



## Letter to the Editor

Cardiovascular events and *de novo* AF following Legionnaires disease

Dear Editor,

Cardiovascular (CV) diseases are a worldwide major cause of death. This fact relates to a number of risk factors [1], but infection might be pointed as one of utmost importance as it triggers inflammation, thrombosis and endothelial dysfunction, leading to atherosclerosis. This is true not only in the acute phase of the infection, but also in the following years. Low respiratory tract infections, specially if severe, have been associated with CV events [2].

Recently, Kwong *et al* [3]{Kwong, 2018 #1} have identified a significant association between respiratory infections and acute myocardial infarction, especially viral infections. Nonetheless, the association with specific bacterial infections is less clear.

We aimed to describe CV events (stroke and myocardial infarction) and *de novo* atrial fibrillation (AF) within the range of one year after Legionnaires disease (LD) has been diagnosed, and intended to find any association between the severity of the disease and these events. Disease severity was defined in accordance to the admission into high dependency units, as CURB-65 score has low performance in LD [4]. Follow up was assessed by clinical and administrative databases.

For this purpose we have performed a retrospective single-center analysis of all patients with LD admitted to our university hospital from 2008 to 2015. During the first year after LD diagnosis, all documented CV events and *de novo* AF were collected as well as risk factors for cardiovascular CV diseases. LD was defined by a positive Legionella Urinary Antigen Test (serotype 1) with a clinical picture suggestive of acute lower respiratory tract infection and new infiltrate on chest x-ray. Study protocol was approved by a local ethics committee.

Our cohort included 110 patients with a median age of 58 years old (IQR 25); 68% ( $n = 75$ ) were male and median Charlson comorbidity index was 1 (IQR 3). Sixty-one patients (55%) were admitted to a general ward while the remaining were admitted to the Intensive Care Department (ICD). Three patients refused hospital admission and were briefly reassessed. Median hospital stay was 13 days (IQR 9). Patients' characteristics as well as classical vascular risk factors in accordance with CV events or *de novo* AF are described in Table 1. Relevant clinical characteristics were similar between patients that had CV events or *de novo* AF and the control group.

In the year following LD diagnosis we have documented one type-two myocardial infarction (1%), two ischemic strokes (2%) and three patients with *de novo* AF (3%). Both *de novo* AF and myocardial infarction occurred within the first 24 h after hospital admission and solely in patients admitted to ICD. Strokes were diagnosed exclusively in patients admitted to general ward. Events were attributed by assistant physicians.

Five patients (4,5%) died during hospital admission but no single death was attributed to CV event. Seven patients (6,3%) were not followed-up regarding CV events due to lack of medical data, but they were alive after 1-year follow-up (follow-up was performed according

clinical data; these seven patients with no clinical data available were followed-up using national administrative data). All-cause one-year mortality was 11%.

In our cohort the rate of CV events was low, which reinforces the different pathogenesis of CV events after viral and specific bacterial infections. Interestingly, non-ICU patients had more CV events (particularly stroke) one year after LD, but they had less incidence of *de novo* AF and MI, both of which occurred earlier, probably related to hemodynamic instability.

Certainly that our study has some limitations. Severity in LD is difficult to define, as commonly used scoring systems are not accurate for this disease. Also, this study represents a single-center cohort with a small sample size and mostly composed by young-adults with low comorbidities. Sampling was also made out of any outbreak, which could limit its validity. Furthermore, due to the retrospective nature of this analysis, more specific data concerning risk factors (stratification of hypertension, smoking load, quantification of alcohol consumption) were not addressed, because they were not commonly specified in medical registries. Nonetheless, according to our knowledge, this is the first study exploring CV events and *de novo* FA following LD and it represents real-life data (without interventions besides usual care), which can better represent the natural history of this disease. Despite its

Table 1

Patients characteristics and comparison between patients with and without CV events or *de novo* AF.

Patients characteristics	CV events or <i>de novo</i> AF ( $n = 6$ ) <sup>a</sup>	No events ( $n = 97$ )	<i>P</i> value
Age yo, median, IQR	69 (31)	57 (18)	0,294
Sex, male, n(%) <sup>b</sup>	4 (67)	68 (70)	0,859
CURB-65, median (IQR)	2 (2)	1 (2)	0,935
SOFA, median, (IQR)	4 (4)	2 (3)	0,048
ICD admission, n (%)	4 (66,7)	40 (43)	0,249
Ratio, median (IQR)	283 (60)	282 (90)	0,725
Macrolide, n (%)	3 (50)	57 (59)	0,234
Length of stay, days, median (IQR)	12 (12)	9 (7)	0,275
1-year mortality	1 (17)	9 (9)	0,597
Vascular risk factors			
Obesity, n (%)	1 (17)	16 (17)	0,991
HTN, n (%)	4 (67)	44 (45)	0,310
Diabetes, n (%)	1 (17)	22 (23)	0,731
Dyslipidemia, n (%)	2 (33)	35 (36)	0,892
Smoking, n (%)	1 (17)	48 (50)	0,118
Alcohol abuse, n (%)	2 (33)	33 (24)	0,594

ICD - Intensive Care Department; HTN - arterial hypertension.

Note: Statistical Analysis: Chi-square test was used to compare categorical variables. Mann-Whitney *U* test was used for continuous skewed variables (none variable was normally distributed).

<sup>a</sup> 7 patients were not followed-up regarding to CV events or *de novo* AF.

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limitations, the information we gathered can be a trigger to future studies on the role of bacterial infection in the pathogenesis of cardiovascular disease.

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Study agrees to the ethical guidelines of the Helsinki declaration and was approved by the local Ethics Committee.

None of authors have conflicts of interest to declare.

All authors have contributed to this work.

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