One Year Follow-up after Liver Transplantation in Children with Cystic Fibrosis

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Background: Although pulmonary insufficiency is the most common cause of death in patients with cystic fibrosis (CF), about 10% of CF patients develop affection of the liver[1] leading to biliary cirrhosis and portal hypertension and may require liver transplantation (LTx). Cystic fibrosis liver disease accounts for 2,7% of overall mortality in CF patients[2].

Methods: We report on 7 children with CF (median age 13.5 years, range 8-18 years, 3 female, 4 male) who underwent LTx (6 whole organs, 1 living donation) at University Hospital Essen from 2006 till 2017. Pre-, peri- and postoperative data were analyzed retrospectively with a follow-up period of 12 months.

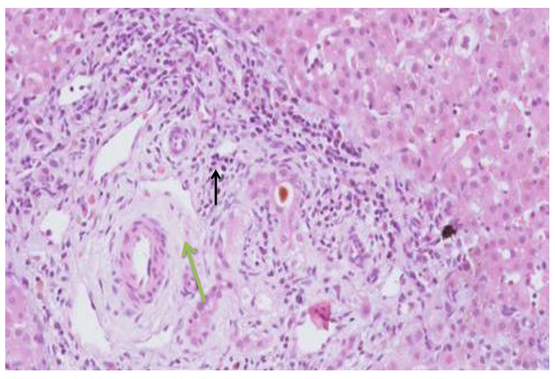


Figure 1: Histologic H&E stain of a liver previous to LTx showing biliary cirrhosis: portal inflammation (leukocite infiltration) ⟶ , portal fibrosis ⟶

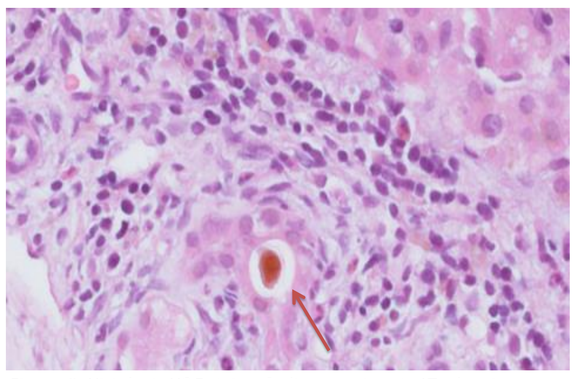


Figure 2: Histologic H&E stain of a liver previous to LTx showing biliary cirrhosis: bile duct with inspissated bile , bile cast ⟶

Genotype confirming CF	Number of Alleles Affected	Number of Patients (n/N)
F508del	homozygous	4/7
F508del and dele 2,3	compound heterozygous	2/7
deletion of exon 22 (reference sequence NM_000492.3)	homozygous	1/7

Table 1: Genetical genotype of the 7 patients confirming the diagnsosis of cystic fibrosis

Indication and Survival: Indications for LTX are shown in table 2.
3 operative revisions were required in 2 patients because of hematoma, leaking bile duct and donor bile duct obstruction.
Liver function normalized in all patients within the first 3 months. Patient and graft survival after 12 months was 100%.

Indications for LTx	Number of Patients (n/N)
Portal Hypertension:	
Splenomegaly	7/7
Bi-/or Pancytopenia	5/7
Esophageal varices > Grade 2	5/7
History of variceal bleeding	3/7
Reduced Liver Function	
Ascites	3/7
Increased prothrombin time	6/7
Reduced albumin level	2/7
Hyperammonemia	4/7
Encephalopathy	1/7
Other	
Dystrophy	5/7
Pancreatic insufficiency	7/7

Table 2: Distribution of Symptoms previous to LTx which lead to listing for LTx

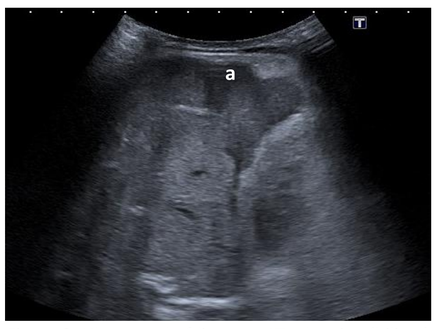


Figure 3: Ultrasound of liver pre LTx showing (biliary) cirrhosis: nodular surface (a), heterogenous echo-texture, rarefied liver veins

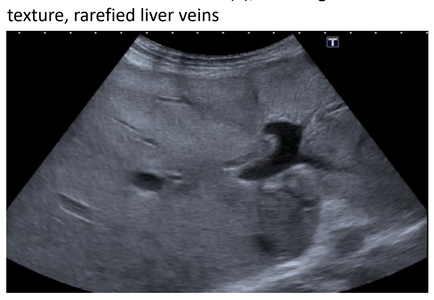
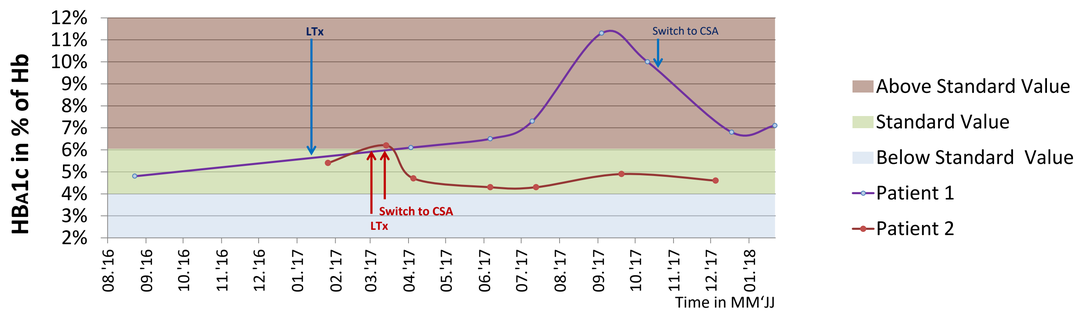


Figure 4: Ultrasound of liver after LTx, parenchyma is homogenous

Comorbidities: Insulin dependent diabetes and antihypertensive drug therapy were documented in 2 and 3 patients respectively. Elevated HbA1c-levels dropped after switching immunosuppressive therapy from Tacrolimus (standard treatment) to Cyclosporin A in 2 patients (see graph 1).



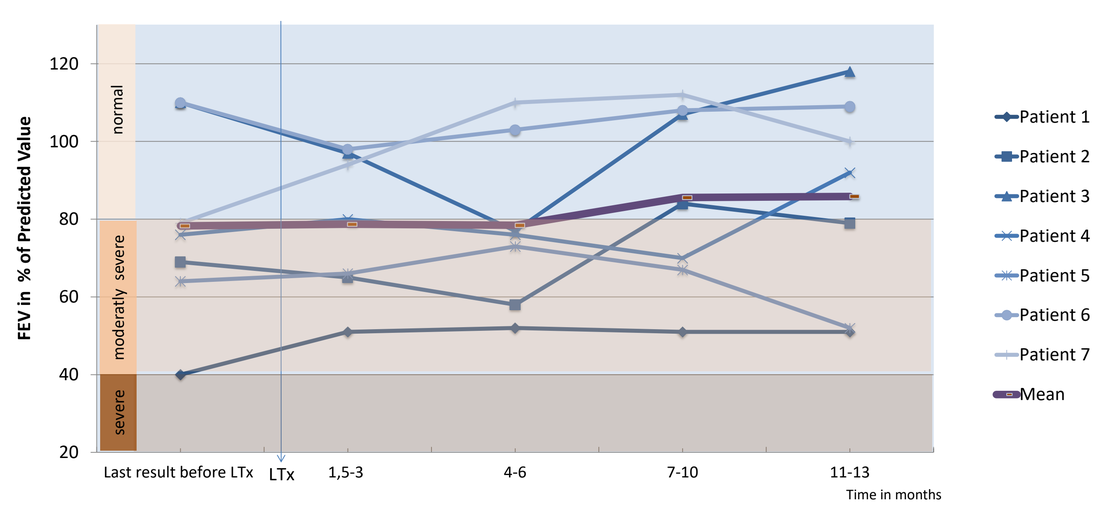
Graph 1: HbA1c Values after LTx in 2 patients were immunosuppressive therapy was switched from Tacrolimus to Cyclosporin A (CSA)

References: [1]Rowland, Marion; Bourke, Billy (2011): Liver disease in cystic fibrosis. In: *Current opinion in pulmonary medicine* 17 (6), S. 461–466. DOI: 10.1097/MCP.0b013e32834b7f51. [2]Marshall, Bruce; Faro, Al; Elbert, Alexander; Fink, Aliza; Sewall, Ase; Loeffler, Deena et al.: 2016 Annual Data Report. Hg. v. Maryland Bethesda. Cystic Fibrosis Foundation Patient Registry 2016.

Pulmonary Outcome: Postoperative pulmonary infection occurred in 2 patients. Preoperative colonisation with pseudomonas aeruginosa, aspergillus fumigatus and stenotrophomonas maltophilia was present in both patients (see table 3)
Pre LTx lung function was formally normal in 2 patients. 5 patients showed an obstructive lung disease with reduced Forced Expiratory Volume in 1 Second (FEV1). Lung function was preserved or improved within 12 months after transplantation in all patients (see graph 2).

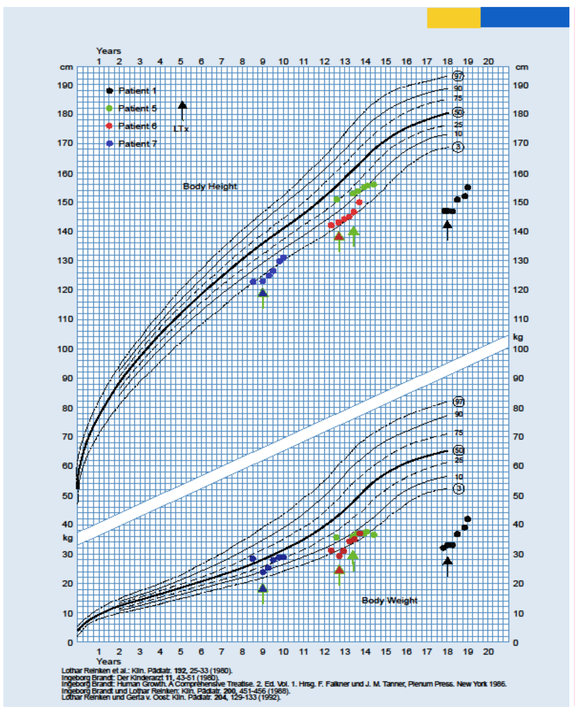
	Pathogens Detected in Throat Swab or Sputum pre LTx	FEV1 pre LTx	Postoperative Pneumonia
Patient 1	Alcaligenes Xylosoxydans, Pseudomonas Aeruginosa, Candida Albicans, Aspergillus species	40%	Pneumonia 5 days after operation, Chest X-Ray: bilateral multifocal consolidations
Patient 2	Achromobacter Xylosoxidans, Candida Albicans,	67%	no
Patient 3	none	109%	no
Patient 4	Candida Glabrata, Bacillus Cereus Bacillus Megaterium, Aspergillus fumigatus, Raoultella planticola, Stenotrophomonas maltophilia	76%	Alveolar hemorrhage 3 days after LTx, Reintubation, Chest X-Ray: bilateral diffuse consolidations
Patient 5	Stphylococcus aureus	64%	no
Patient 6	Staphylococcus auerus, Candida albicans, Haemophilus species,	108%	no
Patient 7	Candida Albicans	78%	no

Table 3: Patients who developed postoperative pneumonia in relation to pre LTx detected colonisation and pre LTx lung function

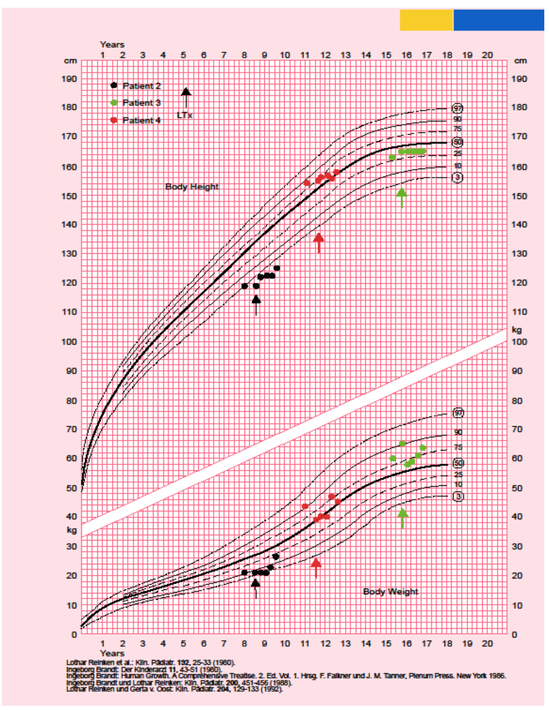


Graph 2: Lung function as Forced Expiratory Volume in 1 Second (FEV 1) as % of the predicted value before and after LTx

Thriving: Failure to thrive improved in all patients with dystrophy (5/7) after LTx.



Graph 3: Growth and Weight Curve as Percentiles
(Boys Age 0-18 years)



Graph 4: Growth and Weight Curve as Percentiles
(Girls Age 0-18 years)

Conclusion: Children with cystic fibrosis requiring liver transplantation had a good overall and a good graft one year survival. Pulmonary function was preserved or even improved and patients showed better thriving.