statistical analyses were performed with SAS software, version 9.4 (SAS Institute).

### **3. RESULTS**

#### **3.1 Patient Characteristics:**

We included 250 patients with a mean age of  $66.7 \pm 15$  years, mostly men (67.2%, n=168). Median duration of pain before diagnosis was 25 days (interquartile range [IQR], 11-51 days). Demographic characteristics and comorbidities are described in Table 1.

On clinical examination at diagnosis, 25.6% patients (n=64) had minor neurological signs and 9.2% (n=23) major neurological signs. The imaging technique used for diagnosis was mainly magnetic resonance imaging (MRI), performed in 87.2% of patients, other imaging modalities were computed tomography, positron emission tomography (PET) and bone scan. In our cohort, the lumbo-sacral level was the most frequently involved (56.4%), followed by the thoracic level (23.2%), and the cervical level (13.3%). Epidural inflammation was the most frequent imaging anomaly, found in 61.1% of patients. Epidural abscesses were found in 19.6% of cases. A structural lesion (destruction > 50% of the vertebral body, destruction of the posterior arch or sagittal angulation) was found in 27.6% of patients, and a compressive lesion (spinal cord hypersignal, subarachnoid space effacement, or dural sac compression) in 26.5%.

Blood cultures were performed in 97.6% of cases, 69.2% of them were positive. Vertebral biopsies were performed in 33.2% of patients, with 74.4% of positivity and surgical biopsies in 8.4% of patients with 81% of positivity. *Staphylococcus aureus* was the most frequent pathogen found (33.6% of the patients). Microbiological samples remained sterile in 5.6% of cases. Endocarditis was diagnosed in 22.4% (n=56) of patients. Patients with endocarditis had significantly fewer minor neurological symptoms at diagnosis (supplementary data). Median duration of antibiotic therapy was 45 days (IQR 42-62 days), with a median

administration of 21 days intravenously (IQR 10-42 days) and 35 days orally (IQR 14-52 days). In our cohort, 11.2% of patients (n=28) underwent spine surgery, those patients had more often major neurological complications or compressive and inflammation lesions, and the cervical level was more often involved (Table S1, See the supplementary material associated with this article online).

### 3.2 Immobilization Findings:

In 76.7% (n=191) of cases, strict bed rest was prescribed, with median duration of 8 days (IQR 5-14 days). A verticalization table was used in 3.6% of patients. Rigid bracing was prescribed in 65.3% (n=162) of patients, with median duration of 6 weeks (IQR 6-12), the duration was 6 weeks for 61 (42.7%) patients and 12 weeks for 37 (25.9%). Initial use of soft bracing was prescribed in 4.0% (n=11) of patients.

In order to explore factors associated with the prescription of immobilization, we compared patients immobilized with rigid bracing with patients not immobilized (Table 2). In univariate analyses, the clinical factors significantly associated with prescription of rigid bracing were: younger age (65.1 years old in the immobilization group and 69.3 in the non-immobilized group,  $p<0.05$ ), less frail patients on the autonomy scale ( $p<0.05$ ) and male gender (71.6% and 58.1% respectively,  $p<0.05$ ). Prescription of immobilization was significantly different between centers ( $p<0.001$ ) with a variation of the prescription rate of rigid bracing from 13.3% (n=2/15) and even 0% (n=0/4) to 100% (n=13/13). Imaging factors associated with rigid bracing were epidural inflammation ( $p<0.01$ ), spinal cord hypersignal ( $p<0.05$ ), subarachnoid space effacement ( $p<0.05$ ), and dural sac compression ( $p<0.05$ ). Patients with endocarditis were less likely to be immobilized than others (17.9% (n=29) and 31.7% (n=27) respectively,  $p<0.05$ ). We found no significant association between the level involved (lumbar, thoracic, or cervical), pain score, neurological complications at diagnosis, recorded comorbidities and the prescription of a rigid immobilization.



In multivariate analysis (table 2), the only independent factor positively associated with rigid spine immobilization was inflammatory lesion on imagery (OR=2.33 and IC [1.21-4.52],  $p=0.01$ ). Endocarditis was negatively associated with rigid bracing (OR=0.42 and IC [0.21-0.87],  $p<0.05$ ), as was frailness (OR=0.65 and IC [0.48-0.88]), which was highly correlated to older age.

Some patients in the immobilized group (35.1%,  $n=57/162$ ) received a soft bracing prescription to follow on from the rigid one at the end of the initial hospitalization, or at 3 months. This relay bracing was more frequently prescribed in patients with a higher pain scale score on activity ( $p=0.001$ ). Of the patients with an initial prescription for rigid bracing, 23.3% ( $n=30/129$ ) were still wearing a soft or rigid brace at 6 months. Observance was considered good for 83.0% ( $n=112/135$ ) of patients, who declared that they complied with the prescription fully.

### 3.3 Immobilization and Clinical Evolution:

During the 6-month follow-up, new minor neurological complications occurred in 9.2% ( $n=23$ ) of cases, at a median of 22 days (IQR, 6-181) after diagnosis, 12.6% ( $n=20$ ) in the immobilized group and 3.5% ( $n=3$ ) in the other group (Figure 2). Major neurological complications occurred in 6.8% of patients ( $n=17$ ), with a median onset of 11 days (IQR, 3-23), 6.2% ( $n=10$ ) in the immobilized group and 8.1% ( $n=7$ ) in the other group (Table S2). At the end of the follow up, minor neurological complications persisted in 8.1% ( $n=15/186$ ) patients and major neurological complications in 5.4% ( $n=10/186$ ) of patients. Among patients with minor neurological complication at baseline, 15.7% (8/51) still had a minor sign at 6 months. A major sign persisted at 6 months in 30.8% (3/13) of the patient with a major neurological complication at baseline. The mortality rate was 6.4% ( $n=16$ ).

We analyzed factors associated with major neurological complications during-follow-up (Table 3, Table S3). Factors significantly associated were mostly imaging features such as destruction of the posterior arc ( $p<0.05$ ), or sagittal angulation ( $p<0.05$ ). Signs of

compression were also associated with major neurological complications: spinal cord hypersignal ( $p < 0.05$ ), anterior effacement of the subarachnoid space ( $p < 0.01$ ), and dural sac compression ( $p < 0.01$ ). Patients who underwent surgery had significantly more major complications during follow-up ( $p < 0.001$ ). These patients were more severe at initial presentation (Table S1). We found no impact of prescribing rigid bracing on major neurological complications during follow-up ( $p = 0.56$ ).

#### **4. DISCUSSION**

To our knowledge, SPONDIMMO is the first study to assess spine immobilization during VO. The lack of literature on this subject is surprising as immobilization remains a frequent question in everyday practice and aims to prevent neurological complications, and to accelerate improvement of pain and inflammation associated with this serious condition. With this large, prospective, multicenter cohort we were able to describe both the prescription of spine immobilization, and the neurological evolution of the patients during a 6-month follow-up period, in both medical and surgical departments.

There is a lack of clear guidelines on spine immobilization. Most studies mention rigid spine immobilization for at least 6 weeks [7,10–12] for all patients, and even sometimes for 6 months or until spine ankylosis occurs [13]. In our study, only two-thirds of our patients received a prescription for rigid bracing and the duration of this prescription varied considerably, with only half of the patients (48%) wearing their rigid bracing for 6 weeks or more. In their retrospective cohorts, Bettini et al. used a plaster brace for all patients for 8 weeks with a canvas corset for 4 more weeks [7]. Legrand et al. described bracing for 89.1% of patients for 81.5 days [14]. Rutges et al. noted that bed rest and orthosis have not been investigated in detail, and suggested a pragmatic approach: bed rest until pain and infection decrease, then start mobilization with a thoracolumbosacral orthosis for all patients, without mentioning any duration [15]. Finally, the French Infectious Diseases Society (SPILF) recommends using rigid bracing for 1 to 3 months depending on the localization [6]. Our data shows that these recommendations are rarely followed in clinical practice.

Strict bed rest is also part of the standard treatment in VO, for a duration of 1 or 2 weeks, or for some authors until improvement in the pain [16] and to reduce inflammation. The aim of using spine bracing is to avoid prolonged bed rest [5] and its well-known morbidities, such as bedsores, deep vein thrombosis, pulmonary embolism, muscle loss, and cardiopulmonary disadaptation, especially in the elderly [17].

We next sought the factors associated with the prescription of a rigid bracing. We first found that the presence of inflammatory lesions (epidural inflammation or epidural abscess) but not compressive ones was a major determinant for the prescription of rigid bracing in multivariate analysis. This is in opposition with the fact that compressive and structural lesions are clearly identified in the literature as risk factors for neurological impairment [3], [18] as confirmed in this cohort. These results highlight that physicians give more credit to inflammatory lesions although the association between inflammatory lesions and neurological complications remains debated. Frailer and older patients received fewer prescriptions for rigid spine immobilization, probably in order to avoid immobilization complications in this vulnerable population known to have poorer outcomes, but without an increased risk of neurological complication [19]. Endocarditis was also negatively associated with rigid bracing, probably because VO was an incidental diagnosis on body-scan imaging performed in the extension check-up of patients with endocarditis. Those patients most often did not have VO symptoms (nor backpain neither stiffness), which is consistent with the 41% of asymptomatic cases of VO in endocarditis found by Carbone et al.[20]. Another determinant for the decision of the type and duration of spine immobilization was the hospital center, highlighting the importance of local custom and experience. This shows the need for consensual recommendations based on evidence-based data to harmonize practices. Of note, we found no association with cervical level or major neurological complications at diagnosis and rigid immobilization. However, those patients were more often managed surgically.

The aim of spine immobilization is to reduce the risk of neurological complications. We thus studied the occurrence of new neurological symptoms during follow-up in relation to the

prescription of rigid bracing. We found a similar rate of new major neurological complications in patients immobilized with (6.2%) and those without (8.1%) rigid bracing. Likewise, occurrence of minor neurological complications was similar with (12.6%) or without (3.5%) rigid bracing. The observational design of our study and the absence of any randomization preclude drawing any definite conclusions regarding the effect of immobilization on neurological complications. However, this shows the low rate of such complications in the non-immobilized group and also the possibility of the occurrence of complications, even in cases of rigid immobilization. As structural and compressive lesions were significantly associated with neurological complications, patients with this type of anomaly should therefore be carefully monitored. An important finding was the short delay after diagnosis before the occurrence of new major neurological complications, with a median of 11 days in our cohort. This enhances the requirement for strict clinical monitoring during the first two weeks, in addition to controlling normalization of inflammatory markers such as C-reactive protein dosage (CRP) [21]. Consistently with other cohorts of VO [22], the neurological outcome was favorable for most patients, with only 5.4% of major neurological signs persistent at 6 months.

In conclusion, we showed that spine immobilization prescriptions are highly heterogeneous between centers and seems associated with inflammatory lesions on imaging but negatively associated with frailness and simultaneous endocarditis. Our data suggest that, in absence of any factor associated with neurological complication, spine bracing might not be systematically indicated. Therefore, bracing should be discussed for each patient after systematic analysis of clinical and imaging information. While Bernard et al. investigated modified antibiotic practices in a randomized trial [23], spine immobilization deserves proper investigation in randomized controlled studies to better define its indications and benefits for patients.

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Declaration of interest: none.

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**Figure 1: Illustration of structural, inflammatory and compressive damage in Vertebral Osteomyelitis**

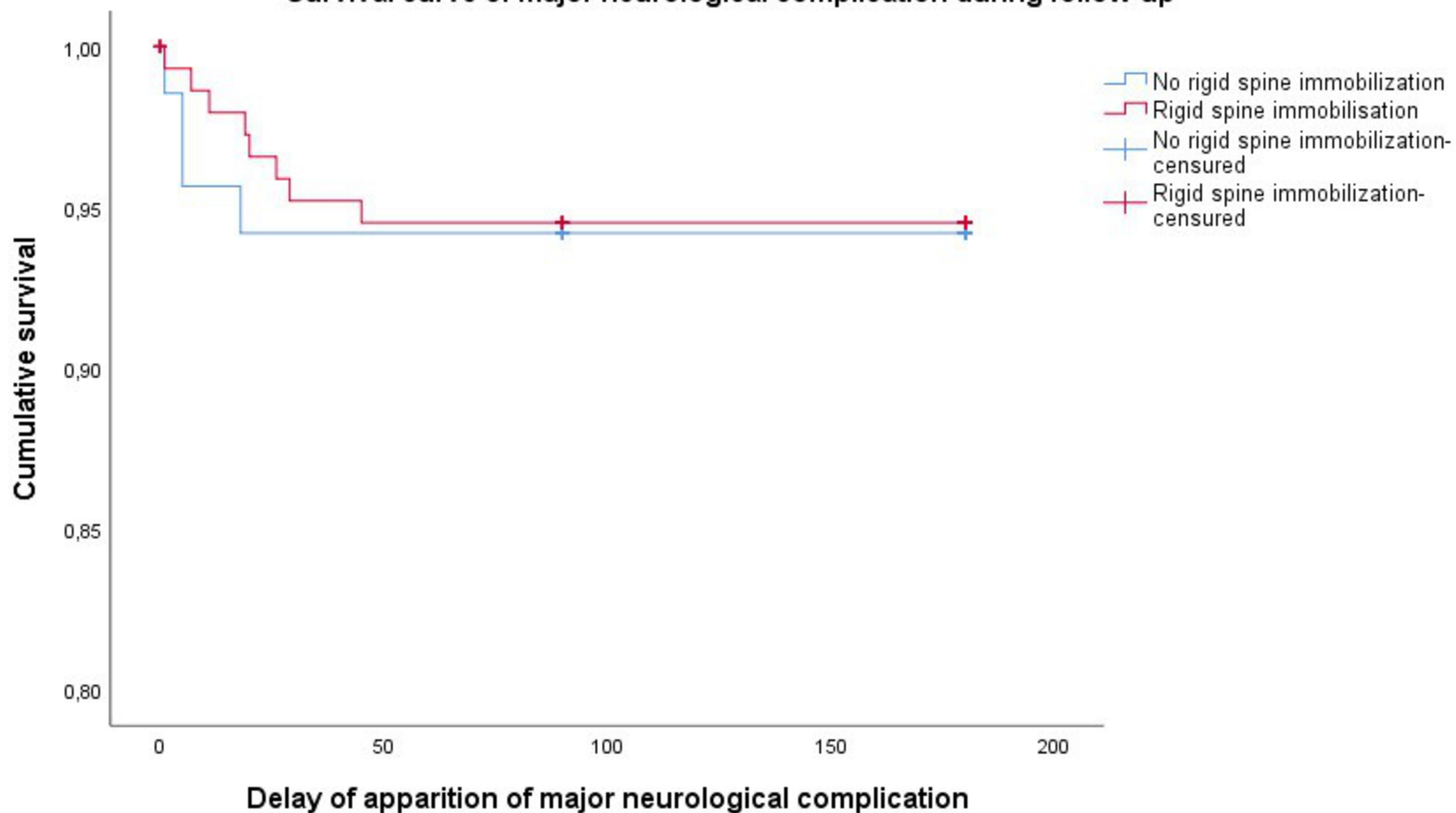
Legend: A. Inflammatory lesion on MRI: epidural abscess. B. Structural lesion on MRI: destruction > 50% of the C6 vertebrae. C. Compressive lesion on MRI : dural sac compression and spinal chord hypersignal

**Figure 2: Survival curve of minor and major neurological complications during the follow-up of patients with Vertebral Osteomyelitis**

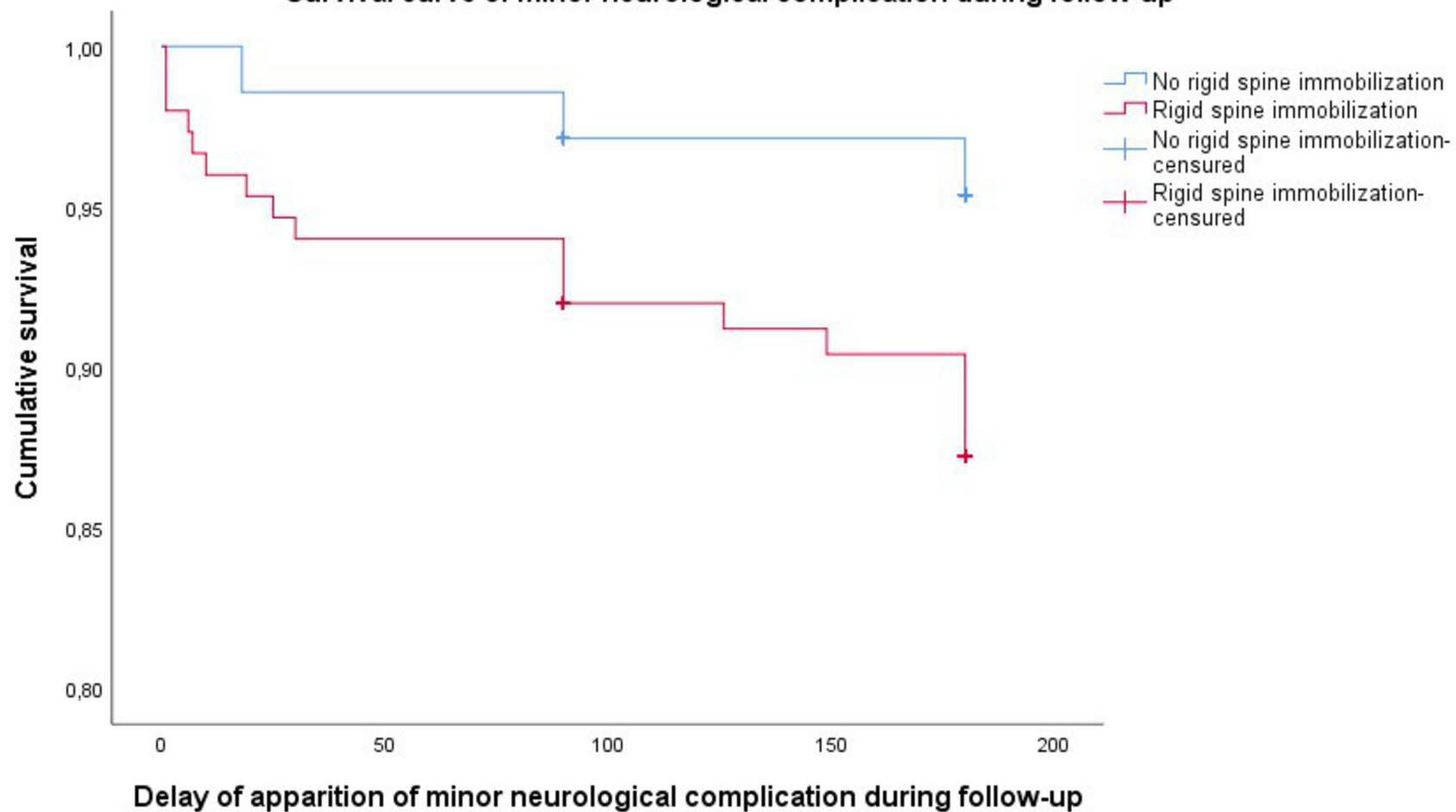




Survival curve of major neurological complication during follow-up



Survival curve of minor neurological complication during follow-up



**Table 1 : General characteristics of patients with Vertebral Osteomyelitis**

	<b>Total % (n=250)</b>
<b>Male, % (n)</b>	67.2 (168/250)
<b>Age, years, mean (SD)</b>	66.7 (15.0)
<b>Diagnosis delay, median [IQR]</b>	25 [11-51]
<b>History of spine surgery, % (n)</b>	5.6 (14/250)
<b>Frailty (0 “very fit” to 5 “severely frail”), median [IQR]</b>	1.0 [1-2]
<b>Diabetes, % (n)</b>	20 (50/250)
<b>Cancer, % (n)</b>	22 (55/250)
<b>Immunosuppressive treatment, % (n)</b>	8.4 (21/250)
<b>Renal insufficiency, % (n)</b>	4.8 (12/249)
<b>Obesity, % (n)</b>	22.9 (57/249)
<b>Blood culture, % (n)</b>	97.2 (243/249)
<b>Positive blood culture, % (n)</b>	69.2 (173/243)
<b>Percutaneous biopsy, % (n)</b>	33.2 (83/249)
<b>Positive percutaneous biopsy, % (n)</b>	74.4 (61/82)
<b>Surgical biopsy, % (n)</b>	8.4 (21/249)
<b>Positive surgical biopsy, % (n)</b>	81.0 (17/21)
<b>Microbiological findings:</b>	
Staphylococcus aureus and Coagulase-negative staphylococci, % (n)	40.8 (102/250)
Streptococcus sp., % (n)	18.0 (45/250)
Escherichia coli and other Gram-negative bacilli, % (n)	13.2 (33/250)
Enterococcus sp., % (n)	7.2 (18/250)
Mycobacterium tuberculosis, % (n)	5.6 (14/250)
Other or multiple bacterial findings, % (n)	9.6 (24/250)
No bacterial identification or missing data, % (n)	5.6 (14/250)
<b>Endocarditis, % (n)</b>	22.4 (56/249)
<b>Level involved:</b>	
Cervical (C2-C3 to C6-C7), % (n)	13.3 (32/241)

Cervico-thoracic (C7-T1), % (n)	1.7 (4/241)
Thoracic (T1-T2 to T11-T12), % (n)	23.2 (56/241)
Thoraco-lumbar (T12-L1), % (n)	5.4 (13/241)
Lumbar (L1-L2 to L5-S1), % (n)	56.4 (136/241)
Multifocal, % (n)	25.5 (61/239)
<b>Imaging anomaly</b>	
Structural lesion, % (n)	27.6 (61/223)
Vertebral destruction > 50%, % (n)	9.8 (23/234)
Destruction of posterior arc, % (n)	8.4 (19/226)
Sagittal angulation, % (n)	20.1 (47/224)
Inflammatory lesion, % (n)	62.6 (139/222)
Epidural inflammation, % (n)	61.1 (135/221)
Epidural abscess, % (n)	19.6 (44/224)
Compressive lesion, % (n)	26.5 (58/219)
Spinal cord hypersignal, % (n)	8.7 (19/218)
Subarachnoid space effacement, % (n)	19.9 (44/221)
Dural sac compression, % (n)	22.5 (50/222)
<b>Duration of antibiotherapy: median [IQR]</b>	45 [42-62]
<b>Surgery, % (n)</b>	11.2 (28/249)
<b>Pain scale evaluation (/100), mean (SD)</b>	53.6 (28,65)
<b>Minor neurological symptom, % (n)</b>	25.6 (64/250)
<b>Major neurological symptom, % (n)</b>	9.2 (23/250)

Legend: SD = standard deviation, Obesity = Body Mass Index > 30 kg/m<sup>2</sup>, IQR = interquartile range, Q1=25%, Q3=75%

**Table 2: Univariate and multivariate analysis of factors associated with the prescription of rigid spine immobilization in Vertebral Osteomyelitis**

	Univariable analysis			Multivariable analysis		
	Rigid Immobilization	No rigid immobilization	p	Odds Ratio	95% Confidence Interval	p
Population characteristics	63.5% (n=162)	34.7% (n=86)				
Centers			<0.001	take into account as random effect in multivariate analysis		
Male, % (n)	71.6 (116)	58.1 (50)	<b>&lt;0.05</b>			
Age, mean (SD)	65.1 (15.2)	69.3 (14.2)	<b>&lt;0.05</b>			
Diagnosis delay, median [IQR]	24 [11-52]	25 [11-44]	0.98			
History of spine surgery, % (n)	6.8 (11/162)	3.5 (3/86)	0.39			
Frailty (0 “very fit” to 5 “severely frail”), median [IQR]	1.0 [1-2]	1.0 [0-2]	<b>0.05</b>	0.65	[0.48 ; 0.88]	<b>&lt;0.01</b>
Diabetes, % (n)	19.8 (32/162)	20.9 (18/86)	0.83			
Cancer, % (n)	25.3 (41/162)	16.3 (14/86)	0.10			
Immunosuppressant treatment, % (n)	10.5 (17/162)	4.7 (4/86)	0.12			
Renal insufficiency, % (n)	3.1 (5/161)	8.1 (7/86)	0.12			
Obesity, % (n)	22.4 (36/161)	24.4 (21/86)	0.72			
Endocarditis, % (n)	17.9 (29/162)	31.7 (27/85)	<b>&lt;0.05</b>	0.42	[0.21 ; 0.87]	<b>&lt;0.05</b>
Level involved:						
Cervical, % (n)	16.2 (25/154)	8.1 (7/86)	0.16			
Cervico-thoracic, % (n)	2.0 (3/154)	1.2 (1/86)	1.00			
Thoracic, % (n)	21.4 (33/154)	26.7 (23/86)	0.54			
Thoraco-lumbar, % (n)	5.2 (8/154)	5.8 (5/86)	1.00			
Lumbar, % (n)	55.2 (85/154)	58.1 (50/86)	0.82			
Multifocal, % (n)	24.0 (37/154)	26.5 (22/83)	0.67			
Imaging anomaly						

Structural lesion, % (n)	30.1 (44/146)	22.7 (17/75)	0.24
Inflammatory lesion, % (n)	69.7 (101/145)	48.0 (46/75)	<0.01
Compressive lesion, % (n)	31.7 (45/142)	17.3 (13/75)	<0.05

2.33	[1.21 ; 4.52]	<b>0.01</b>
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<b>Duration of antibiotherapy, median</b>			
<b>[IQR]</b>	45 [42-62]	46 [42-61]	0.96
<b>Surgery, % (n)</b>	14.2 (23/162)	5.9 (5/85)	0.05
<b>Pain scale evaluation (/100): mean</b>			
<b>(SD)</b>	54.7 (27.01)	51.2 (31.46)	0.57
<b>Minor neurological symptom, % (n)</b>	25.9 (42/162)	24.4 (21/86)	0.80
<b>Major neurological symptom, % (n)</b>	11.1 (18/162)	5.8 (5/86)	0.17

Legend: SD = standard deviation, IQR = interquartile range, Q1=25%, Q3=75

**Table 3: Factors associated with the apparition of neurological complications during follow-up of patients with Vertebral Osteomyelitis in univariable analysis**

	Apparition of major neurological complications 7.2% (18/250)	No major neurological complications 92.8% (232/250)
<b>Male, % (n)</b>	47.1 (8/17)	68.7 (160/233)
<b>Age, years, mean (SD)</b>	65.6 (11.86)	66.7 (15.25)
<b>Diagnosis delay, median [IQR]</b>	21.8 (20.51)	42.2 (54.1)
<b>History of spine surgery, % (n)</b>	5.9 (1/17)	5.6 (13/233)
<b>Frailty (0 “very fit” to 5 “severely frail”):</b>		
<b>mean (SD)</b>	1.35 (1.17)	1.26 (1.02)
<b>Diabetes, % (n)</b>	17.6 (3/17)	20.2 (47/233)
<b>Cancer, % (n)</b>	35.3 (6/17)	21.0 (49/233)
<b>Immunosuppressive treatment, % (n)</b>	0 (0/17)	9 (21/233)
<b>Renal insufficiency, % (n)</b>	0 (0/17)	5.2 (12/233)
<b>Obesity, % (n)</b>	41.2 (7/17)	21.6 (50/232)
<b>Endocarditis, % (n)</b>	23.5 (4/17)	22.4 (52/232)
<b>Level involved:</b>		
<b>Cervical, % (n)</b>	18.8 (3/16)	12.9(29/225)
<b>Cervico-thoracic, % (n)</b>	6.3 (1/16)	1.3 (3/225)
<b>Thoracic, % (n)</b>	31.3 (5/16)	22.7 (51/225)
<b>Thoraco-lumbar, % (n)</b>	0 (0/16)	5.8 (13/225)
<b>Lumbar, % (n)</b>	43.8 (7/16)	57.3 (129/225)
<b>Multifocal, % (n)</b>	43.8 (7/16)	24.2 (54/223)
<b>Imaging anomaly</b>		
<b>Vertebral destruction &gt; 50%, % (n)</b>	12.5 (2/16)	9.6 (21/218)
<b>Destruction of posterior arc, % (n)</b>	25.0 (4/16)	7.1 (15/210)*
<b>Sagittal angulation, % (n)</b>	43.8 (7/16)	19.2 (40/208)*



Epidural inflammation, % (n)	81.3 (13/16)	59.5 (122/205)
Epidural abscess, % (n)	37.5 (6/16)	18.3 (38/208)
Spinal cord hypersignal, % (n)	25.0 (4/16)	7.4 (15/202)*
Subarachnoid space effacement, % (n)	50.0 (8/16)	17.6 (36/205)**
Dural sac compression, % (n)	56.3 (9/16)	19.9 (41/206)**
<b>Duration of antibiotherapy, median [IQR]</b>	43 (7-102)	45 (5-417)
<b>Surgery, % (n)</b>	47.1 (8/17)	8.6 (20/232)***
<b>Pain scale evaluation (/100), mean (SD)</b>	53.6 (25.3)	53.6 (28.9)
<b>Minor neurological symptom, % (n)</b>	11.8 (2/17)	26.6 (62/233)
<b>Major neurological symptom, % (n)</b>	0 (0/17)	9.9 (23/233)

Legend: SD = standard deviation, IQR = interquartile range, Q1=25%, Q3=75%

\* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$