Primary Sclerosing Cholangitis in Pediatrics

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PSC in Children - Definition

- Chronic liver disease of unknown etiology
- Probable autoimmune process
- Irregular damage and scarring of extrahepatic and medium to large intrahepatic bile ducts
- Progresses to biliary cirrhosis

Differences: Children vs. Adults

- Cause
- Age and Course
- Auto-antibodies
- Response to immunologic suppression therapy

Causes of Sclerosing Cholangitis in Children

- Immune deficiencies
- Cystic Fibrosis
- Infections of bile ducts
- Autoimmune
  - 30-50%
- Primary SC

} Associated with Ulcerative colitis or Crohn's disease = 50-80%

Clinical Differences Child vs. Adult

- Incidence
  - < 18 years old .23 per 100,000
  - Adults 1.11 per 100,000

- Males = Females in young children
- Females > Males in teens
- Males > Females in adults

Symptoms of PSC in Children

- Initial Symptoms
  - Fatigue, poor appetite, nausea, weight loss, itching
  - Delayed puberty
  - Jaundice is rare
  - No symptoms – elevated liver blood tests found on testing
    - Ulcerative colitis and Crohn's diease
  - Large liver or spleen on exam
  - Gastrointestinal bleeding

Diagnosis

- Blood tests suggestive (elevated GGT)
- Imaging of bile ducts
  - Ultrasound
  - CT scan
  - Magnetic resonance chlangiography (MRCP)
  - Endoscopic retrograde cholangiography (ERCP)
- Liver biopsy
  - look for damage to bile ducts
  - how much scarring is present?
  - exclude other liver diseases

Autoimmune SC (overlap) – common in children

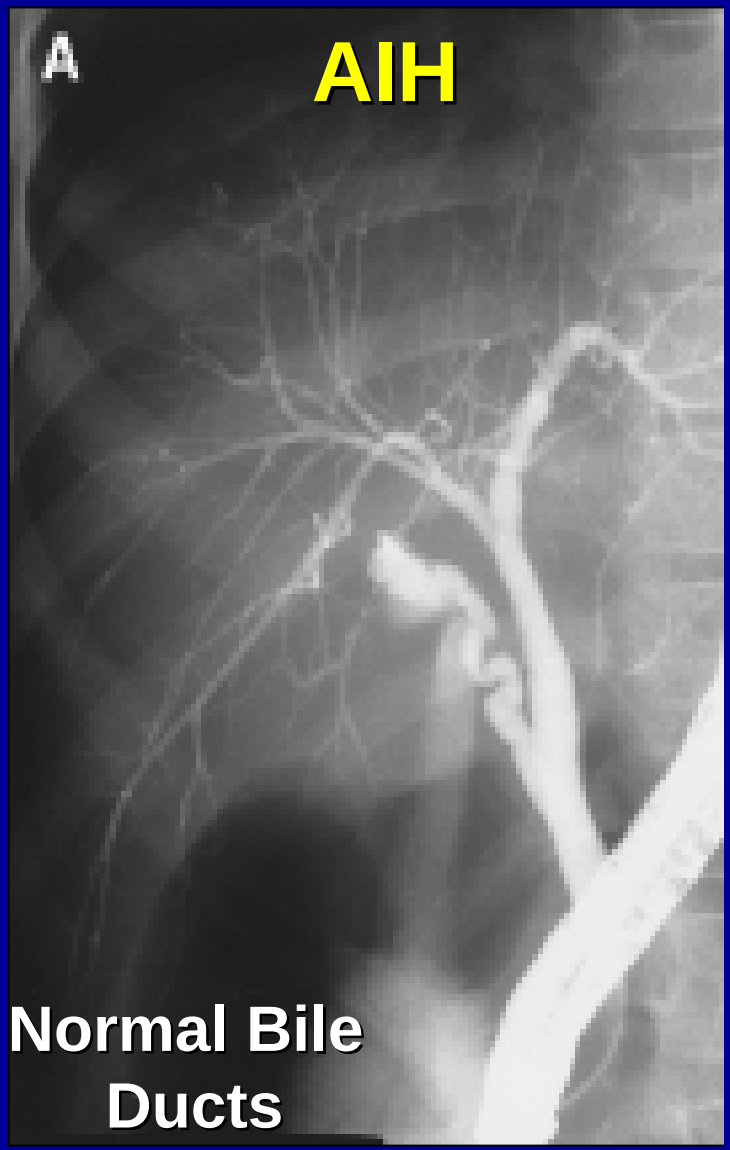
- **Autoimmune Hepatitis (AIH)**
  - chronic liver disease
  - NO bile duct injury!!!
  - elevated IgG
  - presence of autoantibodies in blood
  - characteristic appearance to liver biopsy
  - teen age girls – most common
  - associated with other autoimmune diseases (40%) such as IBD
  - felt to be a true autoimmune disease

Autoimmune SC (overlap)

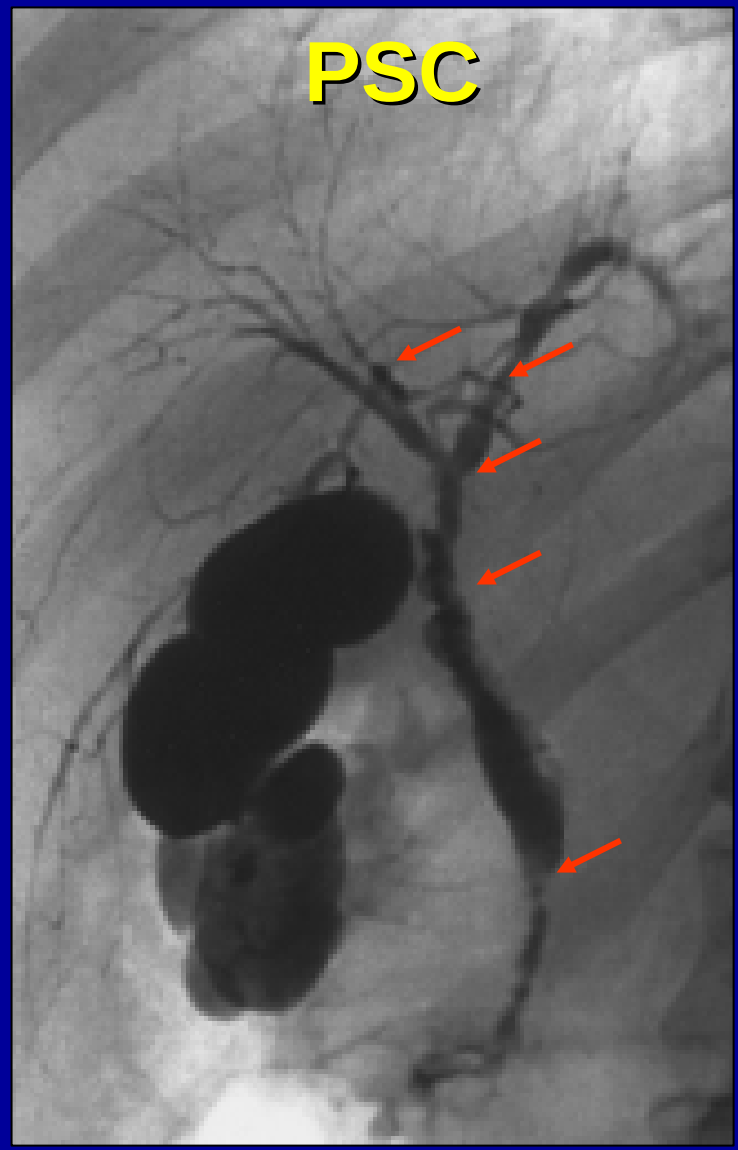
- **ASC/overlap**
  - About one third or more of PSC children present with picture of AIH (vs. 10% of adults)
  - elevated IgG
  - liver biopsy - AIH
  - auto antibodies present

    ANA, anti-smooth muscle antibody, p-ANCA, rarely anti-LKM
  - Eventually, evidence of bile duct injury and strictures present on MRCP or ERCP

Teen with ulcerative colitis



8 Years



Autoimmune SC (overlap)

- Treatment Response of ASC
  - Steroids and Imuran: 70-90% normalized Liver Blood Tests
  - Progression of bile duct injury can still happen in many

Treatment

- If ASC/AIH overlap
  - Treat for AIH component (not done in adults)
  - Corticosteroids and Imuran (azathioprine)
  - If normal blood tests for 1-2 years, attempt to wean off therapy if liver biopsy is normal
- Ursodeoxycholic acid: 10-20 mg/kg/day
  - no proof of long-term benefit, but improves liver blood tests and some symptoms

Treatment

- Fatigue
  - Exclude low thyroid or adrenal gland function, or other autoimmune disease
  - Exclude anemia
  - Daytime somnolence
  - Did not work: fluoxetine, ondansetron
- Itching
  - Urso, rifampicin, cholestyramine, others
  - Exclude bile duct stricture that needs to be dilated
- ? Use of probiotics, Remicaide, others

Treatment

- Complications of PSC
  - strictures
  - cholangitis
- Complications of Cirrhosis
  - Varices
  - Ascites
  - Fatigue
  - Others
- Bile Duct cancer extremely rare in children
- Liver Transplantation

Liver Transplant

- Ultimate treatment for majority, if not all, children with PSC
- Outcome very good
  - SPLIT data under evaluation
- Surveillance for Colitis and its complications post-liver transplant
- Recurrent disease a concern, as in adults

Survival in Children with PSC

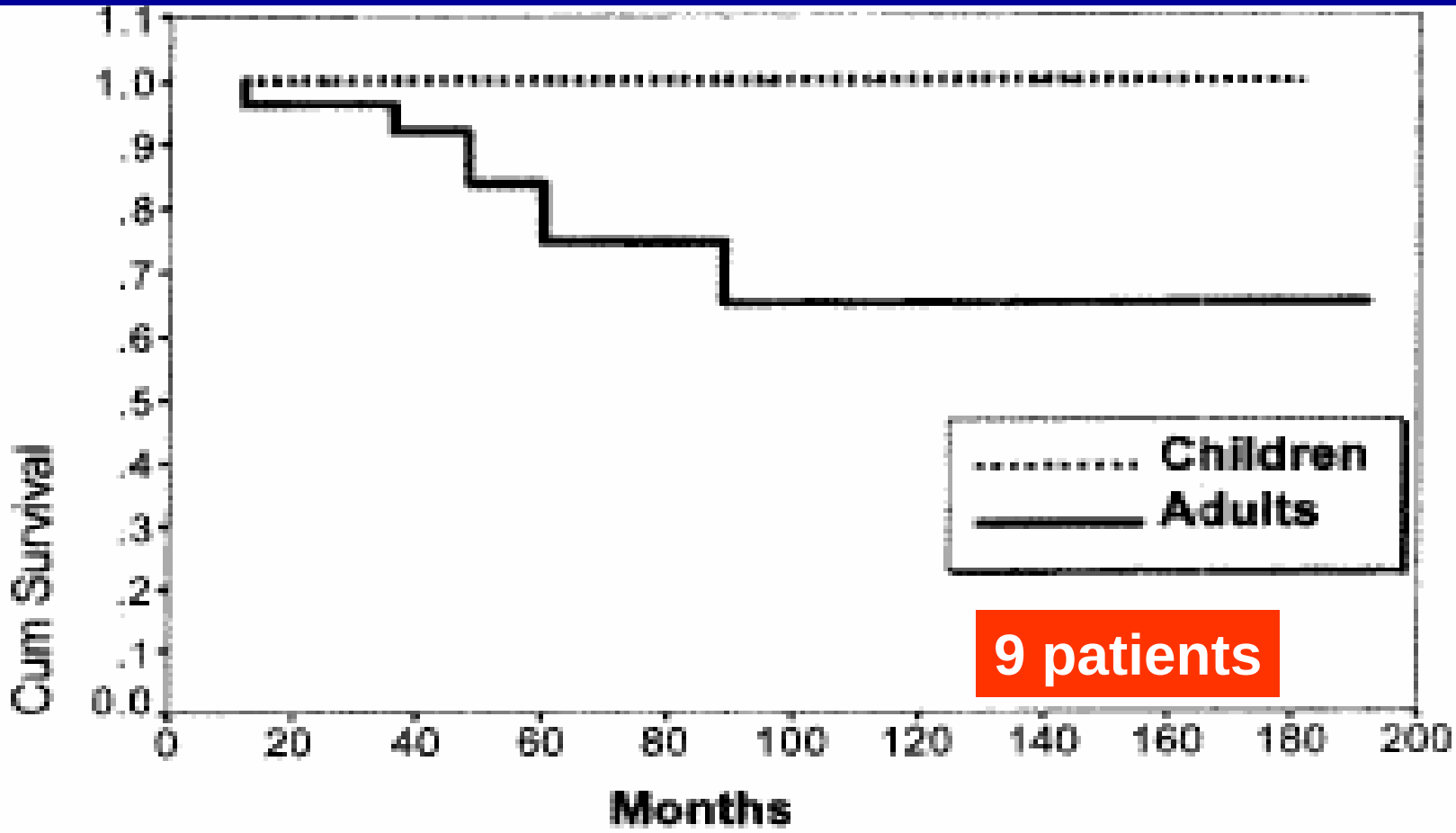


Fig. 2. Survival analysis.

Liver 1999;19:228

Survival – Mayo Series

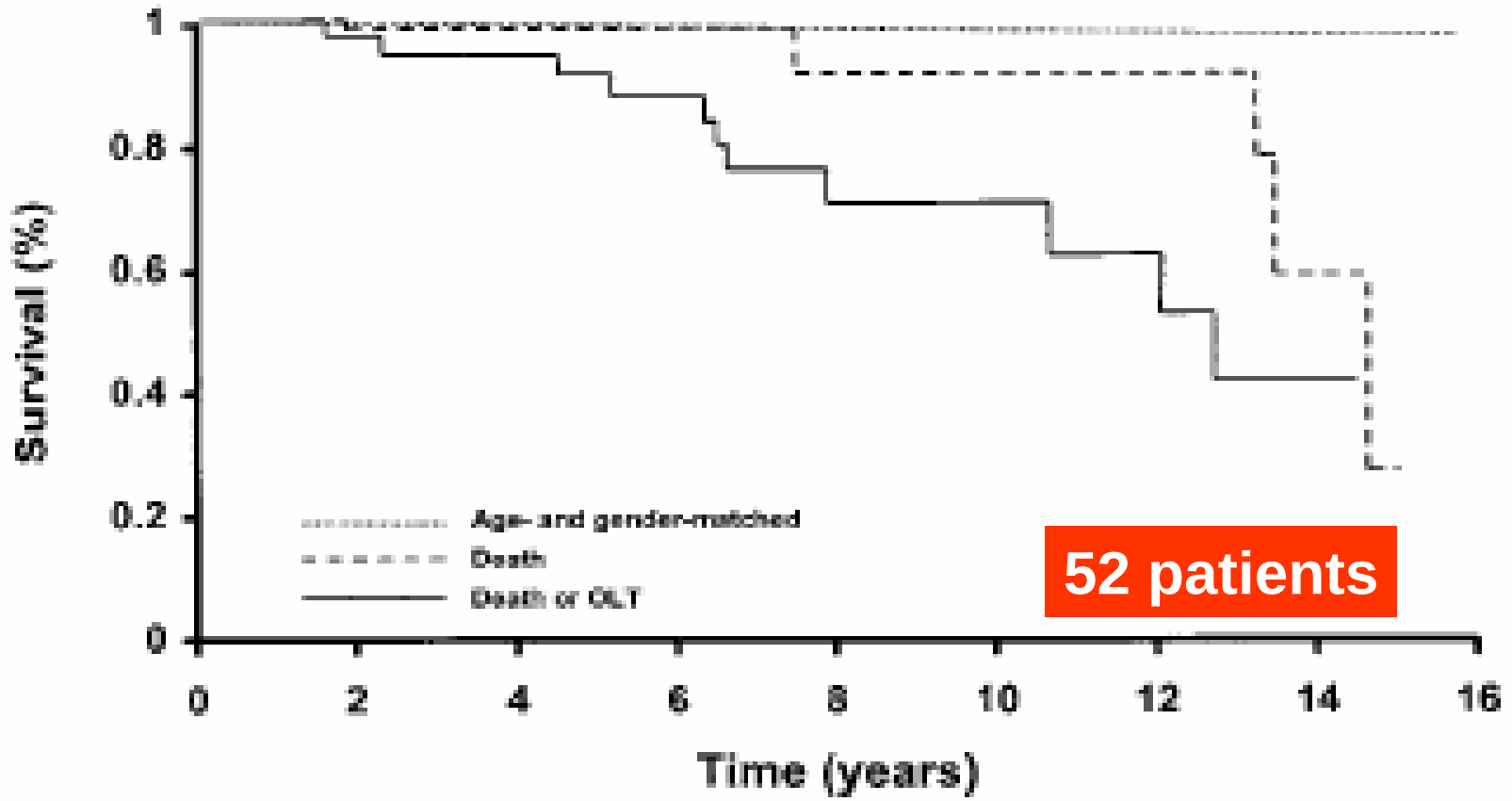


Fig. 1. Actual survival of children with PSC and the expected survival for a cohort of a U.S. Caucasian population matched by age and sex and

Hepatology 2003;38:210

Survival - PSC vs. ASC

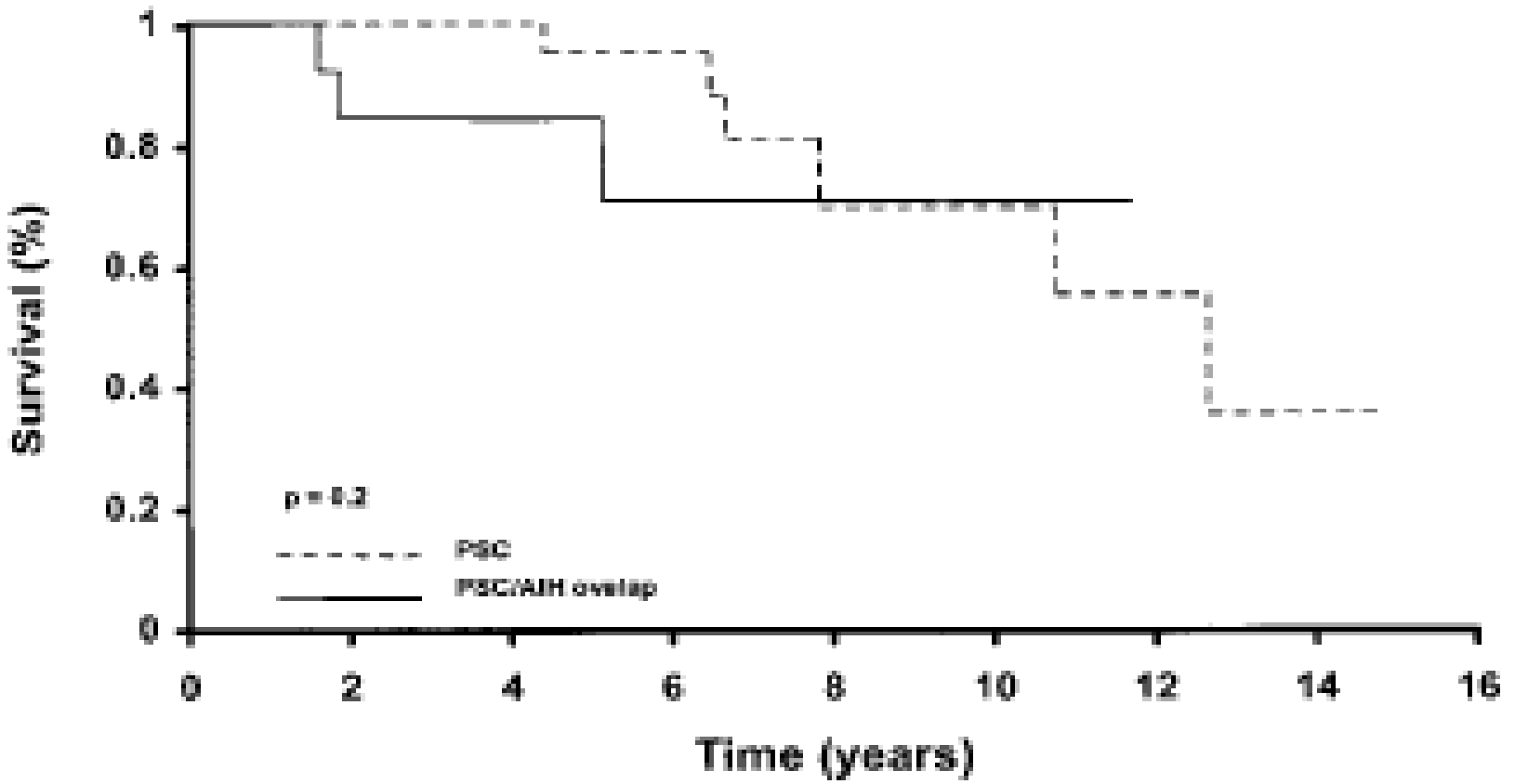


Fig. 3. Actual survival free of liver transplantation in children with PSC alone (**dashed line**) and those with PSC/AIH overlap (**solid line**). $P = .2$.

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Survival – Effect of Treatment

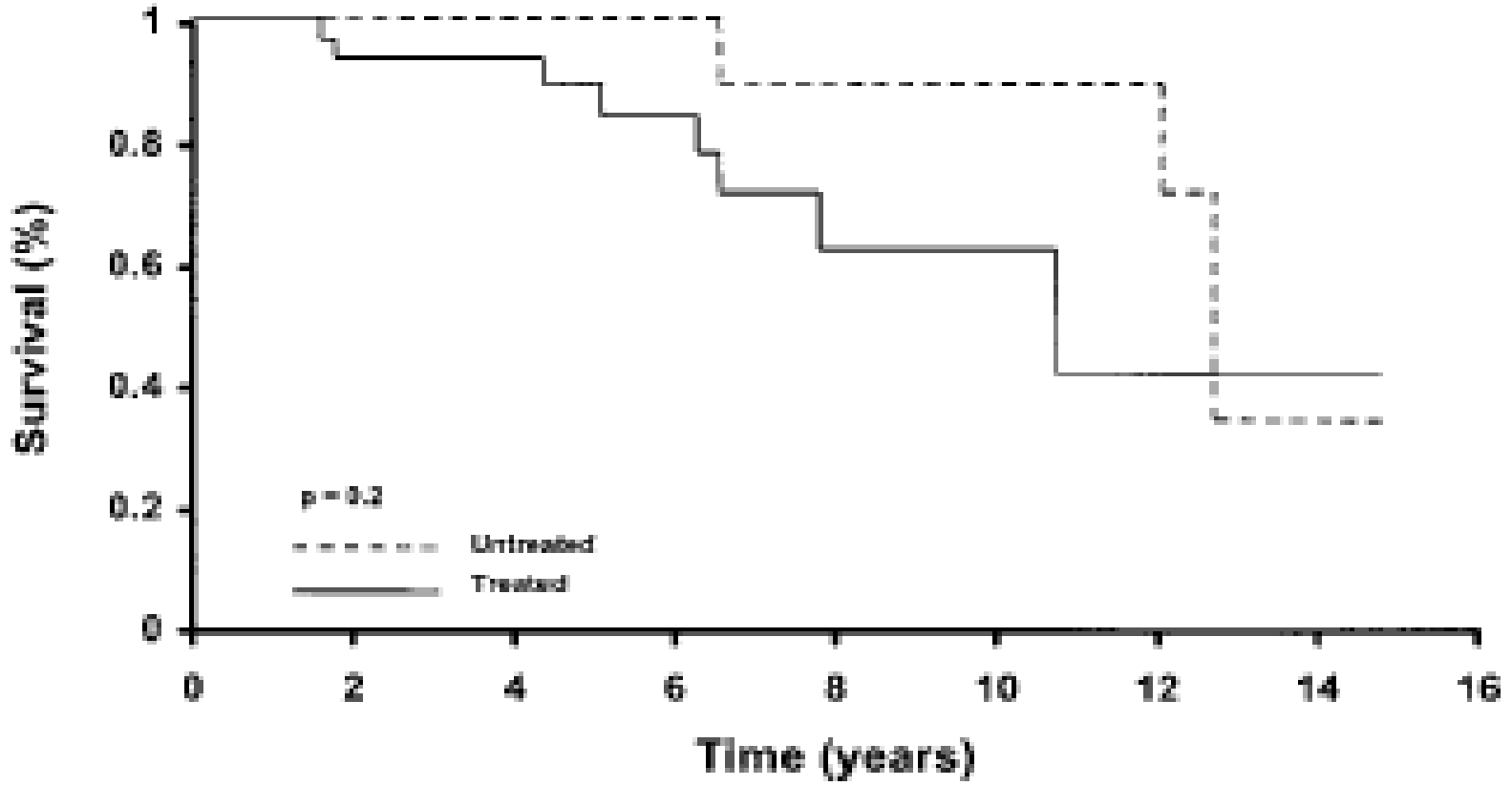

Fig. 2. Actual survival free of liver transplantation in treated (**solid line**) and untreated (**dashed line**) children with PSC. $P = .2$.

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Bottom Line

- PSC is a Rare Disease in children
- No controlled clinical trials yet performed
- Need multi-center collaboration to learn more about cause, ASC overlap, why disease progresses, test treatments
- STOPSC study is now attempting to do this