Jugular Vein Thrombosis and Anticoagulation Therapy in Lemierre's Syndrome—A Post Hoc Observational and Population-Based Study of 82 Patients

David Nygren,[1] Johan Elf,[2] Gustav Torisson,[3] and Karin Holm[1]

[1]Division of Infection Medicine, Department for Clinical Sciences Lund, Lund University, Lund, Sweden, [2]Center of Thrombosis and Haemostasis, Skåne University Hospital, Malmö, Sweden, and [3]Clinical Infection Medicine, Department of Translational Medicine, Lund University, Malmö, Sweden

Background. Lemierre's syndrome is typically caused by *Fusobacterium necrophorum* where an oropharyngeal infection is followed by septic internal jugular vein thrombophlebitis with subsequent septic embolization. Yet, the pathogenesis of septic thrombophlebitis, differences dependent on the presence of jugular vein thrombosis, and the role of anticoagulant therapy are insufficiently understood.

Methods. Patients with invasive infection with *F. necrophorum* and Lemierre's syndrome who had been investigated for jugular vein thrombosis were included from a previous population-based observational study in Sweden. Medical records were reviewed and compared in patients with and without jugular vein thrombosis. Then, patients with jugular vein thrombosis were compared by exposure to therapeutic, prophylactic, or no anticoagulation. Outcomes examined were thrombosis progression, early or late peripheral septic complications, chronic major sequelae, 30-day mortality, and major bleeding.

Results. Fifty-one of 82 (62%) radiologically investigated patients with Lemierre's syndrome had jugular vein thrombosis. Patients with jugular vein thrombosis had lower platelet levels (median, 76 vs 112 $\times 10^9$/L; P = .04) on presentation and more days to defervesence (12 vs 7 days; P = .03) yet similar rates of major sequelae and 30-day mortality. No significant differences in outcomes were seen between patients with jugular vein thrombosis exposed to therapeutic, prophylactic, or no anticoagulation therapy, yet study outcomes were rare.

Conclusions. Patients with Lemierre's syndrome with jugular vein thrombosis were more severely affected, yet had similar prognosis. Most patients with jugular vein thrombosis recovered well without therapeutic anticoagulation therapy, though adverse events were similarly rare in anticoagulated patients. The observational design and rarity of study outcomes require cautious interpretation.

Keywords. *Fusobacterium necrophorum*; jugular thrombosis; Lemierre; Lemierre's syndrome; septic thrombophlebitis.

Fusobacterium necrophorum is a gram-negative anaerobic rod causing oropharyngeal infections, notably tonsillitis and peritonsillar abscess, which can occasionally be complicated by Lemierre's syndrome in adolescents or young adults [1–6]. This syndrome is characterized by a substantial thrombotic burden following oropharyngeal infections, with typical involvement of the internal jugular vein and septic embolization to the lungs [4]. Whether all patients develop occlusive thrombosis at some point during the course of disease is uncertain, though septic thrombophlebitis in Lemierre's syndrome is more likely to develop at a range from endothelial vegetations to occlusive thrombosis. Although the syndrome refers to a specific group

of patients with oropharyngeal infection and direct signs of jugular vein thrombosis or indirect signs through septic embolization to the lungs, *F. necrophorum* infections at other anatomical sites are responsible for similar manifestations of septic thrombophlebitis, including pelvic [7], splanchnic [8], and cerebral vein thrombosis [4], as well as lower-limb deep vein thrombosis [3]. In addition, arterial thromboses have occasionally been reported [9].

In Lemierre's syndrome, a phlegmon or abscess may be surrounding the internal jugular vein, and pathology reports from excised jugular veins have found abscesses within the thrombi [10, 11]. However, little is known about the pathogenesis of thrombosis. One study has shown that *F. necrophorum* subsp. *funduliforme* can activate the intrinsic pathway of coagulation [12], and *F. necrophorum* supsp. *necrophorum,* although mainly seen in bovine infections, has been shown to cause platelet aggregation [13]. In addition, thrombocytopenia as a clinical feature is very common in invasive infections with *F. necrophorum* [6].

In line with international guidelines on the prevention and treatment of acute but nonseptic venous thromboembolism [14, 15], anticoagulation therapy appears to be frequently used in septic thrombophlebitis in patients with Lemierre's syndrome

[16, 17]. Yet, the evidence concerning the efficacy and safety of anticoagulation therapy of septic thrombophlebitis, including Lemierre's syndrome, is limited due to the lack of information from interventional studies, and controversies persist regarding its role [4, 17–20].

In this nationwide population-based post hoc observational study, the main aim was to describe outcomes in patients with and without anticoagulation therapy in Lemierre's syndrome with jugular vein thrombosis. The secondary aim was to compare clinical characteristics in Lemierre's syndrome with or without jugular vein thrombosis, as the presence of septic thrombophlebitis could reflect different stages or levels of severity of disease in Lemierre's syndrome.

METHODS

Study Design and Setting
For this post hoc analysis, we used data collected in a previous nationwide population-based observational study of all diagnosed invasive infections with *F. necrophorum* in Sweden from January 1, 2010, to December 31, 2017 [6]. Invasive infection with *F. necrophorum* was defined as a positive blood culture or sequencing of 16S rDNA, targeted PCR, or culture from normally sterile sites. Review of medical records was performed from presentation due to infection with 6 months of follow-up. Patients were identified and data collected as previously described [6].

Participants
Case eligibility was based on a diagnosis of Lemierre's syndrome, which was defined using the following criteria: (I) invasive infection with *F. necrophorum*, (II) oropharyngeal symptoms preceding presentation with invasive infection, and (III) presence of septic thrombophlebitis, either as a radiologically visualized thrombosis or septic embolization. Finally, patients who fulfilled these criteria yet had not been investigated radiologically for jugular vein thrombosis by ultrasound, computerized tomography, or magnetic resonance imaging were excluded from the study.

Data Collection
Baseline Characteristics, Initial Presentation, and Hospitalization
Baseline, clinical, laboratory, and radiological characteristics and outcomes were recorded from medical records. Comorbidities were evaluated on admission using the updated Charlson Comorbidity Index (uCCI) [21]. SOFA score was calculated on admission, and sepsis and septic shock were defined according to Sepsis 3.0 [22]. Lemierre-associated complications were defined as multifocal pneumonia, septic pulmonary embolization, pleural empyema, lung abscess, arthritis, and central nervous system (CNS) infection. Patients with Lemierre's syndrome with or without jugular vein thrombosis at the time of diagnosis were compared with examination of differences relating to presence of jugular vein thrombosis.

Exposure
Patients with jugular vein thrombosis were then divided into 3 categories according to exposure to therapeutic dose, prophylactic dose, or no anticoagulation therapy. If anticoagulation therapy was given secondary due to a complication of an initial conservative approach, such as progression of thrombosis, these patients were considered not exposed. For all outcomes except for chronic major sequalae, anticoagulation status at the time of the outcome was used.

Direct oral anticoagulation, warfarin, heparin, low–molecular weight heparin, and fondaparinux were considered effective anticoagulation therapy, and if >1 dose was given, patients were considered exposed. Anticoagulation therapy was categorized retrospectively as either therapeutic or prophylactic according to doses given, weight, and renal function.

Outcomes
Study outcomes measured in patients with Lemierre's syndrome with jugular vein thrombosis were progression or new occurrence of thrombosis including cerebral venous sinus thrombosis, peripheral septic complication after diagnosis, peripheral septic complication after discharge, 30-day mortality, chronic major sequelae at 6 months, and major bleeding.

Progression or new occurrence of thrombosis was defined as radiologically visualized local progression or occurrence. Peripheral septic complication after diagnosis and after discharge was defined as radiologically diagnosed new septic complications or clinically obvious complications, such as arthritis or CNS infection. Any objective respiratory, cardiovascular, neurological, renal, or orthopedic functional impairment noted in medical charts at 6 months after presentation was defined as chronic major sequelae. Major bleeding was defined according to the International Society on Thrombosis and Haemostasis [23].

Statistical Methods
No power calculation was performed, as the study size was limited to the total number of patients with invasive infection due to *F. necrophorum* who fulfilled the criteria for Lemierre's syndrome in Sweden during the study period. In the case of missing data, complete case analysis was performed. For the clinical binary variables CNS infection, arthritis, septic embolization, and other venous thrombosis, lack of clinical and radiological signs was regarded as a negative finding. Statistical significance was defined as $P < .05$. Normally distributed continuous variables were described as mean with standard deviation and analyzed using the Student t test or analysis of variance where appropriate. Pairwise comparisons were performed with Bonferroni correction to control for alpha error. Non–normally distributed variables were described as median with interquartile range (IQR) and analyzed using the Kruskal-Wallis test. Binary variables were described as counts and percentages and analyzed

using the Fisher exact test. Statistical analyses were performed using STATA (StataCorp, College Station, TX, USA).

RESULTS

Baseline Characteristics and Initial Presentation

During 2010–2017, 104 patients fulfilled the criteria of Lemierre's syndrome in Sweden. Of these, 22 patients were not radiologically examined for jugular (internal or external) vein thrombosis. Thus, 82 patients were included in this study, among whom jugular vein thrombosis was identified in 51/82 (62%).

Patients with Lemierre's syndrome with and without jugular vein thrombosis were similarly young, without comorbidities according to uCCI scores, and had equal duration of symptoms on presentation (Tables 1 and 2). Lemierre-associated complications were similar independent of the presence of jugular vein thrombosis except for typical pulmonary septic emboli, which were more commonly identified in patients with jugular thrombosis. While not significantly different, cerebral venous sinus thrombosis (n = 2) was exclusively seen in patients with jugular vein thrombosis. In patients without jugular vein thrombosis, other types of venous thrombosis were diagnosed at the time of diagnosis in 6 cases. While most patients with Lemierre's syndrome presented with thrombocytopenia, platelet counts were lower among patients with jugular vein thrombosis, and subsequently, a trend was seen where patients who had jugular vein thrombosis had higher SOFA scores (Table 3).

Patients with Lemierre's syndrome with jugular vein thrombosis (n = 51) were compared depending on treatment with therapeutic, prophylactic, or no anticoagulation therapy. Patients in these 3 groups were equally young, had no comorbidities, and had similar SOFA scores on presentation (Tables 1, 2 and 4).

Treatment

All patients with Lemierre's syndrome received effective antibiotics on admission. In patients with Lemierre's syndrome with jugular vein thrombosis, 20/51 (40%) were not treated with anticoagulation therapy, while 17/51 (33%) received therapeutic doses and 14/51 (27%) received prophylactic doses (Table 4). Anticoagulation therapy in Lemierre's syndrome with jugular

vein thrombosis was given to 8/16 (50%) patients in 2010–2013 and to 23/35 (66%) patients in 2014–2017, an increase mainly accounted for by prophylactic anticoagulation therapy, which increased from 2/16 (12.5%) to 12/35 (34%). No patient received antiplatelet therapy or jugular ligation.

Hospitalization

Patients with jugular vein thrombosis had a longer time to defervescence and yet, not significantly, more often required intensive care unit (ICU) admission and slightly longer hospitalization than those without jugular vein thrombosis. Data on prognosis in patients with or without jugular vein thrombosis can be found in Table 3; both sequelae and mortality at 30 days were similar independent of presence of jugular vein thrombosis. Sequelae included 3 cases with neurological deficits due to palsy, critical illness-associated neuropathy, or mental fatigue, 2 patients with chronic renal failure, 1 patient with chronic respiratory exertional decompensation, and 1 patient with functional impairment of the hip joint. No patient developed septic peripheral complications after discharge.

Despite similar SOFA scores on presentation, patients with jugular vein thrombosis who were not treated with anticoagulant therapy were less often admitted to the ICU, had shorter length of hospital stay, and had fewer days to defervescence (Table 4). However, diagnostic evaluation was generally performed simultaneous to or after ICU admission. Thus, initiation of anticoagulation therapy after identification of jugular vein thrombosis generally started after ICU admission.

Study Outcomes

The associations between no exposure, exposure to prophylactic or therapeutic anticoagulation therapy, and outcomes were studied in patients with Lemierre's syndrome with jugular vein thrombosis at the time of diagnosis. Complications defined as our study outcomes were rare, and no significant differences were identified between groups. Progression or new occurrence of thrombosis was seen in 1 patient who developed cerebral venous sinus thrombosis despite treatment with a therapeutic dose of anticoagulation, while 1 patient who was not treated developed local progression of jugular vein thrombosis. Peripheral septic complications after diagnosis during hospitalization were seen in 2 patients who developed arthritis; both were not on anticoagulation therapy. Chronic major sequelae at 6 months were seen in 2 patients who received prophylactic and therapeutic doses of anticoagulation therapy, respectively. One patient with Lemierre's syndrome with jugular vein thrombosis died within 30 days. This patient was not on anticoagulation therapy. One patient suffered major bleeding while on a therapeutic dose of anticoagulation therapy; this patient was thrombocytopenic on admission and during hospitalization (Table 4).

Table 1.   Lemierre's Syndrome by Presence of Jugular Vein Thrombosis

Baseline Characteristics	Jugular Vein Thrombosis (n = 51)	No Jugular Vein Thrombosis (n = 31)
Age, mean [SD], y	23 [11]	26 [12]
Female sex, No. (%)	26 (51)	17 (55)
uCCI score [21], median (IQR, range)	0 (0–0, 0–5)	0 (0–0, 0–2)
Duration of symptoms before presentation, mean [SD], d	7 [4]	6 [3]

Table 2. Lemierre's Syndrome With Jugular Vein Thrombosis by Anticoagulation Therapy

Baseline Characteristics	No Anticoagulation (n = 20)	Anticoagulation, Prophylaxis Dose (n = 14)	Anticoagulation, Treatment Dose (n = 17)
Age, mean [SD], y	26 [12]	24 [12]	21 [9]
Female sex, No. (%)	9 (45)	8 (57)	9 (53)
Duration of symptoms before presentation, mean [SD], d	7 [4]	6 [2]	7 [4]

Abbreviations: IQR, interquartile range; uCCI, updated Charlson Comorbidity Index.

DISCUSSION

In this nationwide population-based observational study, we highlight differences in clinical characteristics dependent on the presence of jugular vein thrombosis in patients with Lemierre's syndrome and unadjusted correlations between anticoagulation treatment and outcomes in patients with Lemierre's syndrome with jugular vein thrombosis. We believe that the most valuable information from this study can be gathered from its descriptive statistics.

First, we showed that patients with Lemierre's syndrome with jugular vein thrombosis at the time of diagnosis had more severe thrombocytopenia and longer time to defervescence, as well as a trend for higher SOFA scores, frequency of ICU admission, and longer hospital stay, yet no significant differences were seen in chronic major sequelae or mortality (Table 3). We believe that rather than illustrating different entities of disease by presence of jugular vein thrombosis, our findings show that Lemierre's syndrome occurs on a continuous spectrum where septic thrombophlebitis likely ranges from small venous endothelial vegetations to occlusive jugular vein thrombosis. In this study, the latter has been shown to have more severe coagulopathy and a trend for more severe disease,

Table 3. Lemierre's Syndrome by Presence of Jugular Vein Thrombosis

Initial Presentation	Jugular Vein Thrombosis (n = 51)	No Jugular Vein Thrombosis (n = 31)	P
SOFA score on admission, median (IQR)	5 (3–7)	4 (2–7)	.05
Sepsis [22] on admission, No. (%)	46 (90)	26 (84)	.49
Septic shock [22] on admission, No. (%)	11 (22)	7 (23)	1
Thrombocytopenia on admission <150 ×10⁹/L, No./total (%)	39/47 (83)	21/28 (75)	.55
Platelet count on admission, median (IQR), ×10⁹/L	76 (43–130)	112 (69–159)	**.04**
Maximum CRP, mean [SD], mg/L	307 [78]	316 [89]	.63
Other venous thrombosis at the time of diagnosis			
Cerebral venous sinus thrombosis, No. (%)	2 (4)	0	.52
Lower-limb deep venous thrombosis, No. (%)	0	2 (6)	.14
Ovarian vein thrombosis, No. (%)	0	2 (6)	.14
Facial vein thrombosis, No. (%)	0	1 (3)	.38
Visualized pulmonary venous embolism, No. (%)	0	1 (3)	.38
Lemierre-associated complications			
Multifocal pneumonia, No. (%)	47 (92)	27 (87)	.47
Pulmonary septic emboli, No. (%)	35 (69)	10 (32)	**<.01**
Pleural empyema, No. (%)	15 (29)	9 (29)	1
Lung abscess, No. (%)	13 (25)	5 (16)	.41
Arthritis, No. (%)	3 (6)	1 (3)	1
CNS infection, No. (%)	1 (2)	0	1
Treatment			
Full dose anticoagulant therapy (%)	17 (33)	4 (13)	.07
Prophylactic dose, anticoagulant therapy (%)	14 (27)	5 (16)	.29
Duration of anticoagulant therapy, median (IQR), d	44 (14–90)	90 (10–90)	.68
Hospitalization and prognosis			
ICU admission, No. (%)	28 (55)	12 (39)	.18
Length of hospital stay, median (IQR), d	13 (10–22)	11 (6–18)	.09
Days to 50% decrease of CRP, mean [SD]	5 [3]	5 [3]	.83
Days to defervescence, mean [SD]	12 [10]	7 [5]	**.03**
Chronic major sequelae at 6 mo, No. (%)	2 (4)	3 (10)	.36
30-d mortality (%)	1 (2)	0	1

P values for any difference between groups are provided. Significant P values (≤.05) are highlighted in bold.

Abbreviations: CNS, central nervous system; CRP, C-reactive protein; ICU, intensive care unit; IQR, interquartile range.

Table 4. Patients With Lemierre's Syndrome With Jugular Vein Thrombosis by Anticoagulation Therapy

Initial Presentation	No Anticoagulation (n = 20)	Anticoagulation, Prophylactic Dose (n = 14)	Anticoagulation, Treatment Dose (n = 17)	P
SOFA score on admission, median (IQR)	5 (3–6.5)	6 (3–7)	6 (4–9)	.54
Sepsis [22] on admission, No. (%)	18 (90)	12 (86)	16 (94)	.85
Septic shock [22] on admission, No. (%)	4 (20)	3 (21)	4 (24)	1
Creatinine on admission, mean [SD], μmol/L	133 [101]	176 [116]	135 [81]	.43
Thrombocytopenia on admission <150 ×10^9/L, No./total (%)	13/18 (72)	10/12 (83)	16/17 (94)	.27
Platelet count on admission, median (IQR), ×10^9/L	90.5 (60–155)	79 (40.5–134.5)	75 (19–39)	.65
Maximum CRP, mean [SD], mg/L	298 [88]	325 [81]	304 [63]	.59
Other venous thromboses at the time of diagnosis				
Cerebral venous sinus thrombosis, No. (%)	0	1 (7)	1 (6)	.51
Lemierre-associated complications				
Multifocal pneumonia or pulmonary septic emboli, No. (%)	17 (85)	13 (93)	17 (100)	.29
Pleural empyema, No. (%)	1 (5)	6 (43)	8 (47)	**<.01**[a+b]
Lung abscess, No. (%)	3 (15)	5 (36)	5 (29)	.36
Arthritis, No. (%)	1 (5)	2 (14)	0	.27
CNS infection, No. (%)	0	0	1 (6)	.61
Treatment				
Warfarin, No. (%)	-	0	3 (18)	.23
Direct oral anticoagulants, No. (%)	-	1 (7)	2 (12)	1
Heparin (incl. low–molecular weight heparin), No. (%)	-	14 (100)	14 (82)	.23
Duration of anticoagulant therapy, median (IQR), d	-	35 (10–90)	53 (23–90)	.06
Hospitalization				
ICU admission, No. (%)	5 (25)	10 (71)	13 (76)	**<.01**[a+b]
Ventilator, No. (%)	3 (15)	8 (57)	5 (29)	**.03**[a]
Vasopressor, No. (%)	4 (20)	8 (57)	7 (41)	.08
Length of hospital stay, median (IQR), d	10 (7.5–12)	20.5 (12–24)	19 (13–31)	**<.01**[a+b]
Days to 50% decrease of CRP, mean [SD]	4 [2]	6 [3]	5 [2]	.14
Days to defervescence, mean [SD]	6 [5]	14 [10]	16 [12]	**<.01**[b]
Outcomes	None (n = 20)	Prophylaxis Dose (n = 14)	Treatment Dose (n = 17)	P
Progression or new occurrence of thrombosis after diagnosis, No. (%)	1 (5)	0	1 (6)	1
Peripheral septic complication after diagnosis, No. (%)	2 (10)	0	0	.33
Chronic major sequelae at 6 mo, No. (%)	0	1 (7)	1 (6)	.51
30-d mortality, No. (%)	1 (5)	0	0	1
Major bleeding during hospitalization, No. (%)	0	0	1 (6)	.61

P values for any difference between groups are provided. If a significant difference was present (P < .05), pairwise comparisons were performed between all groups, and where significant differences were seen, [a], [b], or [c] is marked. Significant P values (≤.05) are highlighted in bold.

Abbreviations: CNS, central nervous system; CRP, C-reactive protein; ICU, intensive care unit; IQR, interquartile range.

[a]Pairwise comparison between no anticoagulation and prophylactic dose.

[b]Pairwise comparison between no anticoagulation and treatment dose.

[c]Pairwise comparison between prophylactic and treatment dose.

possibly representing a more advanced stage of the syndrome. Second, we showed that patients with Lemierre's syndrome with jugular vein thrombosis in Sweden are often treated with anticoagulation therapy, and increasingly so, though its role is not clear [4, 16–19]. This increase could be due to improved adherence to guidelines on prophylactic anticoagulation therapy in immobilized patients [24], as prophylactic therapy was the main cause for the increase. In addition, despite the presence of thrombocytopenia and renal failure, major bleeding events were rare in patients treated with anticoagulation therapy. In our study, the rates of adverse outcomes in patients with and without anticoagulation treatment were similar. However, important to note, these results come with substantial uncertainty due to the rarity of events.

Consequently, the limitations of this study are evident. Despite being the largest population-based study as of yet with a nationwide design over 8 years, it is based on 104 patients with Lemierre's syndrome, of whom 82 were investigated for jugular vein thrombosis and subsequently included in this study. In a larger study, it is likely that risk estimates in patients treated or not treated with anticoagulation therapy would be more accurate. Yet, indication bias would remain. In our study,

patients with more severe presentations of Lemierre's syndrome were more likely to receive anticoagulation therapy compared with patients with less complicated clinical manifestations of Lemierre's syndrome, introducing significant confounding by indication. In addition, the risk of bias in a time-dependent manner is also evident, where clinicians might have been more likely to start anticoagulation therapy in deteriorating rather than in stable patients, which likely affected our results.

Furthermore, while outcomes such as 30-day mortality and major bleeding are reliable, outcomes such as local thrombosis progression are not as reliable. Due to the observational design, serial evaluation of progression of jugular vein thrombosis was not performed systematically, so it is possible that these numbers are underestimated. In addition, patients might have developed or resolved thrombosis before or after initial diagnostic evaluation, introducing a risk of misclassification bias.

Septic pulmonary embolization is often followed by multifocal pneumonia, lung abscesses, and empyema and differs from venous nonseptic embolization in that it causes inflammatory changes secondary to infection. Thus, progression of radiological findings can be difficult to assess in terms of whether they are secondary to new embolization or local progression of multifocal pneumonia. In addition, in patients with known septic thrombophlebitis, it is possible that the radiologist would be biased when classifying a pulmonary infiltrate as a septic pulmonary emboli, possibly overestimating the difference described in Table 3. As described in Table 4, anticoagulation therapy was more frequently started in patients admitted to the ICU; likewise these patients more often developed pleural empyema and consequently had longer hospital stays. Yet, due to the observational design and, accordingly, the lack of structured serial visualizations, evaluation of empyema or other pulmonary complications as an outcome was not considered appropriate. Finally, anticoagulant treatment timing, duration, dosing, and type of anticoagulant varied, which likely affected our results.

The observational design of this study is its major limitation. Due to the lack of consensus on anticoagulation therapy in Lemierre's syndrome, we originally believed that therapy would be guided by local traditions and guidelines in different regions of the country and thereby slightly randomized; if this were not found to be the case, we considered performing a propensity-matched regression-based analysis. However, in addition to confounding by indication, numbers and outcomes were also less than expected. Thus, regression-based analysis was deemed inappropriate as it was not possible to adequately adjust for confounders or outliers.

Speculatively, as septic thrombophlebitis in Lemierre's syndrome consists of infected debris [11], it is not clear that nonseptic and septic venous thromboembolism should be considered equal in terms of treatment, and fears have been raised of facilitating spread of infection through anticoagulation therapy [20]. On the other hand, in an impressive recent large compilation of previously published cases of Lemierre's syndrome [17], it was suggested that anticoagulant therapy may reduce new in-hospital peripheral septic lesions. However, the issue of indication bias described above also applies here, and data on severity of presentation in patients with or without anticoagulation were not available. In our study, 2 patients with Lemierre's syndrome with jugular vein thrombosis who did not receive anticoagulation therapy developed peripheral septic complications after diagnosis, in both cases arthritis, while 1 patient developed cerebral venous sinus thrombosis despite treatment with a therapeutic dose.

To settle the question of the role of anticoagulation therapy in Lemierre's syndrome, a multinational prospective randomized trial is likely required. While this will be difficult due to the low yet increasing incidence [6], it is possible that prospective enrollment could be performed through the early identification of cases with bacteremia due to *F. necrophorum* with the involvement of several large microbiological laboratories.

In conclusion, we describe a difference between patients with and without presence of jugular vein thrombosis in Lemierre's syndrome, where the former developed more severe thrombocytopenia and appeared to be more severely affected. In addition, we show that most patients with Lemierre's syndrome with jugular vein thrombosis clinically recover well without therapeutic doses of anticoagulant therapy but also that adverse events are rare in patients with anticoagulation therapy. While prophylactic anticoagulation therapy should be given according to estimated risk of venous thromboembolism with consideration of contraindications [24], the role of anticoagulation therapy in treatment doses in Lemierre's syndrome will likely remain unclear until addressed by an interventional study.

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