Table 13 Index tests (transient elastography and biopsy) for prognosis of CFLD and portal hypertension

Index Prognostic factors	Included studies	Study design	Setting	N	Adjusted OR/HRs	Quality	Notes
CFLD (includes cirrhosis)							
Liver stiffness measurement (kPa)	1 study (Kitson 2013)	Case control study	CF referral centre for adults	50	adjOR: 2.74 (95% CI 1.53-4.89, p=0.001)	LOW	Multiple logistic regression model of variables with p<0.05 on univariate analysis was performed to identify independent predictors of CFLD presence
Liver enzymes: AST ≥ 1.5 ULN	1 study (Woodruff 2017)	Prospective cohort	CF clinic in a children's hospital	278	aHR: 6.53 (2.02–21.1)	HIGH	Hazards Ratios for the presence of clinically diagnosed liver disease, adjusted for sex, CFTR

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					Follow-up median: 7.23 years		mutation severity, and the presence of meconium ileus.
Liver enzymes: AST ≥ 2 ULN	1 study (Woodruff 2017)	Prospective cohort	CF clinic in a children's hospital	278	adjHR: 6.52 (0.72–138.5) Follow-up median: 7.23 years	HIGH	Hazards Ratios for the presence of clinically diagnosed liver disease, adjusted for sex, CFTR mutation severity, and the presence of meconium ileus.
Liver enzymes: ALT ≥ 1.5 ULN	1 study (Woodruff 2017)	Prospective cohort	CF clinic in a children's hospital	278	adjHR: 1.95 (0.81–4.27) Follow-up median: 7.23 years	HIGH	Hazards Ratios for the presence of clinically diagnosed liver disease, adjusted for sex, CFTR mutation severity, and the presence of meconium ileus.
Liver enzymes: ALT ≥ 2 ULN	1 study (Woodruff 2017)	Prospective cohort	CF clinic in a children's hospital	278	adjHR: 1.88 (0.82–3.91) Follow-up median: 7.23 years	HIGH	Hazards Ratios for the presence of clinically diagnosed liver disease, adjusted for sex, CFTR mutation severity, and the presence of meconium ileus.
Liver enzymes: GGTP ≥ 1.5 ULN	1 study (Woodruff 2017)	Prospective cohort	CF clinic in a children's hospital	278	adjHR: 4.03 (1.15–13.45) Follow-up median: 7.23 years	HIGH	Hazards Ratios for the presence of clinically diagnosed liver disease, adjusted for sex, CFTR mutation severity, and the presence of meconium ileus.
Liver enzymes GGTP ≥ 2 ULN	1 study (Woodruff 2017)	Prospective cohort	CF clinic in a children's hospital	278	adjHR: 2.44 (0.86-6.13) Follow-up median: 7.23 years	HIGH	Hazards Ratios for the presence of clinically diagnosed liver disease, adjusted for sex, CFTR mutation severity, and the presence of meconium ileus.
Portal Hypertension							
Increasing fibrosis detected by biopsy	1 study (Lewindon 2011)	Cohort study	CF clinic in a city hospital	40	From birth adjHR: 3.9 (p<0.001, no 95% CI given)	HIGH	Fibrosis stages (Scheuer 2002): F0 no fibrosis; F1 mild fibrosis; F2 moderate fibrosis; F3 advanced fibrosis; F4 cirrhosis Multivariate analysis was adjusted for age, FEV at enrolment, URSO treatment, steatosis presence,

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							diabetes mellitus presence. A Cox proportional hazards model was used to determine factors independently associated with time to PHT development
Increasing fibrosis detected by biopsy	1 Lewindon 2011	Cohort study	CF clinic in a city hospital	40	From time of biopsy adjHR: 3.4 (p<0.002, no 95% CI given)	HIGH	Fibrosis stages (Scheuer 2002): F0 no fibrosis; F1 mild fibrosis; F2 moderate fibrosis; F3 advanced fibrosis; F4 cirrhosis Multivariate analysis was adjusted for age, FEV at enrolment, URSO treatment, steatosis presence, diabetes mellitus presence. A Cox proportional hazards model was used to determine factors independently associated with time to PHT development

Abbreviations: adjOR: adjusted odds ratio; CFLD: cystic fibrosis liver disease; CI: confidence interval; ALT: alanine aminotransferase; AST: aminotransferase; GGT: gamma glutamyltransferase