Accuracy of controlled attenuation parameter (CAP) measurement for the detection of steatosis in autoimmune liver diseases

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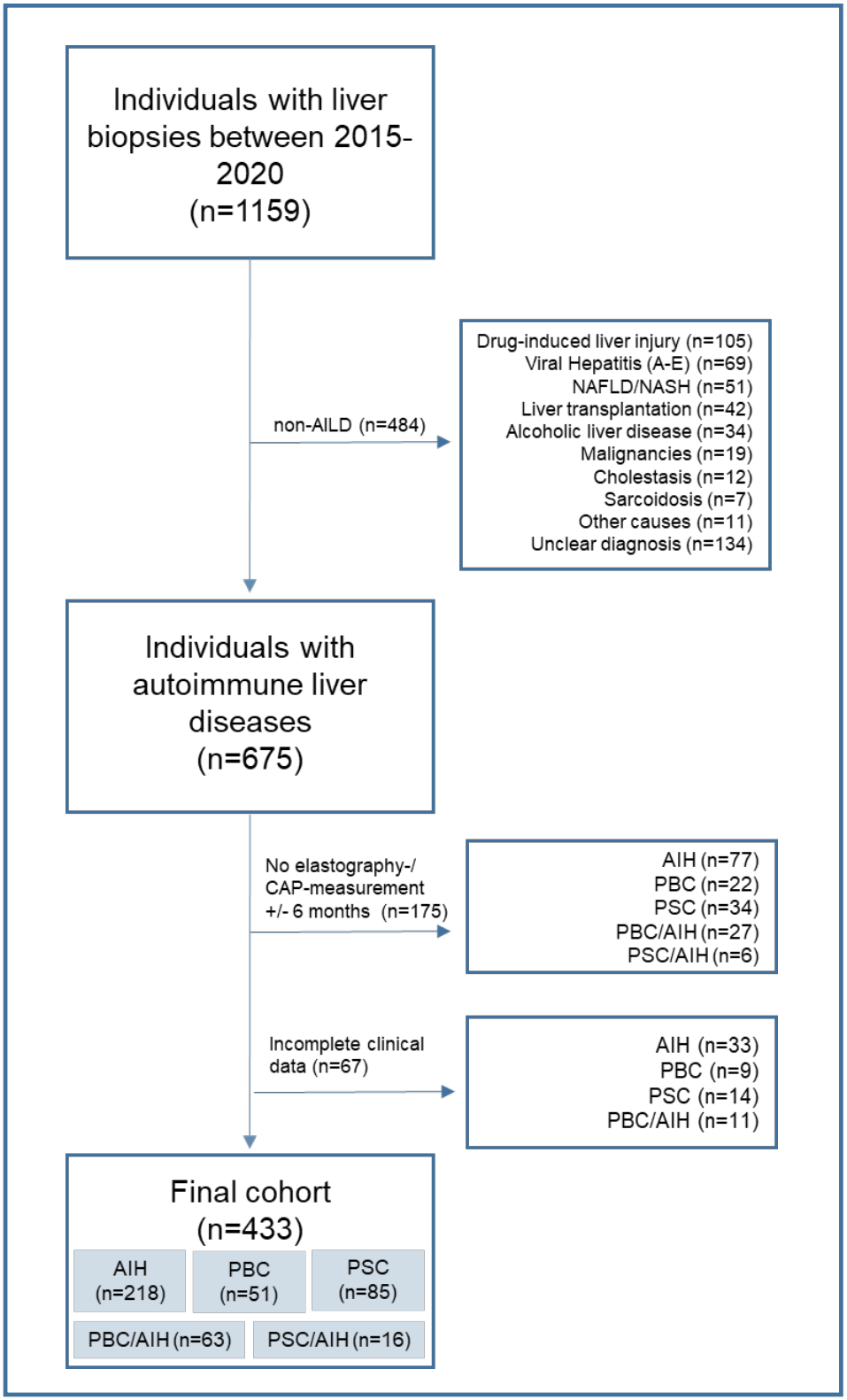

Fig. S1: Flowchart of participant selection for the evaluation of CAP accuracy.

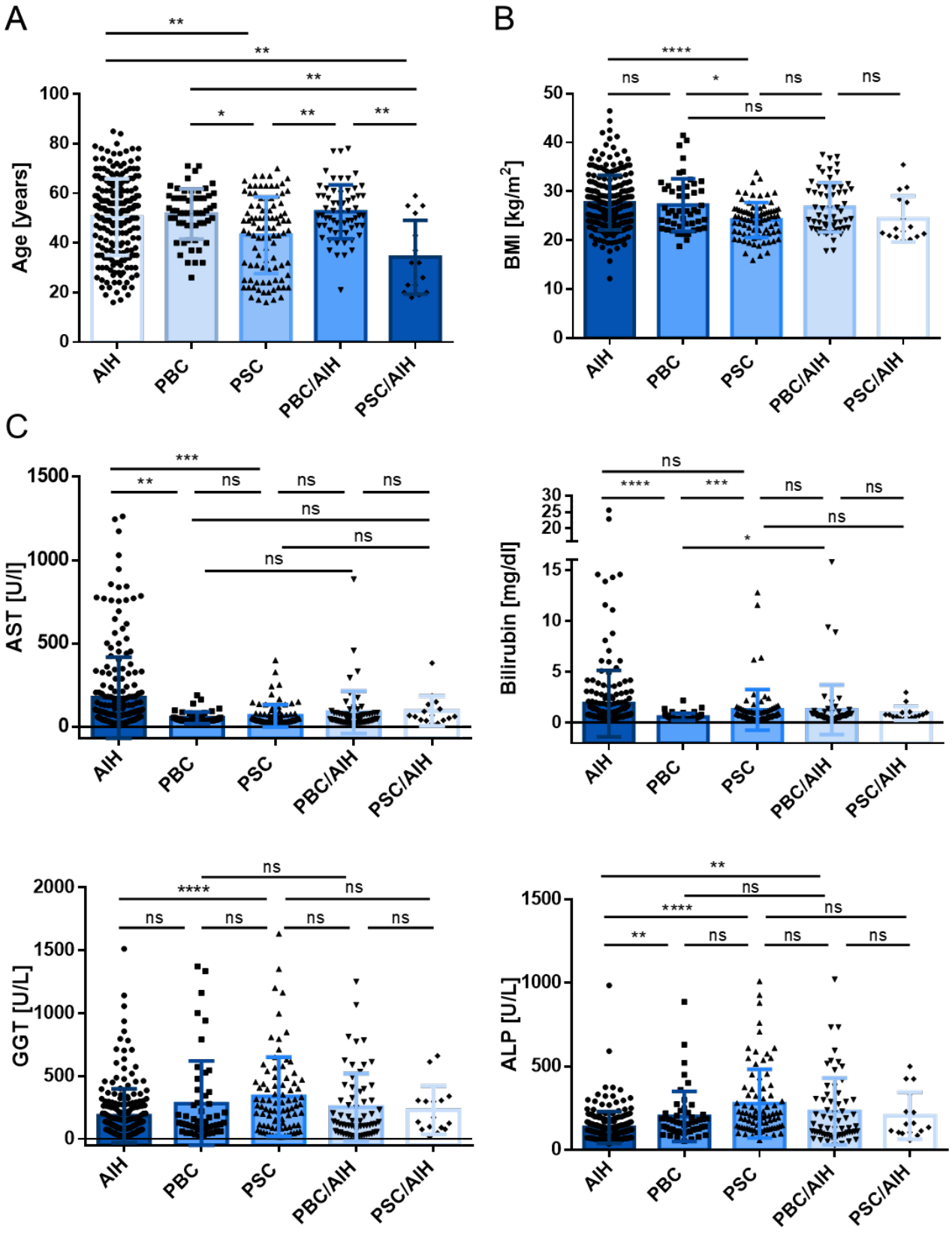

Fig. S2: Clinical characteristics of liver-biopsied people with AILD.

Demographical (A) clinical (B) and laboratory (C) characteristics of the study cohort. Differences between subpopulations were compared by Kruskal-Wallis-test; ns=not significant; *=p<0.05; **=p<0.01; *** =p<0.001; ****=p<0.0001.

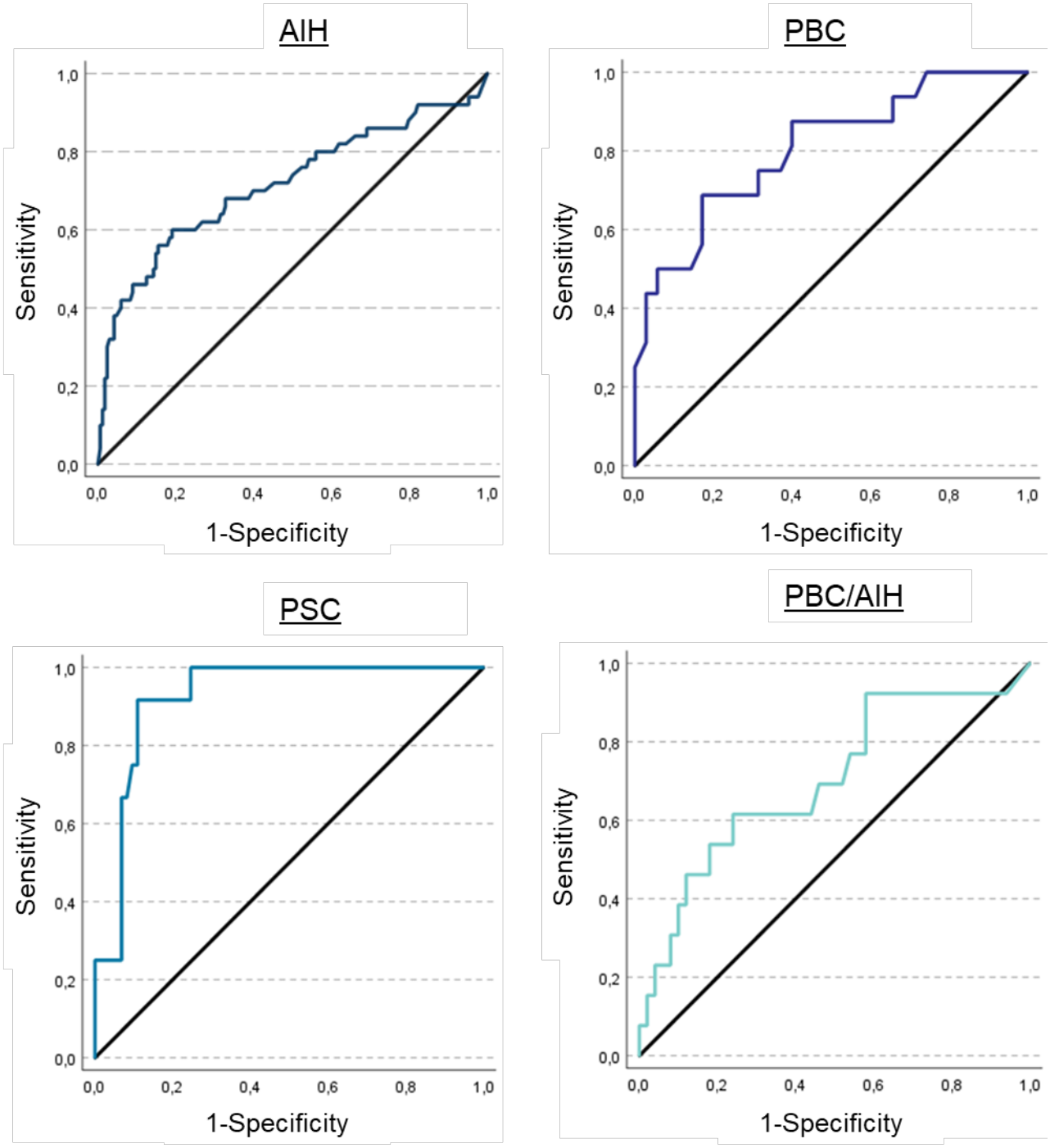

Fig. S3: ROC curves of CAP measurement in people with AILD according to the underlying disease.

AIH: AUROC=0.72; PBC: AUROC=0.81; PSC: AUROC= 0.93; AIH/PBC: AUROC=0.70.

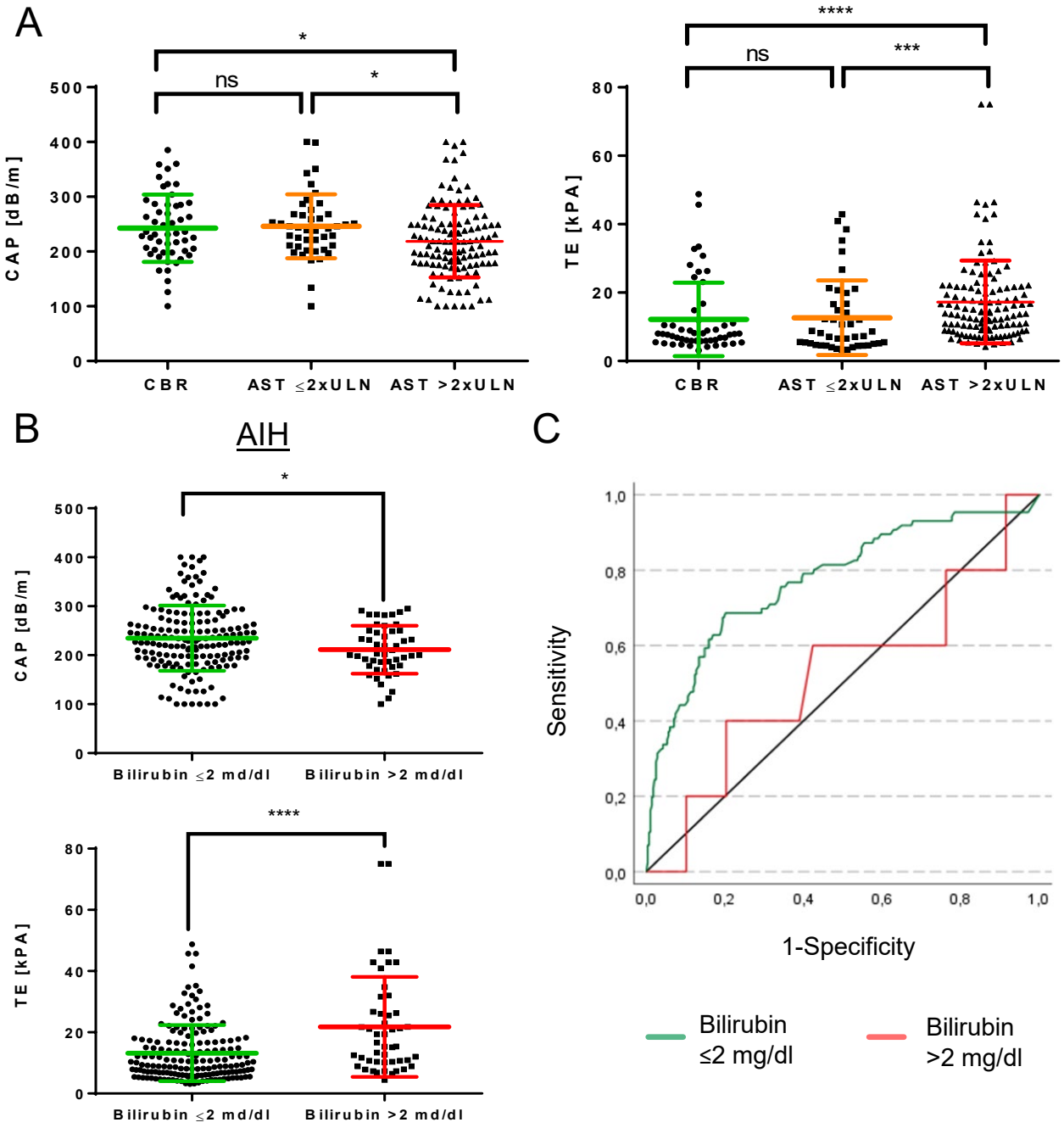

Fig. S4: Effect of hepatic inflammation on elastography measurements in people with AIH.

(A) Elastography measurements differ in people with AIH depending on AST levels (CBR: individuals with complete biochemical response, n= 43; AST <2xULN: people without CBR but AST levels <2xULN, n=41; AST >2xULN: individuals with AST levels >2xULN at time of elastography, n=134). (B) Mean CAP and TE values of individuals with AIH. Patients without jaundice (n=169) show significantly increased CAP (p=0.028) and decreased TE values (p<0.0001) compared to those with bilirubin levels above 2 mg/dl (n=49). (C) In patients with bilirubin levels above 2 mg/dl (red curve) accuracy of CAP to determine hepatic steatosis was lower (AUROC: 0.522) than in individuals without jaundice (AUROC: 0.774; Hanley and McNeil test: p=0.092). Differences between two groups were tested by Mann-Whitney-test. Differences within more than two subpopulations were compared by Kruskal-Wallis-test, ns= not significant, *= p<0.05; *** = p<0.001 ; ****= p<0.0001

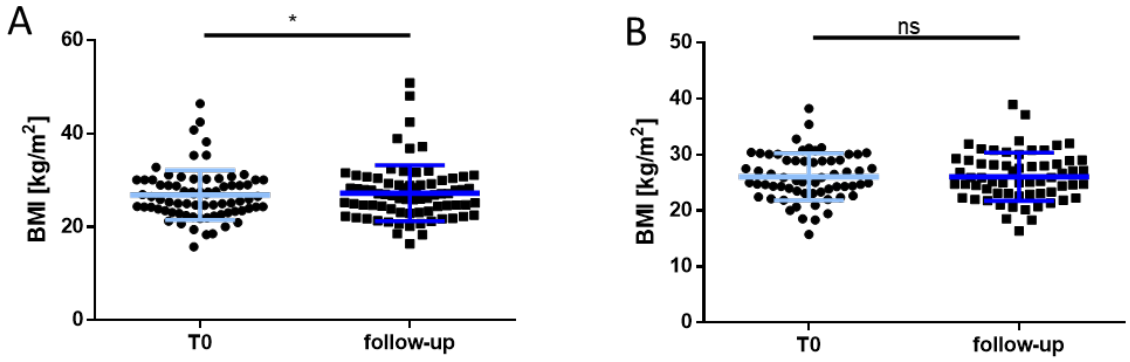

Fig. S5: Changes of BMI in people with AIH upon follow-up.

(A) BMI of all individuals with AIH with high inflammatory activity (T0) and upon elastography follow-up as complete biochemical response (CBR) was achieved, (n=74). (B) BMI of individuals with AIH with high inflammatory activity (T0) and upon follow-up without substantial weight gain (> 10% of initial body weight) (n=62), p=0.3. Wilcoxon matched-pairs signed-rank test was used to test differences of AIH patient upon follow-up. ns=not significant; *=p<0.05.

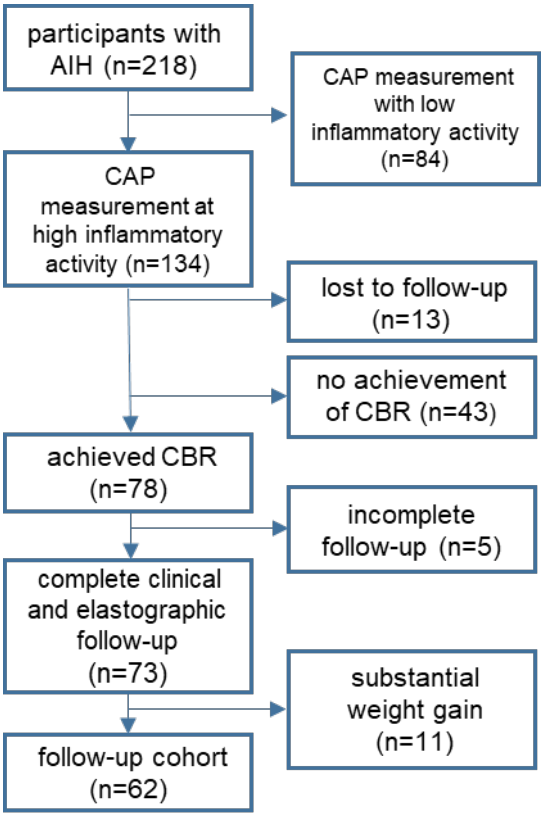

Fig. S6: Flowchart of participant selection for evaluation of follow-up CAP measurement in AIH upon achievement of complete biochemical response (CBR).

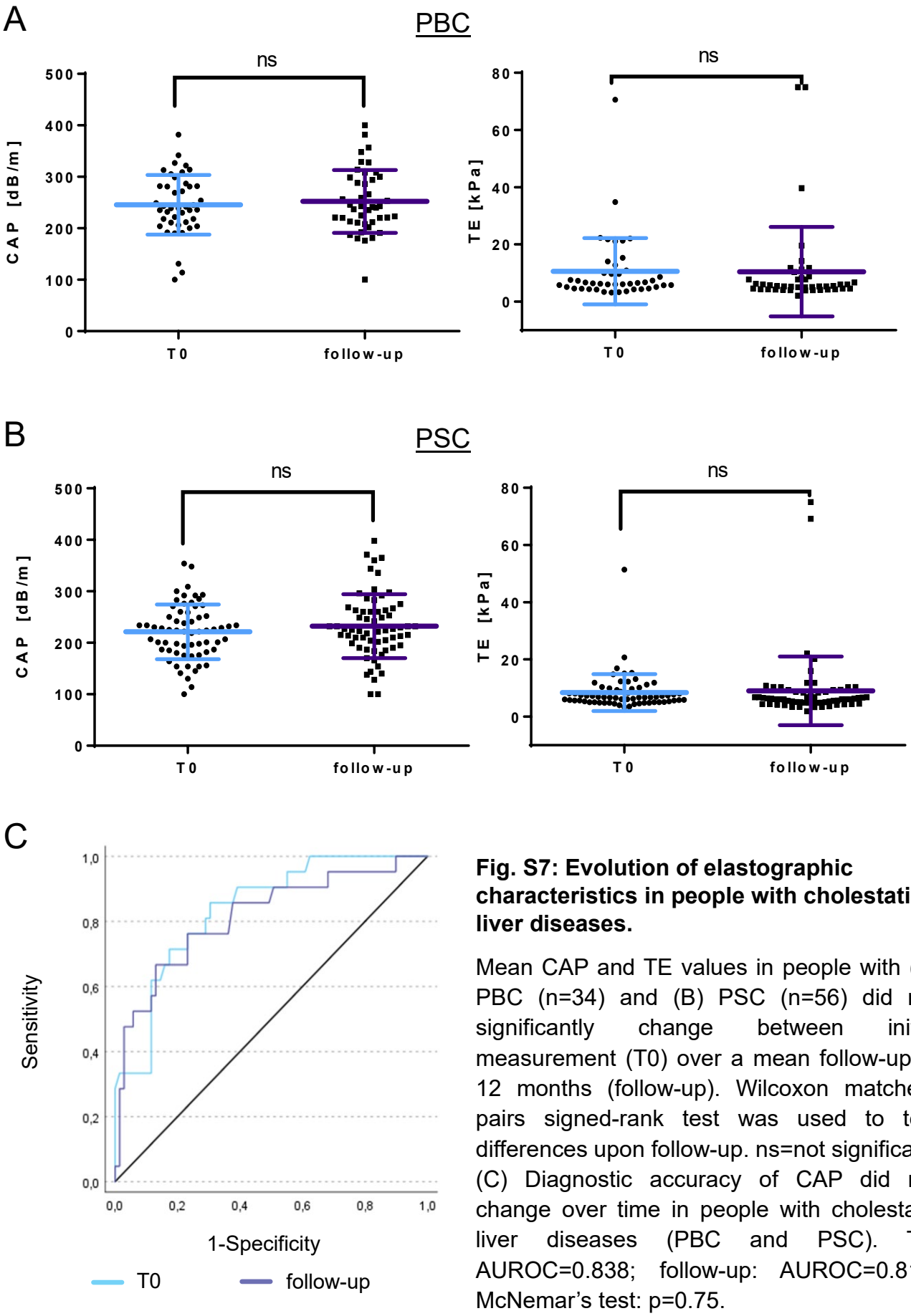

Fig. S7: Evolution of elastographic characteristics in people with cholestatic liver diseases.

Mean CAP and TE values in people with (A) PBC (n=34) and (B) PSC (n=56) did not significantly change between initial measurement (T0) over a mean follow-up of 12 months (follow-up). Wilcoxon matched-pairs signed-rank test was used to test differences upon follow-up. ns=not significant. (C) Diagnostic accuracy of CAP did not change over time in people with cholestatic liver diseases (PBC and PSC). T0: AUROC=0.838; follow-up: AUROC=0.814, McNemar's test: p=0.75.

Table S1: Elastographic characteristics of people with AILD who received a liver biopsy.

Value	**AIH**	**PBC**	**PSC**	**AIH/PBC**	**AIH/PSC**	**p=**
TE kPa	11.0 (3.1;75)	6.7 (3.2;75)	6.9 (3.3;67)	9.2 (3.8;75)	9.1 (4.5;48)	**<0.001**
IQR TE	1.5 (0;33)	1.0 (0;8.4)	1.1 (0;11.7)	1.4 (0.4;23)	1.2 (0.1;4.9)	**0.01**
CAP dB/m	229.6 (±64.2)	245.5 (±62.7)	212.3 (±56.2)	230.6 (±63.0)	205.2 (±62.8)	**0.03**
IQR CAP	39 (0;125)	37 (0;155)	40 (0;113)	38 (0;168)	53 (16;103)	0.87
CAPmedian/IQR	0.18 (0;0.7)	0.14 (0.02;0.52)	0.22 (0.12;0.73)	0.18 (0;0.53)	0.22 (0.07;0.74)	0.33

Data is presented as median (and minimum; maximum) or mean (± SD), as appropriate. Means of groups were compared using Kruskal-Wallis-test.

Table S2: Clinical and elastographic characteristics of people with AIH, PBC and PSC at first time of CAP-measurement (T0) and upon elastographic follow-up assessment.

	AIH (n=153)			PBC (n=34)			PSC (n=56)		
Value	T0	follow-up	p=	T0	follow-up	p=	T0	follow-up	p=
Time between measurements (months)	12 (1;24)			10 (3;22)			12 (1;22)		
BMI (kg/m²)	27.1 (15.8;46.5)	27.5 (16.4;50.9)	0.12	26.1 (18,8;46,5)	274 (18,3;42,5)	0.75	24.7 (17.3;33.9)	24.1 (17.3;32.8)	0.97
hemoglobin (g/dl)	13.6 (±1.5)	13.5 (±1.6)	0.24	13.4 (±1.1)	13.6 (±1.0)	0.38	13.9 (±1.4)	13.8 (±1.9)	0.99
platelets (10^9/l)	220 (±86)	223 (±81)	0.30	263 (±82)	261 (±95)	0.83	267 (±76)	250 (±80)	0.22
albumin (g/l)	36.7 (±4.7)	39.4 (±4.2)	**< 0.001**	38.1 (±3.8)	38.8 (±3.8)	0.20	38.5 (±4.4)	39.1 (±4.8)	0.32
bilirubin (mg/dl)	0.8 (0.2;14.6)	0.7 (0.2;4.4)	**< 0.001**	0.5 (0.2;2.2)	0.5 (0.2;4.6)	**0.06**	0.7 (0.2;6.4)	0.6 (0,2;7.3)	0.91
cholesterol (mg/dl)	197 (±52)	200 (±43)	0.20	207.6 (±53.5)	203.6 (±38.7)	0.12	204 (±58)	202 (±56)	0.63
triglycerides (mg/dl)	110 (44;552)	102 (33;749)	0.88	142 (50;617)	124 (56;728)	0.74	83 (41;694)	89 (47;536)	0.08
AST (U/l)	62 (14;1262)	30 (10;796)	**< 0.001**	41 (19;188)	27 (14;145)	**< 0.01**	38 (15;399)	27 (11;176)	**< 0.001**
ALT (U/l)	82 (15;2506)	30 (10;909)	**< 0.001**	62 (24;375)	32 (11;171)	**< 0.001**	64 (19;485)	32 (9;291)	**< 0.001**
GGT (U/l)	100 (15;1513)	34 (9;649)	**< 0.001**	110 (20;1334)	71 (11;1040)	**< 0.001**	265 (15;1931)	65 (9;956)	**< 0.001**
AP (U/l)	106 (35;986)	76 (23;419)	**< 0.001**	140 (53;630)	102 (50;586)	**< 0.001**	204 (58;708)	150 (53;712)	**< 0.001**
Gamma Globulin (%)	19.3 (9.7;41.6)	16.8 (8.0;33.4)	**< 0.001**	19.1 (±1.5)	18.3 (±4.7)	**0.03**	18.9 (±5.2)	17.4 (±3.7)	0.14
IgG (g/l)	15.3 (6.2;56.9)	12.1 (5.0;31.6)	**< 0.001**	14.6 (±4.2)	13.3 (±3.9)	**0.01**	14.1 (±4.4)	13.7 (±3.5)	0.33
IgA (g/l)	2.3 (0.1;25.2)	2.0 (0.1;11.4)	**< 0.001**	2.2 (±0.6)	2.1 (±0.7)	0.12	2.4 (±1.1)	2.4 (±1.2)	0.92
IgM (g/l)	1.2 (0.3;7.7)	1.1 (0.2;3.4)	**< 0.001**	1.8 (±0.3)	1.5 (±0.4)	**0.02**	1.3 (±0.9)	1.3 (±0.8)	0.82
Quick (%)	89 (±22)	93 (±24)	**< 0.001**	105 (±11)	105 (±16)	0.64	103 (±18)	100 (±16)	0.16
TE (kPa)	10.7 (3.2;75)	7.3 (3.3;37.2)	**< 0.001**	6.5 (3.2;70.6)	5.8 (3.9;75)	**0.04**	6.8 (3,3;51.4)	6.1 (3.3;75)	0.21
CAP (dB/m)	227 (100;400)	233 (100;398)	**0.04**	237 (114;382)	242 (172;400)	0.45	225 (114;354)	224 (100;398)	0.40

Continuous variables are presented as median (and minimum; maximum) or mean (±SD), as appropriate. Wilcoxon matched-pairs signed-rank test was used to test differences between T0 and follow-up.

Table S3: **Correlation analysis of evolution of CAP and changes of clinical markers.**

	All AILD		AIH		PBC		PSC	
Value	ρ	p	ρ	p	ρ	p	ρ	p
Δ BMI	0.179	0.007	ns		0.369	0.034	0.367	0.006
Δ Bilirubin	-0.226	0.001	-0.244	0.003	ns		-0.389	0.003
Δ AST	-0.187	0.004	-0.241	0.003	ns		ns	
Δ ALT	-0.213	0.001	-0.265	0.001	ns		ns	
Δ GGT	-0.231	<0.001	-0.354	<0.0001	ns		ns	
Δ Gamma globulin	-0.179	0.038	-0.235	0.028	ns		ns	

Changes of CAP in follow-up elastography assessment in people with AIH (n=153), PBC (n=43) and PSC (n=64) was expressed as delta (Δ) of CAP. Differences of clinical parameters between initial and follow-up CAP measurement were expressed as their delta value. Correlation between Δ CAP was estimated using the Spearman's ρ coefficient.

Table S4: Demographic and clinical characteristics of people with AIH at first time of CAP-measurement (T0) and upon CAP-measurement after CBR was achieved (follow-up).

Value	**T0** (n=62)	**follow-up** (n=62)	**p=**
Time between measurements (months)	12.5 (1;26)		
cirrhosis presence of	19.4 % (12)	19.4 % (12)	1.0
TE (kPa)	10.5 (3.2;42.9)	6.2 (2.8;27.0)	**<0.0001**
CAP (dB/m)	199.5 (100;321)	236.5 (113;373)	**<0.0001**
BMI (kg/m^2)	25.3 (15.8;38.3)	26.1 (±4.3)	0.93
hemoglobin (g/dl)	13.8 (±1.2)	13.6 (±1.6)	0.92
platelets (10^9/l)	214 (±68)	225 (±81)	0.42
albumin (g/l)	36.9 (±4.9)	41.0 (±3.8)	**<0.0001**
bilirubin (mg/dl)	1.1 (0.4;21)	0.6 (0.3;2.5)	**<0.001**
HbA1c (%)	5.3 (±0.6)	5.5 (±0.4)	0.1
cholesterol (mg/dl)	193.4 (±48.6)	208.0 (±42.9)	**<0.05**
triglycerides (mg/dl)	127.1 (±78.5)	119.4 (±62.3)	0.75
AST (U/l)	144 (40;1262)	24 (13;46)	**<0.0001**
ALT (U/l)	277 (60; 2506)	24 (10;48)	**<0.0001**
GGT (U/l)	190 (30;1213)	24 (9; 204)	**<0.0001**
AP (U/l)	126 (40;1513)	73 (32;275)	**<0.0001**
IgG (g/l)	15.9 (6.2;30)	10.6 (8.6;23.5)	**<0.0001**

Cirrhosis was determined based on histopathological findings. Nominal variables are presented as frequencies (and total numbers). Continuous variables are presented as median (and minimum; maximum) or mean (±SD), as appropriate. Wilcoxon matched-pairs signed-rank test was used to test differences between T0 and follow-up.