Relevance of inflammation as a driver of further decompensation in compensated cirrhosis

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Worsening of low-grade systemic inflammation heralds decompensation in patients with compensated cirrhosis

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1 Introduction

- **Portal hypertension** is a major driver of **progression and decompensation** in cirrhosis.
- **Systemic inflammation** has been well described in decompensated, where it contributes to further progression[1].
- The **information** regarding systemic inflammation in **compensated cirrhosis is limited.**

2 Aims

To investigate:

1. Whether **systemic inflammation** is present in patients with **compensated cirrhosis**.
2. If so, whether its worsening associates with the development of **decompensation**.

3 Methods

Nested cohort study within the PREDESCI trial[2]:

Double blind multicentre, RCT in patients with compensated cirrhosis and clinically significant portal hypertension -CSPH- (HVPG > 10mmHg)

Efficacy of beta-blockers to prevent decompensation.

- Healthy controls (n= 35).
- **Assessment of blood biomarkers:** baseline and 1 year follow-up (F/U).

Register of **cirrhosis complications** during F/U.

4 Results

Baseline characteristics

	Compensated cirrhosis and CSPH (n=201)
Male, n (%)	123 (61.2)
Age (years) mean, sd	62.5, ±10.5
Etiology of cirrhosis, n (%)	
Alcohol	33 (16.4)
Hepatitis C virus	113 (56.2)
Alcohol + Hepatitis C	17 (8.5)
NASH	13 (6.5)
Others	25 (12.4)
CTP score, n (%)	
A	161 (80)
B	40 (20)
Oesophageal varices, n (%)	
None	87 (43.3)
Small	114 (56.7)
HVPG (mmHg) mean, sd	14.8, ± 4

Follow-up characteristics

	Compensated cirrhosis and CSPH (n=201)
Median F/U (months)	37
Decompensation, n (%)	36 (17.4)
Ascites	29 (14.4)
GI bleeding	7 (3.5)
HE	9 (4.5)
Time to event (months), median (p25-p75)	
Ascites	23.5 (13.6-34.4)
GI bleeding	21.8 (11.5-29)
HE	23.5 (19.2-34.6)
Liver transplant, n (%)	4 (2)
Death, n (%)	19 (9.5)

CSPH: clinically significant portal hypertension; sd: standard deviation; NASH: non-alcoholic steatohepatitis; CTP: Child-Turcotte-Pugh; HVPG: hepatic venous pressure gradient; GI: gastrointestinal; HE: hepatic encephalopathy; F/U: follow-up; IQR: interquartile range; P: controls vs cirrhosis; P intra: baseline vs 1-yr; vWF: von Willebrand factor; FABP: fatty acid binding protein.

- 17.4% of patients developed a decompensation during F/U.
- The most common decompensation was ascites in 14.4%.
- Decompensations occurred within a median time of first 2 years during F/U.

Assessment of blood biomarkers

		Baseline				1 year F/U				
	Group	n	Median	IQR	P	n	Median	IQR	P	P intra
IL-6 (pg/mL)	**Controls**	30	1.6	1.01-2.6	**<0.05**				**0.003**	
	Cirrhosis	139	2.3	1.3-3.6		97	3.03	1.39-5.25		**0.02**
TNF-α (pg/mL)	**Controls**	34	6.4	5.3-6.3	0.36				0.95	
	Cirrhosis	149	5.9	3.93-8		97	6.3	4.43-8.1		0.6
CD163 (ng/mL)	**Controls**	34	258.74	210.7- 362.4	**< 0.001**				**< 0.001**	
	Cirrhosis	157	857.72	605.5-1117		101	820.35	524.2-1087.1		0.76
CD14 (ng/mL)	**Controls**	35	1.23	0.84-1.477	0.23				0.34	
	Cirrhosis	163	1.28	1.06-1.6		108	1.27	1-1.6		0.77
vWF (ng/mL)	**Controls**	20	2.95	1.46-5.13	**< 0.001**				**0.005**	
	Cirrhosis	160	6	3.61-9.81		108	4.79	2.78-9.18		0.58
FABP (ng/mL)	**Controls**	30	0.31	0.19- 0.50	**< 0.001**				**< 0.001**	
	Cirrhosis	149	0.72	0.52-1.04		103	0.73	0.419-1.01		0.95
LBP (μg/mL)	**Controls**	35	6	4.1-6.9	0.25				**0.04**	
	Cirrhosis	158	6	4.7-7.4		102	6.3	5.26-7.62		0.89

Low-grade systemic inflammation and intestinal barrier function derangement

- Higher IL-6, vWF and CD163 levels in patients compared to controls.
- IL-6 was higher and increased (p<0.05) at 1-year in patients that decompensated.
- Higher FABP in patients compared to controls.

No association between biomarkers and hemodynamic parameters (blood pressure, HVPG)

5 Conclusions

Low-grade systemic inflammation is present in patients with compensated cirrhosis. In this setting, **worsening** of systemic inflammation heralds **cirrhosis decompensation.**

6 References

[1] Albillos A et al. Cirrhosis- associated immune dysfunction. *Nat Rev Gastroenterol Hepatol 2022*;19(2):112-134.

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