Chronic liver disease negatively affects outcome in hospitalised patients with community-acquired pneumonia

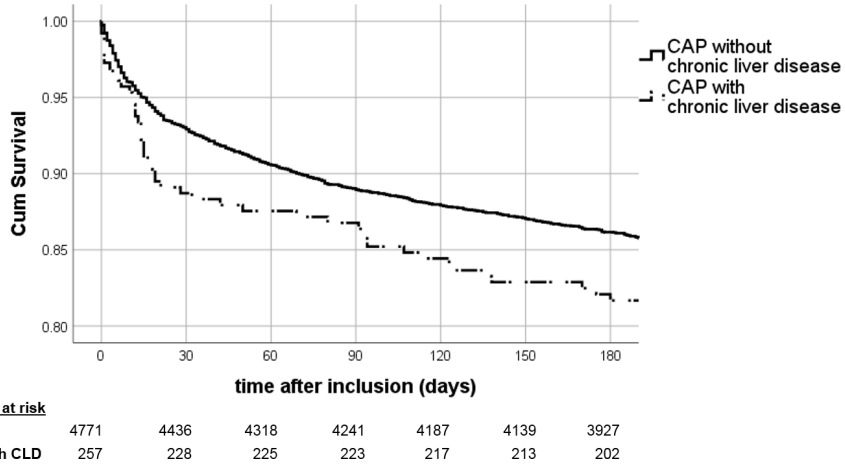

Figure 1 Kaplan-Meier survival curve of hospitalised CAP patients with and without CLD. CAP, community-acquired pneumonia; CLD, chronic liver disease.

We read with great interest the article by Fernández and colleagues[1] which identifies bacterial infections, including pneumonia, not only as a trigger, but also as a common complication of acute-on-chronic liver failure with severe consequences. Moreover, in this and other studies the role of respiratory infections and failure has been shown to be detrimental in patients with chronic liver disease (CLD).[2–4] While it is well established that respiratory infections aggravate the clinical outcome and increase mortality in CLD, there are little to no data from large cohorts analysing the role of CLD in patients with community-acquired pneumonia (CAP). This prompted us to analyse the impact of CLD on the severity of CAP using data from the German Competence Network for Community-acquired pneumonia (CAPNETZ) study, a large multicentre study on CAP conducted between 2001 and 2017.[5 6] The CAPNETZ study included a total of 11 832 patients with episodes of CAP, of whom 5449 hospitalised patients had information available on the presence or absence of CLD. In this cohort, 289 patients with CAP (5.3%; online supplementary figure S1) were identified with CLD. CAP patients with CLD were significantly younger than those without; their median age (IQR) was 64 years (50–73) vs 73 years (64–80) (p<0.001). Possibly due to the lower age in this patient group, cardiac disease, cerebrovascular disease and diabetes mellitus were less frequent in CAP patients with CLD than in those without. By contrast, chronic respiratory diseases were more common in CAP patients with CLD (online supplementary table 1).

Interestingly, despite younger age, which is usually beneficial in the prognosis of CAP, survival of patients with CLD was significantly lower than in those without (figure 1; log-rank (Mantel-Cox) test p=0.020). Thirty-day and 180-day mortality rates were higher than in cases without underlying CLD (30 days: 11.3% vs 7.1%, OR 1.667 (95% CI 1.115 to 2.492), p=0.014; 180 days: 19.0% vs 14.5%, OR 1.383 (95% CI 0.996 to 1.920), p=0.054). Moreover, in a multivariable regression analysis, age ≥65 years, cerebrovascular disease, chronic heart failure and CLD were independently associated with 30-day mortality (table 1). Among these, CLD was associated with the second-highest OR for 30-day mortality in hospitalised CAP (OR 2.350 (95% CI 1.548 to 3.658)), corroborating the significance of CLD on the outcome of patients with CAP. The median length of hospital stay was significantly higher in patients with CLD than in those without, even with other severe comorbidities (12 days (IQR 8–16) vs 10 days (IQR 8–14), p<0.001).

Results of blood cultures were available in 112 and 2265 CAP cases with and without CLD, respectively. The proportion of patients with bacteraemia was more than twice as high in the group of CAP patients with CLD as in those without (19.6% vs 8.9%, p<0.001). This higher prevalence of bacteraemia might be due to increased intestinal permeability, bacterial translocation, changes in the microbiome and immune dysfunction.[7] These findings warrant further investigation regarding the mechanisms of bacterial dissemination, pathogen spectrum and antimicrobial resistance.

The predictive value of the Quick Sequential Organ Failure Assessment (qSOFA) in patients with cirrhosis and bacterial infection has been validated in a recent study.[8] We identified patients at high risk of sepsis-related mortality, defined by suspected infection (pneumonia) and a qSOFA score ≥2. Among CAP cases with CLD, the proportion of patients fulfilling these criteria was higher than in those without (49 of 264 (18.6%) vs 605 of 4789 (12.6%), p=0.005). In both groups, a qSOFA score ≥2 was strongly associated with an increased risk of 30-day mortality (online supplementary table 2).

Table 1 Multivariable regression analysis for 30-day mortality using backwards variable selection (Wald method) with the covariates chronic liver disease, age ≥65 years, chronic respiratory disease, chronic heart failure, cerebrovascular disease and diabetes mellitus, including 5006 patients with CAP for which data on these variables were available

	OR (95% CI)	P value
Cerebrovascular disease	2.527 (2.003 to 3.189)	<0.001
Chronic liver disease	2.350 (1.548 to 3.568)	<0.001
Age ≥65 years	2.224 (1.559 to 3.093)	<0.001
Chronic heart disease	1.875 (1.501 to 2.341)	<0.001

CAP, community-acquired pneumonia.

In conclusion, the findings presented by Fernández and colleagues[1] together with our data shown in this letter highlight an emerging need and deliver a rationale for preclinical and clinical studies to further elucidate the liver-lung axis, which seems to be increasing mortality in patients with CLD as well as in patients with CAP.

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