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# Severe listeriosis in intensive care units: insights from a retrospective multicentric study

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## Abstract

**Background** Listeriosis is a rare but severe foodborne infection, particularly affecting immunocompromised individuals and older adults. Severe cases may lead to neurolisteriosis and sepsis, necessitating intensive care unit (ICU) admission. This study aims to analyze the demographic characteristics, clinical presentation, microbiological findings, treatments, and outcomes of critically ill patients with *Listeria* infections in the ICU.

**Methods** A retrospective multicenter study was conducted across 23 French hospitals over a 10-year period, including ICU patients with culture-confirmed *Listeria monocytogenes* infections. Data on demographics, comorbidities, ICU admission characteristics, biological and microbiological parameters, treatments, and outcomes were collected. The primary outcome was ICU mortality. A multivariable logistic regression model was used to identify factors associated with mortality in patients with neurological manifestations.

**Results** A total of 110 patients were included, with a median age of 68 years; 61% were male, and 71% were immunocompromised. Neurological involvement was present in most cases. Invasive mechanical ventilation was required in 58% of patients, and vasopressor support in 44%. ICU and in-hospital mortality rates were 25% and 32%, respectively. Among patients with neurolisteriosis, each 1-point decrease in Glasgow Coma Scale score at admission was associated with increased mortality (OR, 1.22; 95% CI 1.05–1.45;  $p=0.009$ ), as were higher cerebrospinal fluid (CSF) protein levels (OR, 1.56; 95% CI 1.15–2.41;  $p=0.028$ ). Steroid use was not significantly associated with reduced mortality (OR, 0.30; 95% CI 0.07–1.05;  $p=0.076$ ).

**Conclusion** Listeriosis requiring ICU admission is associated with high morbidity and mortality, particularly in older and immunocompromised patients. The severity of these infections is reflected by the frequent need for organ support. Further research is needed to clarify the potential role of steroids in neurolisteriosis.

**Keywords** Listeriosis, Intensive care unit (ICU), Neurolisteriosis, Steroids, Immunosuppression, Sepsis

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## Background

Listeriosis, caused by *Listeria monocytogenes*, a Gram-positive bacterium, can manifest as bacteremia, central nervous system involvement, or infection of other organ systems [1, 2]. Despite improvement in survival [3, 4], listeriosis remains a major public health concern, responsible for significant morbidity, mortality, and economic burden [5–7]. A substantial portion of these costs is associated with frequent ICU admissions, particularly in cases of sepsis or central nervous system involvement (neuroinfection).

While recent research has focused extensively on understanding the pathophysiology of listeriosis and host–pathogen interactions, making *L. monocytogenes* one of the most-studied pathogenic bacteria [8, 9], its clinical aspects remain less thoroughly investigated, particularly in critically ill patients. From 2009 to 2013, the MONALISA cohort [10] provided new insights into the prognostic factors of this disease and highlighted the central role of intensivists in the management of listeriosis. Indeed, 20% of patients with bacteremia and 60% of patients with neurological form required ICU admission, mortality rate reaching 45% and 30% at three months, respectively [10]. The therapeutic management of listeriosis remains under debate as illustrated by discrepancy regarding the beneficial impact of corticosteroids in cases of neuroinfection [10, 11]. Thus, uncertainties remain regarding the optimal treatment of this infection, as well as its clinical characteristics, biological markers, and prognostic factors in ICU patients.

This national, multicenter, retrospective study primarily aimed to assess in-hospital mortality in critically ill patients admitted to the ICU with listeriosis. Secondary objectives included describing the demographic and clinical characteristics of this population and analyzing risk factors for in-hospital mortality, particularly in patients with neuroinfection.

## Methods

### Study design and patients

This retrospective multicenter study was conducted across 23 intensive care units (ICUs) in tertiary teaching hospitals throughout metropolitan France. Eligible cases were identified by searching hospital databases for ICD-10 code A32 (as a principal or associated diagnosis). To ensure accuracy, all cases were cross-matched with microbiology laboratory records, and local investigators independently reviewed medical files. A confirmed case was defined as a patient with *Listeria monocytogenes* isolated from a normally sterile site. We included all cases from January 2013 to December 2022, and classified these as bacteremia, neuroinfection, or other forms.

Only adult patients ( $\geq 18$  years old) were included, as all participating ICUs exclusively manage adult patients. Given the severity of listeriosis in critically ill patients, no exclusion criteria were applied to ensure a comprehensive representation of cases.

### Definitions of clinical conditions

Clinical definitions used in this study were based on those proposed in the MONALISA national prospective cohort study (Charlier et al., *Lancet Infect Dis* 2017) [10], complemented by established definitions from international guidelines when available. Bacteremia was defined as the isolation of *Listeria monocytogenes* from blood. Neuroinfection was defined as the isolation of *L. monocytogenes* from cerebrospinal fluid (CSF) by culture and/or PCR, or from blood cultures in a patient presenting with unexplained neurological symptoms such as altered consciousness, seizures, nuchal rigidity, or focal neurological signs. As in the MONALISA study, patients with neuroinfection and concurrent positive blood cultures were classified under neuroinfection. Meningitis was diagnosed in patients with abnormal CSF analysis accompanied by typical symptoms. Meningoencephalitis was defined by abnormal CSF associated with altered vigilance, seizures, or other manifestations consistent with encephalitis, in line with the 2013 International Consensus Definition [12]. Rhombencephalitis was defined as brainstem or cerebellar involvement, based on clinical features such as ataxia or cranial nerve deficits. Immunocompromised status was defined if at least one of the following was present: solid tumor within the last 5 years, hematological malignancy, solid organ transplant, corticosteroid use within the last 3 months, use of other immunosuppressive drugs, cirrhosis, chronic kidney disease, chemotherapy, diabetes mellitus, or chronic alcohol abuse (daily alcohol intake of more than three drinks per day). Fever was defined as a core temperature  $\geq 38.5$  °C. Shock was defined by vasopressor use or a SOFA hemodynamic score  $> 1$  on ICU admission (Vincent et al., 1996) [13]. Organ dysfunction and failure were evaluated using the SOFA score. Acute kidney injury was defined by a renal SOFA score  $\geq 2$  [13]. Neutropenia was defined as an absolute neutrophil count  $< 1.5$  G/L, and severe thrombocytopenia as a platelet count  $< 100$  G/L. Hyponatremia was defined as sodium  $\leq 130$  mmol/L.

### Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes included the analysis of clinical and microbiological features of *Listeria monocytogenes* infections in ICU patients, as well as the identification of factors associated with survival.

### Statistical analysis

All data are presented as medians with interquartile ranges (25th–75th percentiles) for quantitative variables and frequencies (percentages) for qualitative variables. Baseline characteristics were compared between survivors and non-survivors using the Wilcoxon rank-sum test for quantitative variables and Fisher's exact test for qualitative variables. Factors associated with in-hospital mortality were assessed using multivariable mixed logistic regression models, with the center included as a random effect. Two separate models were built: one in the whole cohort, and one in the subgroup of patients with neurological involvement. Two models were built separately, in the whole cohort and in patients with a neurological involvement. For each model, covariates associated with the outcome at the 0.2 significance level in univariate analysis were selected based on clinical relevance and included in the model as fixed effects. The final model was then assessed using a multiple backward stepwise selection procedure, eliminated variables with an exit threshold set at  $p=0.05$ . Log linearity assumption and collinearity were carefully checked. Model calibration and discrimination were evaluated using the Hosmer–Lemeshow goodness-of-fit test and the concordance index (C-index).

As missing data represented less than 10% of the dataset, a complete-case analysis was conducted without imputation. Measures of association are presented as odds ratios (ORs) with 95% confidence intervals (CIs). All statistical tests were two-sided, and a  $p$ -value  $<0.05$  was considered statistically significant. Analyses were performed using R version 3.1.2 (<http://www.R-project.org>).

## Results

### Demographics and comorbidities

Over this ten-year period, 110 patients were included with a median age of 68 years (IQR: 58–77) (Table 1). The cohort consisted of 67 males (61%) and 43 females (39%). Pregnancy was noted in 2 patients (2%). Included patients had frequent comorbidities including chronic heart failure ( $n=22$ , 20%), respiratory disease ( $n=16$ , 15%), cirrhosis ( $n=15$ , 14%), diabetes mellitus ( $n=28$ , 25%), and chronic kidney disease (CKD) ( $n=18$ , 16%). Chronic alcohol abuse was reported in 21 patients (19%) (Table 1).

ICU admission sources included the emergency room (35%), home (15%), hospital wards (27%), and other hospitals (24%). The majority of patients were immunocompromised ( $n=78$ , 71%), with details as follows: 14 patients (13%) had cancer, 35 patients (32%) were on immunosuppressive drugs (25 on steroids and 10 on others immunosuppressive drugs), and 5 patients (5%) were

HIV-positive. Solid tumors were present in 13 patients (12%), with 6 having localized tumors (5%) and 7 having metastatic tumors (6%). Hematological malignancies were observed in 15 patients (14%) (Table 1).

### Clinical manifestations and involvement

Neurological involvement was the most prominent feature, with neurosteriosis identified in 82% of patients. This included meningitis (75%), meningoencephalitis (59%), rhombencephalitis (10%), and cerebral abscesses (6%). Altered mental status was reported in 69% of cases, while focal neurological deficits, primarily motor impairments in the arms and legs, were observed in 23%. Seizures occurred in 14%, including status epilepticus in 5% of cases. Bacteremia was observed in 68% of patients, reflecting its high prevalence in this cohort. Fever was documented in 59 patients (54%). Additional organ involvement included the lungs in 9%, the digestive tract in 9%, and the heart in 3% of cases. Diarrhea was a notable symptom in 17% of patients. Figure 1 provides an overview of the distribution of clinical manifestations.

### Organ support therapy and outcome

Shock was present in 34 patients (31%). Acute kidney injury was identified in 31 patients (28%). The median ICU length of stay (LOS) was 7 days (IQR: 3–16), and the hospital LOS was 24 days (IQR: 14–40.25). ICU mortality was 25%, with hospital mortality at 32%. Therapeutic limitations were implemented in 25% of the cases (Table 1).

### Biological characteristics

The biological parameters of the study cohort are summarized in Table 2. The study cohort showed severe thrombocytopenia in 26% of patients, with no significant leukocytosis. Marked lymphopenia was present with a median of  $0.8 \times 10^9/L$ . Inflammatory markers were elevated, with a median CRP level of 117 mg/L and a procalcitonin level of 1.9 ng/mL. Hyponatremia was observed in 16% of patients.

Cerebrospinal fluid (CSF) analysis revealed a median protein level of 2.54 g/L [IQR, 1.71 to 3.965] and a median WBC count of 397 cells/ $\mu$ L [IQR, 187.8 to 880], with a median percentage of neutrophils at 66.5% [IQR, 40.25 to 81] and a median percentage of lymphocytes at 25% [IQR, 10 to 50]. The median CSF to blood glucose ratio was 0.3 [IQR, 0.1 to 0.39].

### Microbiology and antibiotic usage

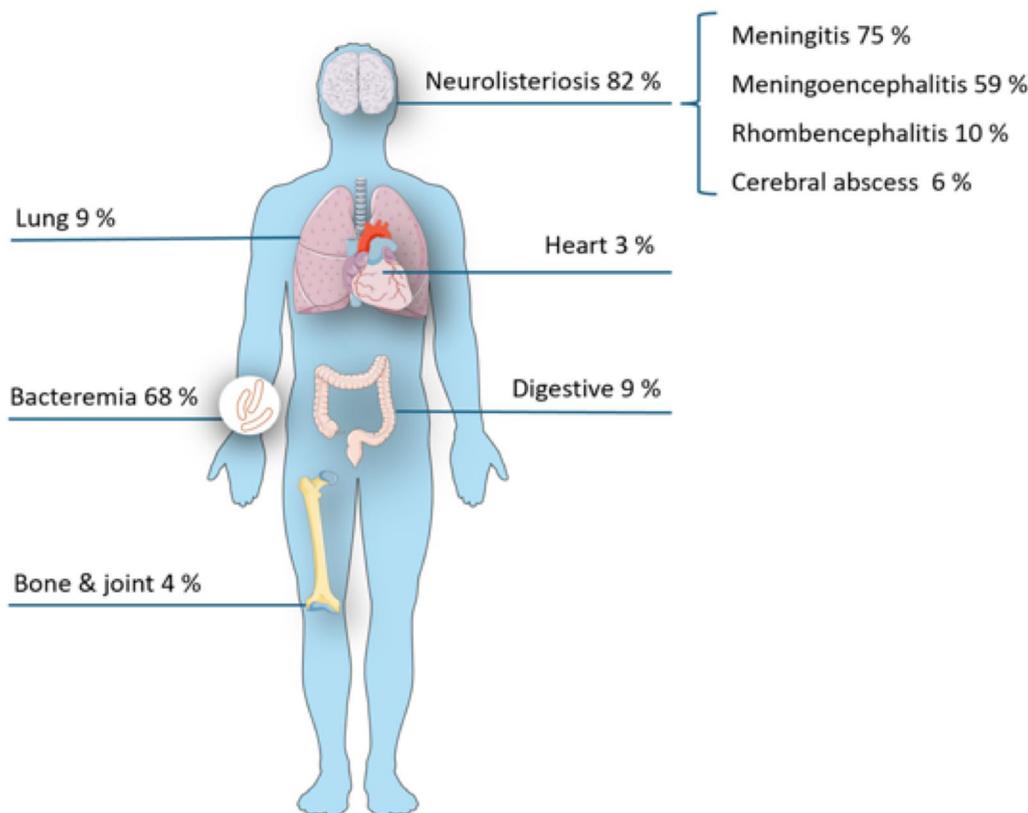
The microbiological parameters and treatments for the study cohort are detailed in Table 3. Cerebrospinal fluid (CSF) analysis showed that 30% of patients had a positive direct exam, while 80% had a positive CSF culture. PCR testing of CSF was positive in 71% of cases. Blood

**Table 1** Variables are presented as number of patients (N), percentages (%), or medians with interquartile ranges (IQR)

Variable	Value (n [%] or median [IQR])	Missing values
Age (years)	68 [58.25–77]	0
Male gender	67 (61%)	0
BMI (kg/m <sup>2</sup> )	25 [22–28]	0
Pregnancy	2 (2%)	0
Chronic heart failure	22 (20%)	0
Respiratory disease	16 (15%)	0
Cirrhosis	15 (14%)	0
Diabetes mellitus	28 (25%)	0
Chronic kidney disease	13 (12%)	0
• End-stage CKD	5 (5%)	0
Chronic alcohol abuse	21 (19%)	0
Immunocompromised state	78 (71%)	0
• HIV	6 (5%)	0
• Solid tumor – localized	6 (5%)	0
• Solid tumor – metastatic	7 (6%)	0
• Hematological malignancy \$	16 (15%)	0
• Solid organ transplant	3 (3%)	0
• Immunosuppressive drugs £	35 (32%)	0
ICU Admission Characteristics		
Time from symptoms to ICU admission (days)	2 [1–5]	2
Time from hospital to ICU admission (days)	1 [0–1]	1
ICU admission source ER / home / ward / other	35% / 15% / 27% / 24%	1
Core temperature (°C)	38.6 [37.5–39.2]	1
Fever	59 (54%)	1
SAP (mmHg)	125 [103–148]	4
DAP (mmHg)	68 [59.25–80.75]	4
MAP (mmHg)	88 [74.5–102.5]	4
Heart rate (bpm)	97 [82–112]	4
Shock	34 (31%)	0
Acute kidney injury	31 (28%)	1
SpO <sub>2</sub> (%)	98 [96–99]	1
Respiratory rate (bpm)	22 [18–25]	19
Oxygen device used None / O <sub>2</sub> -mask / HFNC / ETI	32% / 38% / 1% / 29%	7
Glasgow Coma Scale	10.5 [7–14]	0
SOFA score (admission)	6 [3–9]	1
Higher SOFA (day 1)	6 [4–10]	7
SAPS II (day 1)	52 [38–65]	1
ICU Stay Characteristics		
IMV	64 (58%)	0
IMV length (days)	5 [0–11]	23
Renal replacement therapy	16 (15%)	0
Vasopressor use	48 (44%)	4
Vasopressor length (days)	0 [0–2]	0
VAP	10 (9%)	0
ICU length of stay (days)	7 [3–16]	1
Hospital length of stay (days)	24 [14–40.25]	10
ICU mortality	28 (25%)	0
In-hospital mortality	35 (32%)	0
Therapeutic limitations	28 (25%)	0

**Table 1** (continued)

Key abbreviations: *BMI* Body Mass Index, *CKD* Chronic Kidney Disease, *HIV* Human Immunodeficiency Virus, *ICU* Intensive Care Unit, *ER* Emergency Room, *SAP* Systolic Arterial Pressure, *DAP* Diastolic Arterial Pressure, *MAP* Mean Arterial Pressure, *SpO<sub>2</sub>* Peripheral Capillary Oxygen Saturation, *HFNC* High-Flow Nasal Cannula, *ETI* Endotracheal Intubation, *SOFA* Sequential Organ Failure Assessment, *SAPS II* Simplified Acute Physiology Score II, *IMV* Invasive Mechanical Ventilation, *VAP* Ventilator-Associated Pneumonia. \$ hematological malignancy (acute leukemia in 2 [2%], chronic lymphocytic leukemia in 3 [3%], lymphoma in 3 [3%], and multiple myeloma in 7 [6%] patients). £ 25 on steroids and 10 on others immunosuppressive drugs



**Fig. 1** Organ Involvements in patients with *Listeria Monocytogenes* Infection. This figure was created using the SMART Servier Medical Art platform (Servier Medical Art, <https://smart.servier.com>), which provides licensed images under a Creative Commons Attribution 3.0 Unported License

cultures were positive in 64% of patients, highlighting the systemic nature of the infection.

Regarding treatments, steroids were administered to 34 patients (31%). Among them, 26 patients received dexamethasone at a dose of 10 mg four times daily, 6 were treated with hydrocortisone at septic shock doses, and 2 received methylprednisolone, with a median duration of 1 day [IQR, 1 to 4]. The most commonly used antibiotic regimen was amoxicillin combined with gentamicin (48%). Other antibiotic combinations included amoxicillin alone (15%), amoxicillin-cotrimoxazole-gentamicin (11%), amoxicillin-gentamicin-vancomycin (5%), and amoxicillin-cotrimoxazole (5%). Amoxicillin was administered for a median duration of 14 days [IQR, 7 to 17] in cases of bacteremia and 21 days [IQR, 13 to 21] in cases with neuro involvement.

**Factors associated with in hospital mortality:**

**Whole cohort of patients with listeria infection**

In the entire cohort, the following factors were independently associated with in-hospital mortality (Supplemental Tables 1 & 2): immunocompromised status (OR 4.93 [95% CI, 1.44–16.82], p=0.011), shock at ICU admission (OR 4.85 [95% CI, 1.72–13.64]), and meningoencephalitis (OR 3.11 [95% CI, 1.10–8.82], p=0.032).

**Subgroup of patients with neurological involvement**

In the subgroup of patients with neurological involvement mortality (Fig. 2 and Supplemental Tables 3 & 4), immunocompromised status (OR 4.09 [95% CI 1.16–18.02], p=0.04), decrease in Glasgow Coma Scale (GCS) score at ICU admission (OR per 1-point decrease: 1.22 [1.05–1.45]; p=0.009) and high CSF white blood cell

**Table 2** Biological Parameters

Variable	Value (median [IQR])	Missing values
Hemoglobin (g/dL)	12 [10.3–13.2]	1
Platelets (× 10 <sup>9</sup> /L)	170 [97–243]	1
White blood cells (× 10 <sup>9</sup> /L)	12.9 [8.6–16.7]	1
CRP (mg/L)	117 [55–237.5]	39
PCT (ng/mL)	1.9 [0.59–10]	72
Total bilirubin (μmol/L)	14 [10–25.33]	6
Creatinine (μmol/L)	100 [66–184]	1
Urea (mmol/L)	9.5 [5.8–16.45]	2
Sodium (mmol/L)	135 [133–139]	1
Prothrombin time (%)	67 [45–84.25]	10
Lactate (mmol/L)	1.8 [1–3]	17
CSF protein (g/L)	2.54 [1.71–3.97]	11
CSF WBC (× 10 <sup>6</sup> /L)	397 [187.8–880]	8
CSF neutrophils (%)	66.5 [40.25–81]	4
CSF lymphocytes (%)	25 [10–50]	7
CSF blood glucose ratio	0.3 [0.1–0.39]	14

Variables are presented as number of patients (N), percentages (%), or medians with interquartile ranges (IQR)

Key abbreviations: *Hb* Hemoglobin, *WBC* White Blood Cells, *CRP* C-reactive protein; *PCT* Procalcitonin, *PT* Prothrombin Time, *CSF* Cerebrospinal Fluid

**Table 3** Treatments. Variables are presented as number of patients (N), percentages (%), or medians with interquartile ranges (IQR)

Variable	Value (n [%] or median [IQR])	Missing values
Steroids	34 (31%)	0
Steroid duration (days)	1 [1–4]	1
Amoxicillin-Gentamicin	53 (48%)	2
Amoxicillin	17 (15%)	2
Amox-Cotrimoxazole-Gentamicin	12 (11%)	2
Amox-Gentamicin-Vancomycin	6 (5%)	2
Amox-Cotrimoxazole	5 (5%)	2
Amox-Penem-Cotrimoxazole-Gentamicin	4 (4%)	2
Cotrimoxazole-Gentamicin	2 (2%)	2
Linezolid	1 (1%)	2
Amox-Vancomycin	1 (1%)	2
Amox-Cotrimoxazole-Genta-Vancomycin	1 (1%)	2
Amox-Cotrimoxazole-Rifampicin-Gentamicin	1 (1%)	2
Amox-Penem-Vancomycin	1 (1%)	2

count (OR: 1.56, [1.15–2.41],  $p=0.03$ ). Steroid use was not associated with mortality (OR: 0.30 [0.07–1.05],  $p=0.08$ ).

## Discussion

This study demonstrates the severe nature of *Listeria monocytogenes* infections, with high mortality rates observed in our multicentric retrospective cohort. These results provide valuable insights into demographics, comorbidities, particularly immunodeficiency and other chronic conditions, as well as the organ support requirements of critically ill patients. This highlights areas for further optimization in the intensive care management of listeriosis.

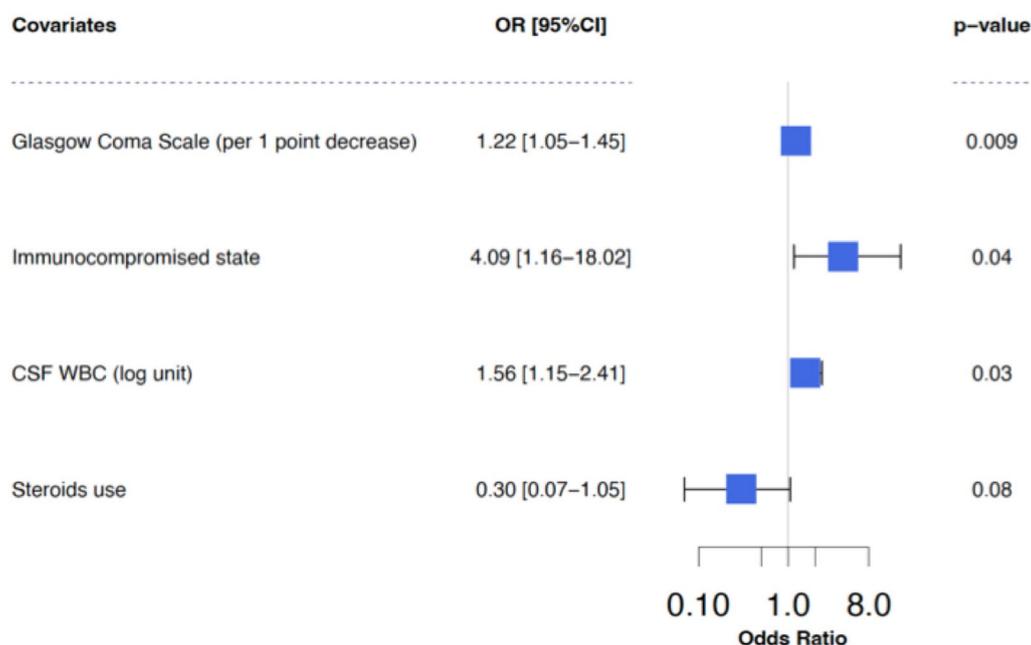
### Comparison with previous studies

The demographics and comorbidities observed in our cohort are consistent with prior reports. The median age of our cohort was 68 years, with a slight male predominance (61%). These findings align with the demographic characteristics reported by *Charlier et al.* in their study of 252 patients with neurolisteriosis, where the median age was similarly high, and there was a slight male predominance [10]. The high prevalence of comorbid conditions such as chronic heart failure (20%), diabetes mellitus (25%), and chronic kidney disease (16%), along with the significant proportion of immunocompromised patients (71%), underscores the extreme vulnerability of this population to severe infections and poor outcomes. Interestingly, fever was absent in a substantial proportion of patients, with only 54% of patients being febrile upon ICU admission. This relatively low prevalence of fever could be attributed to several factors. First, central nervous system involvement, particularly in neurolisteriosis, may impair thermoregulation due to damage to the hypothalamus or other thermoregulatory centers. Second, the use of antipyretics or other treatments that could mask fever, although not systematically collected in our data, may have contributed to this finding. This observation suggests that the absence of fever should not exclude a diagnosis of severe listeriosis, particularly in immunocompromised or neurologically impaired patients.

### Microbiological parameters and treatment regimens

Our microbiological findings showed that blood cultures were positive in 64% of cases, and cerebrospinal fluid (CSF) cultures were positive in 80% of cases, highlighting the importance of these simple diagnostic tools in confirming *Listeria* infections [14]. The presence of bacteremia in cases of *Listeria monocytogenes* meningitis is a key factor that promotes bacterial dissemination and central nervous system invasion, increasing the severity of the infection, especially in immunocompromised patients [15, 16].

The variability in antibiotic regimens, with a notable proportion of patients receiving combination therapies,



**Fig. 2** Factors associated with mortality in the neurological cohort. The plot displays odds ratios (OR) with 95% confidence intervals (CI) for key covariates: Glasgow Coma Scale (OR per 1-point decrease: 1.22 [1.05–1.45];  $p=0.009$ ), immunocompromised state (OR 4.09, 95% CI 1.16–18.02,  $p=0.04$ ), cerebrospinal fluid (CSF) white blood cell (WBC) count in log units (OR 1.56, 95% CI 1.15–2.41,  $p=0.03$ ), and steroid use (OR 0.30, 95% CI 0.07–1.05,  $p=0.08$ ). Variables with significant associations are highlighted by p-values  $<0.05$ . The horizontal lines represent 95% CIs, and squares indicate the point estimates for ORs. Model performance metrics included a Hosmer–Lemeshow statistic with  $X^2=1.7809$  ( $p=0.987$ ), and a C-index statistic of 0.82 [0.72–0.92]. Of note, the following variables were included in the initial model before the selection procedure for the final model: SOFA score at ICU admission, steroid use, white cell count in the CSF, protein concentration in the CSF, Glasgow Coma Scale, immunocompromised status, and white blood cell count

reflects the complexity of Listeriosis treatment in ICU patients. The combination of gentamicin with ampicillin remains a standard and effective treatment for meningitis caused by *Listeria monocytogenes* due to its synergistic effects [17, 18]. However, the use of gentamicin in combination treatment was not associated with lower mortality in our univariate analysis, in contrast to findings from a recent study [19]. It is important to note that this study included only 45 patients, 20 of whom had neurolisteriosis. While the authors reported lower overall mortality in the full cohort, the results were not statistically significant for the neurolisteriosis subgroup.

**Organ support and mortality**

Disease severity was high in our cohort with frequent use of organ support therapy; half of the patients being under mechanical ventilation and receiving vasopressors. These rates are higher than those reported in some previous studies, reflecting the severe nature of the infections in our cohort [20, 21]. The high mortality rates observed—25% in the ICU and 32% in-hospital—are consistent with the significant morbidity and mortality associated with *Listeria* infections, particularly in

immunocompromised and older patients. These mortality rates are significantly higher than those observed in other cases of bacterial meningitis admitted to the ICU, where studies have reported mortality rates ranging between 13 and 20% [22, 23].

Additionally, therapeutic limitations were frequent, affecting 25% of patients. Although the exact reasons for these limitations were not always specified, it is plausible to speculate that they were often related to severe brain damage and the absence of neurological recovery.

**Steroid use in listeriosis**

The use of adjunctive dexamethasone in neurolisteriosis remains controversial. The MONALISA study in France associated dexamethasone with higher mortality (48% vs. 27%,  $p=0.037$ ), identifying it as an independent risk factor for three-month mortality (adjusted OR 4.58; 95% CI 1.50–13.9;  $p=0.008$ ) [10]. Consequently, French guidelines advise against its use in neurolisteriosis since 2018 [24]. Conversely, Brouwer et al. reported improved outcomes with dexamethasone administered according to a strict protocol (10 mg four times daily for four days, starting before or with antibiotics) [11].

Unfavorable outcomes were observed in 46% of patients receiving dexamethasone versus 72% without it (adjusted OR 0.40; 95% CI, 0.19–0.81;  $p=0.017$ ), with reduced in-hospital mortality (adjusted OR 0.40; 95% CI 0.19–0.84;  $p=0.016$ ). In our study, we observed that the use of steroids was relatively common, with 31% of patients receiving them. However, our multivariable model for the neurological cohort did not identify a statistically significant association between steroid use and mortality (OR 0.30; 95% CI 0.07–1.05;  $p=0.076$ ). Given the conflicting findings in previous studies and the lack of a clear effect in our own data, our results do not provide strong evidence to support the use of corticosteroids in neuroinfectious disease. Moreover, we did not observe any benefit of corticosteroids when stratifying by CSF protein levels (data not shown).

Several factors may explain discrepancies between our findings and those of the MONALISA study. Firstly, our study had a larger proportion of patients receiving steroids (31% vs. 13% in the MONALISA study), providing a more robust basis for evaluating their impact. Secondly, the timing and context of dexamethasone administration were not clearly detailed in the MONALISA study, which could introduce bias if steroids were preferentially administered to the most severely ill patients. In contrast, the study by Brouwer et al. reported a potential benefit of dexamethasone in neuroinfectious disease, but several critical aspects of its design merit cautious interpretation. While their strict protocol ensured early and adequate dexamethasone administration with a full four-day course in one group, the control group also received corticosteroids, albeit inconsistently. This raises questions about what is truly being compared. Furthermore, the decision to discontinue corticosteroids in the control group may have been influenced by the perception of unfavorable clinical progression, introducing potential bias. The study design does not eliminate the possibility that patient outcomes could have shaped treatment decisions rather than vice versa. In our cohort, at least half of the patients who received corticosteroids were treated for a maximum of one day, likely reflecting early discontinuation once *Listeria monocytogenes* was identified. This heterogeneity in treatment duration further complicates direct comparisons with studies that followed a standardized four-day protocol. Given these conflicting results, the role of adjunctive dexamethasone in neuroinfectious disease remains uncertain and randomized controlled trials are required to clarify this point.

### Limitations

Our study has several limitations. Firstly, its retrospective design introduces potential biases inherent to observational studies. Secondly, the sample size, particularly for subgroup analyses, limits statistical power and may explain why some findings, such as the borderline significance of steroid use, did not reach statistical significance. Thirdly, variability in the timing and dosing of dexamethasone across centers may have influenced outcomes. Unlike the strict protocol in Brouwer et al., our study did not control for timing relative to antibiotic administration, a critical factor in steroid efficacy. Additionally, while we adjusted for key variables such as Glasgow Coma Scale score and immunocompromised state, other potential confounders, like infection severity at presentation and adequacy of initial antibiotic therapy, were not fully accounted for, leading to possible residual confounding. Furthermore, our study did not systematically collect data on antibiotic dosing, limiting our ability to assess the potential impact of augmented renal clearance in septic critically ill patients. Given the known challenges of aminoglycoside and beta-lactam penetration into the central nervous system, even in the presence of meningeal inflammation, variations in amoxicillin dosing may have influenced outcomes. Lastly, outcomes were assessed only at hospital discharge, unlike the three-month follow-up in MONALISA, potentially missing late complications and long-term neurological outcomes. Due to the retrospective design and ICU-focused approach, systematic follow-up after discharge was not feasible, limiting our ability to assess functional recovery. Despite these limitations, our findings provide valuable insights into the management of severe *Listeria* infections but should be interpreted cautiously. Prospective, randomized controlled trials are needed to confirm the role of dexamethasone in neuroinfectious disease. In the meantime, clinicians should base treatment decisions on current evidence, guidelines, and patient-specific factors.

### Conclusion

Our study provides valuable insights into the clinical characteristics, management strategies, and outcomes of patients with *Listeria monocytogenes* infections. Our findings highlight the high burden of comorbidities, substantial need for organ support, and significant mortality associated with these infections. The role of adjunctive dexamethasone in managing neuroinfectious disease remains controversial, underscoring the need for further prospective studies to delineate its benefits and risks.

**Abbreviations**

CI	Confidence interval
CKD	Chronic kidney disease
CRP	C-reactive protein
CSF	Cerebrospinal fluid
GCS	Glasgow coma scale
HIV	Human immunodeficiency virus
ICU	Intensive care unit
IQR	Interquartile range
LOS	Length of stay
L. monocytogenes	Listeria monocytogenes
OR	Odds ratio
PCR	Polymerase chain reaction
SOFA	Sequential organ failure assessment
WBC	White blood cell

**Supplementary Information**

The online version contains supplementary material available at <https://doi.org/10.1186/s13054-025-05421-8>.

Supplementary file 1.

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**Author contributions**

Antoine Villa: Conceptualization, Methodology, Data Curation, Formal Analysis, Project Administration, Writing – Original Draft, Writing – Review & Editing, Supervision. Hafid Ait-Oufella: Conceptualization, Methodology, Formal Analysis, Project Administration, Writing – Original Draft, Writing – Review & Editing, Supervision. Guillaume Dumas: Data Curation, Formal Analysis, Visualization, Writing – Original Draft, Writing – Review & Editing. All authors: Investigation, Resources, Validation, Writing – Review & Editing, Final Approval of the Version to Be Published.

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**Availability of data and materials**

No datasets were generated or analysed during the current study.

**Declarations****Ethics approval and consent to participate**

This study was conducted in accordance with French legislation and received approval from the local ethics committee (Comité d'Éthique de la Société de Réanimation de Langue Française, CE SRLF 23–095). The study was also registered with the French National Commission on Informatics and Liberty (CNIL) under reference number 2228756. Given the retrospective nature of the study, the requirement for individual informed consent was waived by the ethics committee. This study was conducted in compliance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

**Consent for publication**

Not applicable. This manuscript does not include data from individual persons in any form (including images or videos).

**Competing interests**

The authors declare no competing interests.

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**References**

- Brouwer MC, van de Beek D, Heckenberg SGB, Spanjaard L, de Gans J. Community-acquired listeria monocytogenes meningitis in adults. *Clin Infect Dis*. 2006;43(10):1233–8.
- Koopmans MM, Brouwer MC, Vázquez-Boland JA, van de Beek D. Human Listeriosis. *Clin Microbiol Rev*. 2023;36(1): e0006019.
- Scobie A, Kanagarajah S, Harris RJ, Byrne L, Amar C, Grant K, et al. Mortality risk factors for listeriosis - A 10 year review of non-pregnancy associated cases in England 2006–2015. *J Infect mars*. 2019;78(3):208–14.
- Bennion JR, Sorvillo F, Wise ME, Krishna S, Mascola L. Decreasing Listeriosis Mortality in the United States, 1990–2005. *Clin Infect Dis*. 2008;47(7):867–74.
- Goulet V, Jacquet C, Martin P, Vaillant V, Laurent E, de Valk H. Surveillance of human listeriosis in France, 2001–2003. *Euro Surveill*. 2006;11(6):79–81.
- de Noordhout CM, Devleeschauwer B, Angulo FJ, Verbeke G, Haagsma J, Kirk M, et al. The global burden of listeriosis: a systematic review and meta-analysis. *Lancet Infect Dis*. 2014;14(11):1073–82.
- Huang C, Lu TL, Yang Y. Mortality risk factors related to listeriosis — a meta-analysis. *J Infect Public Health*. 2023;16(5):771–83.
- Pamer EG. Immune responses to *Listeria monocytogenes*. *Nat Rev Immunol*. 2004;4(10):812–23.
- Lecuit M, Vandormael-Pournin S, Lefort J, Huerre M, Gounon P, Dupuy C, et al. A transgenic model for listeriosis: role of internalin in crossing the intestinal barrier. *Science* juin. 2001;292(5522):1722–5.
- Charlier C, Perrodeau É, Leclercq A, Cazenave B, Pilmis B, Henry B, et al. Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study. *Lancet Infect Dis* mai. 2017;17(5):510–9.
- Brouwer MC, van de Beek D. Adjunctive dexamethasone treatment in adults with listeria monocytogenes meningitis: a prospective nationwide cohort study. *EClinicalMedicine*. 2023;58: 101922.
- Venkatesan A, Tunkel AR, Bloch KC, Luring AS, Sejvar J, Bitnun A, et al. Case definitions, diagnostic algorithms, and priorities in encephalitis: consensus statement of the international encephalitis consortium. *Clin Infect Dis*. 2013;57(8):1114–28.
- Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure on behalf of the working group on sepsis-related problems of the European Society of Intensive Care Medicine. *Intensiv Care Med*. 1996;22(7):707–10.

14. Coant PN, Kornberg AE, Duffy LC, Dryja DM, Hassan SM. Blood culture results as determinants in the organism identification of bacterial meningitis. *Pediatr Emerg Care*. 1992;8(4):200.
15. Gantz NM, Myerowitz RL, Medeiros AA, Carrera GF, Wilson RE, O'Brien TF. Listeriosis in immunosuppressed patients: a cluster of eight cases. *Am J Med*. 1975;58(5):637–43.
16. Berche P. Bacteremia is required for invasion of the murine central nervous system by *Listeria monocytogenes*. *Microb Pathog*. 1995;18(5):323–36.
17. Azimi P, Koranyi K, Lindsey KD. *Listeria monocytogenes*: synergistic effects of ampicillin and gentamicin. *Am J Clin Pathol*. 1979;72:974–7.
18. Scheld W, Fletcher DD, Fink F, Sande MA. Response to therapy in an experimental rabbit model of meningitis due to *Listeria monocytogenes*. *J Infect Dis*. 1979;140(3):287–94.
19. Sutter JP, Kocheise L, Kempinski J, Christner M, Wichmann D, Pinnschmidt H, et al. Gentamicin combination treatment is associated with lower mortality in patients with invasive listeriosis: a retrospective analysis. *Infection*. 2024. <https://doi.org/10.1007/s15010-024-02330-w>.
20. Wettervik TS, Howells T, Hedberg AL, Lewén A, Enblad P. Intracranial pressure dynamics and cerebral vasomotor reactivity in community-acquired bacterial meningitis during neurointensive care. *J Neurosurg*. 2021;1:1–9.
21. Fernandes D, Gonçalves-Pereira J, Janeiro S, Silvestre J, Bento L, Póvoa P. Acute bacterial meningitis in the intensive care unit and risk factors for adverse clinical outcomes: retrospective study. *J Critical Care*. 2014;29(3):347–50.
22. Martín-Cerezuela M, Aseginolaza-Lizarazu M, Boronat-García P, Asensio-Martín MJ, Alamán-Laguarda G, Álvarez-Lerma F, et al. Severe community-acquired *Streptococcus pneumoniae* bacterial meningitis: clinical and prognostic picture from the intensive care unit. *Crit Care*. 2023;27(1):72.
23. Georges H, Chiche A, Alfandari S, Devos P, Boussekey N, Leroy O. Adult community-acquired bacterial meningitis requiring ICU admission: epidemiological data, prognosis factors and adherence to IDSA guidelines. *Eur J Clin Microbiol Infect Dis*. 2009;28(11):1317–25.
24. Hoen B, Varon E, de Debroucker T, Fantin B, Grimprel E, Wolff M, et al. Management of acute community-acquired bacterial meningitis (excluding newborns) Long version with arguments. *Med Mal Infect*. 2019;49(6):405–41.

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