	≤ 90-day survival		> 90-day survival		
Parameter	**Av. data**	**No.**	**Av. data**	**No.**	**p-value**
Age (years)[2]	36	60 (54.8 – 65.3)	246	58 (48 – 64.5)	0.099
Gender (male/female)	36	20/16	243	146/97	0.606
Etiology of liver disease	36		243		0.587
Alcohol abuse		12		72	
NASH/ASH/NAFLD		4/1/0		26/5/6	
Cryptogen		5		27	
Hepatitis B/C/E		0/4/0		5/20/1	
PSC/PBC		1/0		17/7	
Drug related		1		5	
Autoimmune hepatitis		2		6	
Secondary sclerosing cholangitis		3		5	
Other		3		41	
Clinical conditions					
AD/ACLF	36	20/16	243	232/11	<0.001
Inflammation (pos./neg.)	36	20/16	242	49/193	<0.001
Ascites (pos./neg.)	36	15/21	242	58/184	0.024
Hepatic encephalopathy	36	14/22	242	31/211	<0.001
Hepatorenal syndrome (pos./neg.)	36	14/22	242	23/219	<0.001
Anemia (pos./neg.)	36	10/26	243	52/191	0.39
Comorbidities					
Coronary heart disease	36	6/30	228	14/228	0.018
Hypertension (pos./neg.)	36	19/17	243	111/132	0.426
Diabetes (pos./neg.)	36	10/26	243	61/182	0.731
Chronic kidney disease	36	21/15	243	44/199	<0.001
Hepatocellular cancer (pos./neg.)	36	3/33	243	39/204	0.227
Alcohol abuse (neg./active/history of)	36	21/3/12	235	150/27/58	0.513
Established clinical scores predicting survival					
CHILD A/B/C	34	2/14/18	210	89/89/32	<0.001
MELD-Score	36	26.2 (± 8.6)[1]	213	13 (8 – 17)[2]	<0.001

AD-Score[1]	20	55.2 (±9.8)	183	46.7 (±10.2)	<0.001
Biomedical characteristics					
WBC (10^9/l)[2]	36	7.1 (5 – 11.4)	239	5.9 (4.3 – 7.9)	0.017
Sodium[2]	33	138 (134 – 141)	238	139 (136 – 142)	0.057
Albumin (g/dl)	25	2.8 (±0.48)[1]	157	3.5 (2.8 – 4.1)[2]	<0.001
Ferritin (µg/l)[2]	36	861 (244.3 – 1876.5)	243	190 (63.5 – 456)	<0.001
Transferrin (mg/dl)	32	102.1 (±46.4)[1]	218	198.5 (137.5 – 262)[2]	<0.001
Transferrin saturation (in %)[2]	32	78 (27.3 – 92)	214	31 (18 – 52)	<0.001
Iron (µg/dl)[2]	33	74 (44 – 108)	234	78 (52.3 – 122.8)	0.366
CRP (mg/dl)[2]	33	3.6 (1.8 – 7.1)	152	1.8 (0.4 – 3.6)	<0.001
AST (U/l)[2]	31	79 (54.5 – 184.5)	212	54.4 (35.8 – 114)	0.01
ALT (U/l)[2]	35	40 (23 – 110)	214	42.5 (27.3 – 84.8)	0.749
GGT (U/l)[2]	36	115.5 (37 – 326.8)	213	122 (56 – 268)	0.519
Creatinine (mg/dl)[2]	36	1.4 (1 – 2.3)	209	0.9 (0.7 – 1.2)	<0.001
Bilirubin (mg/dl)[2]	35	7.9 (2.6 – 16.3)	220	1.3 (0.7 – 2.8)	<0.001
INR[2]	36	1.9 (±0.5)	215	1.2 (1.1 – 1.5)	<0.001

Supplemental Table 1: Demographic data and clinical conditions of included unmatched patients with end-stage liver disease based on 90-day survival (n=286). Non-alcoholic steatohepatitis (NASH), alcoholic steatohepatitis (ASH), non-alcoholic fatty liver disease (NAFLD), primary sclerosing cholangitis (PSC), primary biliary cholangitis (PBC), acute decompensation (AD), acute on chronic liver failure (ACLF)

[1] Mean (± Std. deviation); [2] Median (1^{st} – 3^{rd} quartile)

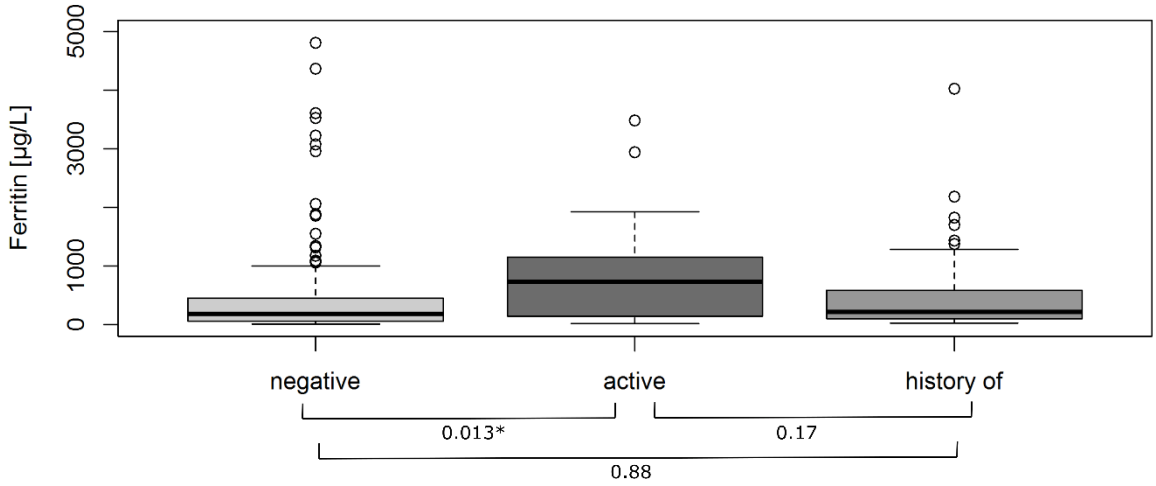
	≤ 90-day survival		> 90-day survival		
Parameter	**Av. data**	**No.**	**Av. data**	**No.**	**p-value**
Age (years)[2]	36	60 (54.8 – 65.3)[2]	36	57.1 (±8.8)[1]	0.157
Gender (male/female)	36	20/18	36	18/18	0.637
Etiology of liver disease	36		36		0.448
Alcohol abuse		12		20	
NASH/ASH/NAFLD		4/1/0		1/1/0	
Cryptogen		5		4	
Hepatitis B/C/E		0/4/0		0/5/0	
PSC/PBC		1/0		0/0	
Drug related		1		2	
Autoimmun Hepatitis		2		1	
Secondary sclerosing cholangitis		3		0	
Others		3		2	
Clinical conditions					
AD/ACLF	36	20/16	36	25/11	<0.001
Inflammation (pos./neg.)	36	20/16	36	20/16	1
Ascites (pos./neg.)	36	15/21	36	24/12	0.033
Hepatic encephalopathy	36	14/22	36	12/24	0.624
Hepatorenal syndrome (pos./neg.)	36	14/22	36	11/25	0.458
Anemia	36	10/26	36	12/24	0.609
Comorbidities					
Coronary heart disease	36	6/30	36	1/35	0.047
Hypertension (pos./neg.)	36	19/17	36	15/21	0.345
Diabetes (pos./neg.)	36	10/26	36	5/31	0.147
Chronic kidney disease	36	21/15	36	8/28	0.002
Hepatocellular cancer (pos./neg.)	36	3/33	36	2/34	0.643
Alcohol abuse (neg./active/history of)	36	21/3/12	35	14/15/6	0.003
Scores predicting survival					
CHILD A/B/C	34	2/14/18	36	7/14/15	0.224
MELD-Score[1]	36	26.2 (± 8.6)	34	20 (± 7.5)	0.003

AD-Score[1]	20	55.2 (± 9.8)	22	53.2 (± 8.7)	0.493
Biomedical characteristics					
WBC (10^9/l)[2]	36	7.1 (5 – 11.4)	36	6.8 (4.9 – 10.7)	0.757
Sodium	33	138 (134 – 141) [2]	36	135.5 (± 6)[1]	0.423
Albumin (g/dl)[1]	25	2.8 (± 0.5)	24	3.0 (± 0.9)	0.257
Ferritin (µg/l)[2]	36	861 (244.3 – 1876.5)	36	251.5 (85.8 – 995.3)	0.017
Transferrin (mg/dl)	32	102.1 (± 46.4)[1]	35	119 (76 – 191.5)[2]	0.108
Transferrin saturation (in %)[2]	32	78 (27.3 – 92)	32	55 (21.8 – 82.5)	0.080
Iron (µg/dl)[2]	33	74 (44 – 108)	33	69 (47 – 116)	0.918
CRP (mg/dl)	33	3.6 (1.8 – 7.1)[2]	27	3.7 (± 2.6)[1]	0.444
AST(U/l)[2]	31	79 (54.5 – 184.5)	32	104 (56.3 – 199)	0.685
ALT (U/l)[2]	35	40 (23 – 110)	32	42.5 (27.8 – 102.75)	0.679
GGT (U/l)[2]	36	115.5 (37 – 326.8)	32	115.5 (48 – 207.3)	0.658
Creatinine (mg/dl)[2]	36	1.4 (1 – 2.3)	33	1.1 (0.8 – 1.7)	0.048
Bilirubin (mg/dl)[2]	35	7.9 (2.6 – 16.3)	33	4.40 (1.6 – 9.9)	0.133
INR	36	1.9 (± 0.53)[1]	33	1.5 (1.3 – 1.7)[2]	0.014

Supplemental Table 2: Propensity score matched demographic data and clinical conditions of the included patients with end-stage liver disease (n=72). Non-alcoholic steatohepatitis (NASH), alcoholic steatohepatitis (ASH), non-alcoholic fatty liver disease (NAFLD), primary sclerosing cholangitis (PSC), primary biliary cholangitis (PBC), acute decompensation (AD), acute on chronic liver failure (ACLF

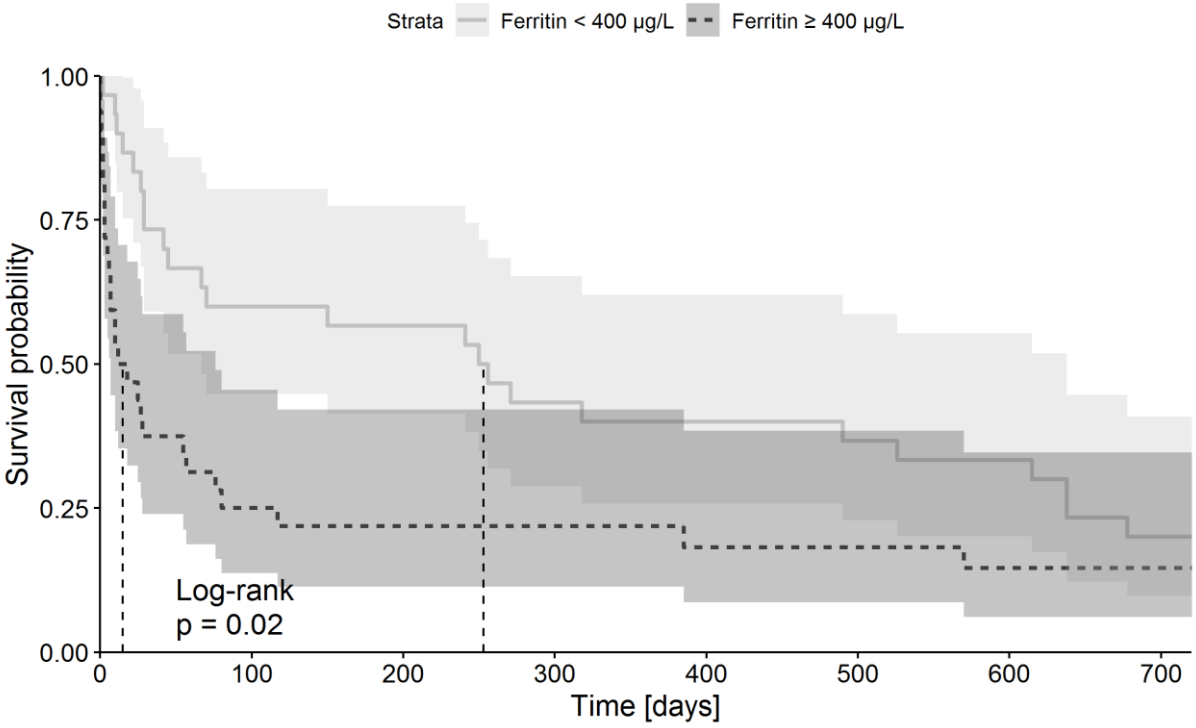
[1] Mean (± Std. deviation); [2] Median (1^{st} – 3^{rd} quartile)

Subgroup analysis of the effect of alcohol abuse upon serum ferritin levels of patients with end stage liver disease.



Supplemental Figure 1: Differences in serum ferritin levels of end-stage liver disease patients based upon alcohol abuse in unmatched analysis. Patients were grouped in patients with no, with active and with a history of alcohol abuse. Pairwise comparisons of serum ferritin levels based upon subgroups of alcohol abuse. There was a significant difference between the serum ferritin value of patients with active alcohol abuse compared to patients with no alcohol abuse (p=0.013). The Y-axis has been limited to a maximum value of 5000 µg/L to allow for better visualization.

Analysis based on hyperferritinemia



Supplemental Figure 2: Overall survival based on hyperferritinemia. The cutoff for hyperferritinemia was chosen based on the upper reference limit of our laboratory. Statistically significant differences between both groups can be demonstrated over the two-year observational period (p=0.02). Vertical lines indicate median survival (serum ferritin level >400 µg/L: 15 days; serum ferritin level <400 µg/L: 253 days). Shaded areas represent the 95% confidence interval.

Parameter	Survival (%)	95% CI (lower – upper)
Serum ferritin ≤ 400 µ/L	60%	44.8% - 80.4%
Serum ferritin > 400 µ/L	25%	13.7% - 45.5%

Supplemental Table 3: 90-day survival expressed as percentage values including lower and upper 95% confidence intervals.

Overview of currently published studies evaluating the role of ferritin and transferrin for the outcome of patients with end-stage liver disease (ESLD).

Author, year (Ref No.)	**Study design**	**No of patients included (n)**	**Parameter**	**Study Titel**	**Results**
Walker 2010[1]	Retrospective cohort	322	SF	SF concentration predicts mortality in patients awaiting LT	- SF ≥200 µg/L independent risk factor for significantly increased 1-y mortality in patients awaiting LT (p=0.01)
Weismüller 2011[2]	Retrospective cohort	410	SF	SF concentration and transferrin saturation before LT predict decreased long-term recipient survival	- Patients with a SF ≥365 µg/L before LT had a significant lower overall survival following LT than patients with a SF <365 µg/L (61.1% vs. 74.4%; p<0.01)
Al-Freah 2013[3]	Retrospective cohort	1079	SF	The association of pretransplant ferritin level with waiting list and post-transplant survival. Does ferritin actually predict outcome?	- ESLD patients with a SF >300 µg/L had a significantly increased 3-, 6- and 12-month mortality compared to ESLD patients with a SF ≤300 µg/L (18.4%; 28.0% and 33.4% vs. 9.7%, 15.4% and 21.5%; all p<0.001)
Maiwall 2014[4]	Retrospective cohort	318	SF	SF predicts early mortality in patients with decompensated cirrhosis	- SF (≥200 µg/L) was a significant predictor of early mortality (15-d and 30-d) in patients decompensated cirrhosis (p<0.05)
Wu 2014[5]	Prospective cohort	172	SF	SF concentration predicts mortality in patient with hepatitis B virus-related acute-on-chronic liver failure	- Patients with hepatitis b virus-related acute-on-chronic liver failure and elevated SF levels (>500 µg/L) had a significant higher 3-month mortality rate than patients with lower SF levels (p<0.01) - The AUROCs for 3-month mortality were 0.64 for SF (p<0.01) and 0.91 for MELD+SF (p<0.001)
Maras 2015[6]	Prospective cohort	160	SF/ST	Dysregulated iron homeostasis is strongly associated with multiorgan failure and early mortality in acute-on-chronic liver failure	- Lower ST levels were found in patients with acute-on-chronic liver failure (with and without multi-organ failure) compared to patients with compensated cirrhosis and healthy controls (p<0.01) - Higher SF levels were found in patients with acute-on-chronic liver failure with multi-organ failure compared to those without and healthy controls (p<0.05)
Ripoll 2015[7]	Retrospective cohort	51	SF	SF in patients with cirrhosis is associated with markers of liver insufficiency and circulatory dysfunction, but not of portal hypertension	- SF was not associated with prolonged survival in patients with liver cirrhosis in univariate analysis (p value not provided) - SF levels were not different in liver cirrhosis patients who died compared to patients who were still alive at the end of follow-up (p value not provided)
Beer 2015[8]	Retrospective cohort	405	SF	Etiologies and short-term mortality in	- Patients with an acute liver injury and SF values >5000 µg/L have a 30-d

				patients with ultraelevated SF	mortality of 33% and a 6-month mortality of 39%
Hagström 2016[9]	Retrospective cohort	222	SF	Elevated SF is associated with increased mortality in non-alcoholic fatty liver disease after 16 y of follow-up	- High SF cutoff values (men >350 µg/L; women >150 µg/L) showed an increased mortality 15 y after diagnosis in patients with non-alcoholic fatty liver disease (hazard ratio 1.1 per y; p<0.05)
Anastasiou 2017[10]	Retrospective cohort	102	SF/ST	Low transferrin and high ferritin concentrations are associated with worse outcome in acute liver failure	- Patients with SF >1510 µg/L had a significant higher mortality in patients with acute liver failure compared to patients with SF <1510 µg/L (p<0.0001) - Patients with ST <155 mg/dL had a significant higher mortality in patients with acute liver failure compared to patients with ST >155 mg/dL (p<0.0001) - The AUROC for 90-d survival were 0.80 for SF, 0.87 for ST, 0.89 for MELD+SF and 0.95 for MELD+ST (all p<0.002)
Bruns 2017[11]	Prospective cohort	292	SF/ST	Low ST correlates with acute-on-chronic organ failure and indicates short-term mortality in decompensated cirrhosis	- 90-d non-survivors presented with higher SF (p=0.03) and lower ST (p=0.02) - The AUROCs for 30-d mortality were 0.68 for ST (p=0.003) and 0.75 for MELD+ST (p value not provided)
Oikonomou 2017[12]	Retrospective cohort	192	SF	High SF is associated with worse outcome of patients with decompensated cirrhosis	- SF was an independent risk factor for mortality (HR 1.001; p=0.005) - SF had a low discriminative ability to the outcome of patients with decompensated cirrhosis (AUROC of 0.61) - Patients with cut-off SF >55 µg/L had a worse outcome (p=0.001)
Umer 2017[13]	Prospective cohort	132	SF	SF as a predictor for 30-d mortality in patients of decompensated chronic liver disease	- Patients with elevated SF levels had a significantly increased 30-d mortality (SF <200 µg/L: 0% mortality; SF 200-400 µg/L: 50% mortality; SF >400 µg/L: 93% mortality; p<0.001)
Viveiros 2018[14]	Retrospective cohort	1851	ST	Transferrin as a predictor of survival in cirrhosis	- In ESLD patients with ST <180mg/dL, 3-month, 1-y, and 5-y transplant-free survival rates were significantly lower (92%, 79% and 31%) compared to ESLD patients with ST ≥180 mg/dL (99%, 96% and 68%; all p<0.001)
Ribot-Hernandez 2019[15]	Prospective cohort	238	SF/ST	Prognostic value of serum iron, ferritin and transferrin in chronic alcoholic liver disease	- ST was significantly associated with survival of patients with chronic alcoholic liver disease (p<0.05 in log-rank test) - No association was found between SF and survival of patient with chronic alcoholic liver disease (p value not provided)

Supplemental Table 4: Overview of currently published studies evaluating the role of ferritin and transferrin for the outcome of patients with end-stage liver disease (ESLD).

After performing a systematic literature search in an electronic database (database: NCBI

pubmed; search items “ferritin AND outcome AND liver”, “transferrin AND outcome AND liver”, “ferritin AND survival AND liver” and “transferrin AND survival AND liver”; date of search: 29/09/2019) 1112 records were identified. After removing duplicates, 925 records were checked for evaluating the role of ferritin and transferrin for the outcome of ESLD patients. Finally, 15 records could be identified. Exclusion of records: Non-English language, case reports, case series, abstracts only, congress abstracts, reviews and animal studies. Abbreviations: D=day; y=year; AUROC=area under the receiver operating characteristic; SF=serum ferritin; ST=serum transferrin; ESLD=end-stage liver disease; LT=liver transplantation; MELD=Model of end-stage liver disease.

REFERENCES:

1. Walker NM, Stuart KA, Ryan RJ, et al. Serum ferritin concentration predicts mortality in patients awaiting liver transplantation. *Hepatology*. 2010; 51: 1683-91.
2. Weismuller TJ, Manns MP and Strassburg CP. Ferritin and liver allocation? Impact on mortality not only on the waiting list but also after orthotopic liver transplantation should be considered. *Hepatology*. 2010; 52: 392-3; author reply 3.
3. Al-Freah MA, Kriese S, Foxton MR, et al. The association of pretransplant ferritin level with waiting list and post-transplant survival. Does ferritin actually predict outcome? *Transpl Int*. 2013; 26: 1070-9.
4. Maiwall R, Kumar S, Chaudhary AK, et al. Serum ferritin predicts early mortality in patients with decompensated cirrhosis. *J Hepatol*. 2014; 61: 43-50.
5. Wu J, Chen L, Chen Y, Yang J and Wu D. Serum ferritin concentration predicts mortality in patients with hepatitis B virus-related acute on chronic liver failure. *Arch Med Res*. 2014; 45: 251-6.
6. Maras JS, Maiwall R, Harsha HC, et al. Dysregulated iron homeostasis is strongly associated with multiorgan failure and early mortality in acute-on-chronic liver failure. *Hepatology*. 2015; 61: 1306-20.
7. Ripoll C, Keitel F, Hollenbach M, Greinert R and Zipprich A. Serum Ferritin in Patients With Cirrhosis is Associated With Markers of Liver Insufficiency and Circulatory Dysfunction, but Not of Portal Hypertension. *J Clin Gastroenterol*. 2015; 49: 784-9.
8. Beer T and Vadakara J. Etiologies and Short-Term Mortality in Patients with Ultraelevated Serum Ferritin. *South Med J*. 2015; 108: 574-8.
9. Hagstrom H, Nasr P, Bottai M, et al. Elevated serum ferritin is associated with increased mortality in non-alcoholic fatty liver disease after 16 years of follow-up. *Liver Int*. 2016; 36: 1688-95.
10. Anastasiou OE, Kalsch J, Hakmouni M, et al. Low transferrin and high ferritin concentrations are associated with worse outcome in acute liver failure. *Liver Int*. 2017; 37: 1032-41.
11. Bruns T, Nuraldeen R, Mai M, et al. Low serum transferrin correlates with acute-on-chronic organ failure and indicates short-term mortality in decompensated cirrhosis. *Liver Int*. 2017; 37: 232-41.
12. Oikonomou T, Goulis I, Soulaidopoulos S, et al. High serum ferritin is associated with worse outcome of patients with decompensated cirrhosis. *Ann Gastroenterol*. 2017; 30: 217-24.
13. Umer N, Makki MU, Kiran SK and Jadoon NA. Serum ferritin as a predictor of 30 days mortality in Patients of decompensated chronic liver disease. *J Ayub Med Coll Abbottabad*. 2017; 29: 415-8.
14. Viveiros A, Finkenstedt A, Schaefer B, et al. Transferrin as a predictor of survival in cirrhosis. *Liver Transpl*. 2018; 24: 343-51.
15. Ribot-Hernandez I, Martin-Gonzalez C, Vera-Delgado V, et al. Prognostic Value of Serum Iron, Ferritin, and Transferrin in Chronic Alcoholic Liver Disease. *Biol Trace Elem Res*. 2019.