Paediatric liver transplantation: an overview

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Abstract

The only definitive treatment for end stage liver disease is transplantation. This has been made possible by advances in vascular surgery and immunosuppression. In the paediatric population, liver transplantation is most commonly performed for liver failure secondary to biliary atresia. Successful transplantation depends on patient preparation by a dedicated multidisciplinary team and meticulous peri-operative care. Improvements in timing of transplantation, immunosuppression advances and peri-operative intensive care have all contributed to improvements in patient survival. Currently the survival rates for children undergoing deceased donor liver transplant in the UK is 95.7% at 1 year and 91.8% at 5 years. These outcomes are reliant on multi-disciplinary care, which is best provided in centres that provide the expertise in each of the specialist fields required to care for these children. This article provides an overview of the entire process. It describes the selection process, the surgery undertaken and early and late post-operative complications.

Keywords Immunosuppression; liver transplantation; organ donation; transplant assessment

Introduction

Liver transplantation is a treatment still in its nascence but remains the only definitive treatment for liver failure. Its success is due not only to the development of technical expertise but also the evolution of effective immunosuppression.

The first liver transplant was completed in 1963 by Dr Thomas Starzl but despite technical success, the first five patients died, the first from bleeding and the others due to sepsis. A self-imposed moratorium ensued whilst he continued work on immunosuppression. The first successful liver transplant was performed in July 1967 using azathioprine and prednisolone as immunosuppressive agents. The 1 year survival rate more than doubled followed the introduction of Ciclosporin thanks to the work of Professor Sir Roy Calne in 1978. A further evolution in immunosuppression followed in Tacrolimus, a drug that is synthesised by the bacteria *Streptomyces tsukubaensis* and first discovered in 1987, equally efficacious but with the absence of cosmetic side-effects and is steroid sparing.

Indications for liver transplantation

The commonest underlying diagnosis leading to paediatric liver transplantation is biliary atresia followed by inborn errors of metabolism and malignant tumours (Figure 1).

NHS Blood and Transplant provides guidance on the conditions that can be considered for liver transplant in children in the UK (Table 1).

Chronic liver failure

The majority of children undergoing liver transplantation will do so for chronic disease. The timing of transplant assessment is crucial. Many children with liver cirrhosis and portal hypertension can have compensated liver disease. However, signs of decompensating disease include deteriorating synthetic function, coagulopathy, variceal bleeding, ascites, faltering growth, increasing fatigue and learning difficulties.

Earlier referral ensures the patient is fit for surgery, allows time to prepare for surgery e.g. optimisation of nutritional status and has been shown to improve transplant outcomes. Assessment and counselling is performed by an experienced multidisciplinary team comprising of hepatologists, transplant surgeons, transplant co-ordinators, anaesthetists, specialist nurses, family support worker, physiotherapist, intensivist and psychologist. Depending on clinical condition, the team may be extended to include other subspecialists.

Clinical investigations include liver function tests including clotting screen, blood group, endoscopy, liver biopsy, viral serology to assess both infection status and efficacy of immunisations, echocardiogram and ECG, creatinine clearance and anthropometry. The team meets at the end of assessment to decide if the patient is a candidate for transplantation with consideration to three things.

- Transplantation will improve the patient's survival.
- Following transplantation the patient should have an expected 5-year survival of more than 50%
- The patient's quality of life may be currently unacceptable due to the underlying condition and that this would be improved by transplantation.

Contraindications to paediatric liver transplant include:

- Active sepsis
- Active extra-hepatic malignancy
- Severe cardiopulmonary or other co-morbid conditions compromising survival
- Likely non-compliance that would not respond to suitable support
- Technical reason precluding transplantation

Following assessment, the patient could be accepted for transplantation, declined for transplantation (on the grounds of one or more of the above contraindications) or considered for reassessment at a later date.

If accepted for transplantation, all live vaccines must be given prior to activation on the list to reduce post-immunosuppression infection.

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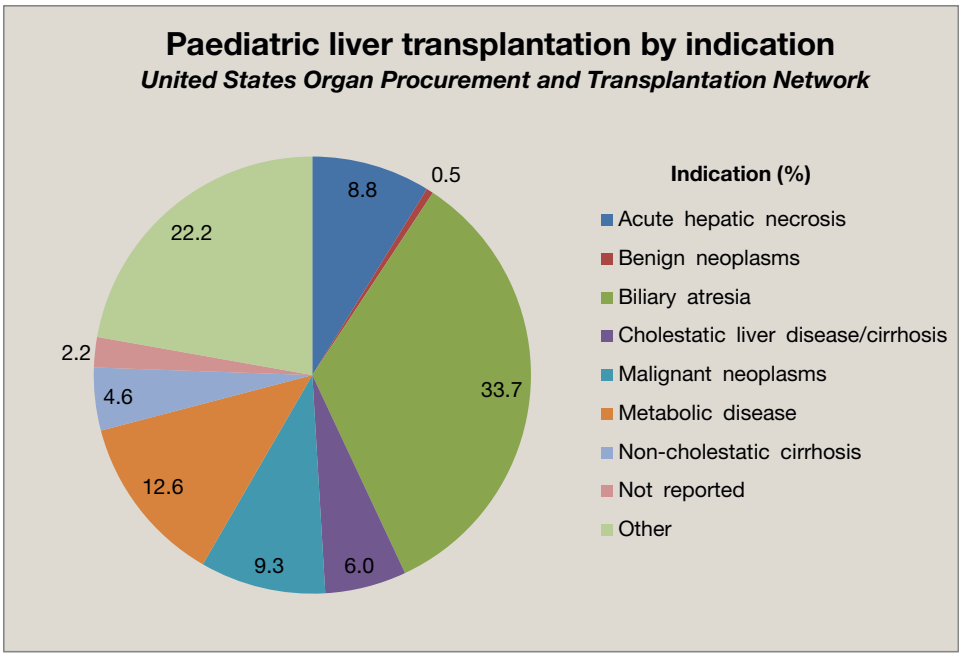

Figure 1 Indications for paediatric liver transplant in the USA 2015–2016.

Indications for liver transplantation in children

Indications for liver transplantation in children (NHS Organ Donation and Transplantation, Liver Transplantation: Selection Criteria and Recipient Registration):

- Acute liver failure
- Chronic liver disease
  - Biliary atresia
  - α-1-antitrypsin deficiency
  - Autoimmune hepatitis
  - Sclerosing cholangitis
  - Caroli's syndrome
  - Wilson's disease
  - Cystic fibrosis
  - Progressive familial intrahepatic cholestasis (all types)
  - Alagille syndrome
  - Glycogen storage disease types 3 and 4
  - Tyrosinaemia type 1
  - Graft versus host disease
  - Budd–Chiari syndrome
  - Any aetiology leading to hepatopulmonary syndrome or portopulmonary hypertension
- Liver tumours
  - Unresectable hepatoblastoma without extrahepatic spread
  - Uresectable benign tumours with disabling symptoms
- Metabolic liver disease
  - Crigler–Najjar syndrome
  - Urea cycle defects
  - Hypercholesterolaemia
  - Organic acidaemias
  - Primary hyperoxaluria
  - Glycogen storage disease type 1
  - Inherited disorders of complement causing atypical haemolytic uraemic syndrome

Table 1

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