Transplant International

Transplant International ISSN 0934-0874

CASE REPORT

Safe use of segmental liver grafts from donors after cardiac death (DCD) in children with acute liver failure

M. Thamara P. R. Perera, Sara Gozzini, David Mayer, Khalid Sharif, James Bennett, Paolo Muiesan and Darius F. Mirza

The Liver Unit, Birmingham Children's Hospital, Birmingham, UK

Keywords
acute liver failure, donation after cardiac death, reduced-liver transplantation.

Correspondence
Darius F. Mirza, Consultant Surgeon, Nuffield House 3rd Floor, Queen Elizabeth Hospital, University Hospital Birmingham NHS Trust, Edgbaston, Birmingham B15 2TH, UK.
Tel.: 0121 6272418; fax: 0121 4141833;
e-mail: darius.mirza@uhb.nhs.uk

Received: 9 February 2009
Revision requested: 6 March 2009
Accepted: 4 April 2009

doi:10.1111/j.1432-2277.2009.00886.x

Summary

Emergency liver transplantation is a life-saving procedure in selected subset of children with acute liver failure (ALF), when most recipients receive a segmental graft from a living or heart-beating deceased donor. The increased use of full-liver grafts from donors after cardiac death (DCD) has had a beneficial impact on elective liver transplantation in adults. These grafts however are more susceptible to poor initial function, and most centres are reluctant to consider their use as segmental grafts, let alone in the situation of ALF where good initial function is imperative. In this short article, we describe the use and successful outcome in two children aged 6 weeks and 6 years with acute liver failure who received reduced-size DCD liver grafts.

Introduction

Acute liver failure (ALF) in children caused by metabolic, infective, autoimmune, drug-induced or unknown reasons is rare and is usually associated with an adverse outcome without transplantation. Emergency liver transplantation in these children is associated with a good outcome in up to 80% [1,2]. Unfortunately around 14–20% of children with ALF die after being listed, mainly because of the lack of availability of cadaver donor organs [1]. Most children undergoing successful transplantation receive segmental grafts using techniques of split-liver transplantation (SLT), live donor liver transplantation (LDLT) or reduced-size liver transplantation (RLT) [3].

The recent resurgence of donation after cardiac death (DCD) with good graft outcomes has provided a viable option to increase the donor pool [4–6]. These DCD livers however are still considered 'marginal', because of the associated higher risk of impaired initial graft function, primary nonfunction, ischaemic type biliary lesions (ITBL) and rejection [7,8].These grafts are therefore believed to be unsuitable for transplantation into high-risk ALF patients [6]. Their use in elective recipients has been shown to have long-term results comparable to deceased or live related liver transplantation, provided care is taken with the donor and recipient selection [9]. Surgical reduction of DCD liver graft potentially further compromises an already marginal graft with the additional cold ischaemia and benching procedure. There is limited data in the literature on the use of DCD reduced-liver grafts in children, and their use as grafts for paediatric ALF has not been described [10,11]. Herein, we report our experience of two children with ALF who were successfully transplanted with reduced ('cutdown') DCD liver grafts.

Case report 1

A 10-week-old female term infant (blood group B +ve) weighing 2.6 kg presented with ALF secondary to giant cell hepatitis. Her condition deteriorated with the development of progressive coagulopathy, encephalopathy and

she was listed for after satisfying criteria for 'super-urgent' transplantation (On admission biochemistry: INR – 2.2, Bilirubin – 476 mmol/l, ALT – 136 IU/l, AST 661 IU/l, gamma GT 64 IU/l, ALP 1261 IU/l). An EEG was compatible with hepatic encephalopathy. In view of her small size, an upper limit of 50 kg donor weight was set and she waited 22 days before receiving an offer from a 35 kg 14-year-old DCD donor with meningitis (blood group O +ve). A decision was made to accept this category III donor offer in view of clinical deterioration and lack of other offers. Recipient biochemical results at the time of transplant were; AST 348 IU/l, ALT 69 IU/l, ALP – 701 IU/l, gamma GT 47 IU/l Bilirubin 382 mmol, Na^+ 139 mmol/l, K^+ 3.6 mmol/l, Hb% 9.3 g, WBC 3.6×10^3, Platelets 75×10^3 and INR 1.5 [supported with fresh-frozen plasma (FFP)]. The donor: recipient weight ratio (DRWR) was 13.5. The donor liver was reduced to obtain a graft containing segments II and an atrophic segment III with a weight of 68 g, and the graft weight:recipient weight (GWRW) ratio was 2.42%. Venous outflow was achieved with a donor left hepatic vein to a triangulated recipient hepatic vein trifurcation (Brisbane method) [12] and portal vein reconstruction involved the donor left portal vein to recipient main portal vein bifurcation. A donor iliac artery conduit from the recipient infra-renal aorta was used as the arterial reconstruction. Biliary reconstruction was done with a Roux loop hepaticojejunostomy. The cold ischaemic time (CIT) was 8 h and 29 min, while the graft warm ischaemia and the implantation times were 22 and 50 min respectively. The intraoperative transfusion requirements were: 320 cc packed red cells, and 760 cc FFP and 100 cc platelets and 300 cc colloids. The early postoperative course was associated with renal dysfunction and fluid overload requiring temporary renal support. Her subsequent course was uneventful, she was discharged on tacrolimus, mycophenelate and prednisolone-based immunosuppression at 33 days. Follow up biochemistry at 6 months was; AST 159 IU/l, ALT 229 IU/l, ALP – 701 IU/l, Bilirubin 13 mmol and gamma GT 455 IU/l. An ultrasound scan showed patent graft vessels and a nondilated biliary system. The most recent liver biopsy ruled out rejection, but showed mild cholestasis.

Case report 2

A 6-year-old girl (weight 15.4 kg, blood group O +ve) diagnosed with primary familial intra-hepatic cholestasis (PFIC) was admitted with sudden-onset acute-on-chronic hepatic failure. On presentation, she was encephalopathic and her serum biochemistry was as follows: AST 454 IU/l, ALT 42 IU/l, ALP – 103 IU/l, Bilirubin 856 mmol/l, Na^+ 130 mmol/l, K^+ 5.2 mmol/l, Hb% 6.2 g, WBC 16.5×10^3, Platelets 155×10^3 and INR of 3.6. She was listed for a 'super-urgent' transplantation and was offered and received a reduced left hemiliver from a 20-year-old deceased donor; blood group O +ve; category III DCD donor; weight 75 kg; cause of death of the donor – trauma; with DRWR of 4.87. The liver was reduced to a graft containing segments II, III and IV. The graft weighed 645 g and the GWRW was 4.18%. The cold ischaemia time was 9 h and 34 min and the graft warm ischaemia and the implantation times were 25 and 36 min respectively. Venous and biliary reconstruction was similar to case 01, and arterial reconstruction was via a direct hepatic artery to hepatic artery anastomosis. Post operatively she developed two episodes of early acute rejection confirmed by biopsy and successfully treated with pulsed steroids. The remainder of her post operative recovery was uneventful and maintained on tacrolimus based immunosuppression. At 3-year post-transplantation, she remains clinically well, although her liver enzymes are elevated (AST 138 IU/l, ALT 213 IU/l, ALP – 1014 IU/l, Bilirubin 8 mmol/l, gamma GT 75 IU/l) with normal appearance of the graft on ultrasonography. A recent liver biopsy has ruled out rejection and shows features of cholestasis, and the deranged liver function has been attributed to mild intra-hepatic biliary fibrosis. Magnetic resonance cholangiography showed minimal segmental intra-hepatic biliary dilatation suggestive of early multiple intra-hepatic strictures.

Discussion

The frequency of DCD transplants has increased over the past several years and account for nearly 14% of all transplants in the United Kingdom at present, with an increase of 94% over the last year [13]. Graft and patient survival figures following LT from controlled DCD in larger series approached 80% at 1 year, which is not different to deceased heart-beating donor transplantation [14]. These outcomes and organ shortage have led to expansion of the recipient pool, with DCD transplantation being considered in patients who were previously considered less suitable to receive such grafts. Sometimes DCD may be the only option for a patient who is severely ill; waiting for an ideal graft may result in irreversible brain injury, multi-organ failure and mortality in patients with ALF.

The increased susceptibility of DCD organs to primary nonfunction and initial poor function is attributed to the initial warm ischaemia incurred by hypotension and subsequent circulatory arrest followed by obligatory stand-off time and vascular congestion [6,15]. Improved graft and patient survival is reported when the warm ischaemia time is below 30 min [16]. Moreover, prolongation of the cold ischaemia time has been shown to increase this ischaemic

injury [17]. This affects early graft function, and graft failure rates have been reported to increase by approximately threefold when the cold ischaemia time exceeds 8 h [14]. Reduction of a DCD liver graft to the appropriate size further lengthens cold ischaemia time, and as a result both our grafts were implanted with a CIT > 8 h.

The reported successes of DCD transplantation have in part relied on careful patient selection. The overall results after DCD transplantation have historically been inferior when the recipients are more ill, resulting in higher operative mortality and graft failure rates. There is clearly an additional risk in performing a LT using a graft from DCD donor in a child with acute liver failure, adding additional challenges to the management of encephalopathy, sepsis, coagulopathy and renal impairment associated with ALF. However, a major concern in DCD transplantation is the long-term biliary complications and in particular ITBL, with a reported incidence of up to 50% [18]. This was confirmed in one of the children in this report, and in the other, the short follow up may preclude a definitive conclusion. The successful use of thrombolytic agents prior to cardiac death may reduce the biliary complications after DCD transplantation [19].

This report also raises the possibility of considering the use of segmental DCD grafts for more elective recipients either as reduced- or even as split-liver grafts thereby increasing the donor pool. From a technical point of view, bench times are shorter for graft reduction when compared with liver splitting. Understandably, use of DCD livers as split grafts for two recipients would add to the logistic pressures, as both split grafts would need to be transplanted simultaneously, keeping cold ischaemia times shorter than 8 h. Therefore, local/regional rather than national allocation of DCD liver grafts would help to minimize the cold ischaemia times, and early commencement of the recipient operation before arrival of the graft may also help to save vital time.

In conclusion, this paper describes the first successful use of segmental DCD liver grafts in children with acute liver failure. The early results are promising with both patients surviving the crucial early perioperative period and one child completing a 3-year follow up. Although the limited follow up in this case series does not allow us to draw conclusions on the long-term outcome and the necessity for re-transplantation, we have demonstrated that the use of DCD segmental grafts is a definitive life-saving option for children with ALF. The use of these DCD livers as segmental grafts should be increasingly considered.

Authorship

MTPRP: wrote the paper. SG: data collection/co-writer. DM, KS, JB and PM: contributed important suggestions/helped co-write. DFM: conceptualised the paper/lead author.

Funding

None.

References

1. Lee WS, McKiernan P, Kelly DA. Etiology, outcome and prognostic indicators of childhood fulminant hepatic failure in the United Kingdom. *J Pediatr Gastroenterol Nutr* 2005; **40**: 575.
2. Lu BR, Gralla J, Liu E, Dobyns EL, Narkewicz MR, Sokol RJ. Evaluation of a scoring system for assessing prognosis in pediatric acute liver failure. *Clin Gastroenterol Hepatol* 2008; **6**: 1140.
3. Otte JB. History of pediatric liver transplantation. Where are we coming from? Where do we stand? *Pediatr Transplant* 2002; **6**: 378.
4. Kootstra G, Daemen JH, Oomen AP. Categories of non-heart-beating donors. *Transplant Proc* 1995; **27**: 2893.
5. Kootstra G. Statement on non-heart-beating donor programs. *Transplant Proc* 1995; **27**: 2965.
6. Reddy S, Zilvetti M, Brockmann J, McLaren A, Friend P. Liver transplantation from non-heart-beating donors: current status and future prospects. *Liver Transpl* 2004; **10**: 1223.
7. Abt P, Crawford M, Desai N, Markmann J, Olthoff K, Shaked A. Liver transplantation from controlled non-heart-beating donors: an increased incidence of biliary complications. *Transplantation* 2003; **75**: 1659.
8. Reich DJ, Munoz SJ, Rothstein KD, *et al.* Controlled non-heart-beating donor liver transplantation: a successful single center experience, with topic update. *Transplantation* 2000; **70**: 1159.
9. Manzarbeitia CY, Ortiz JA, Jeon H, *et al.* Long-term outcome of controlled, non-heart-beating donor liver transplantation. *Transplantation* 2004; **78**: 211.
10. Muiesan P, Girlanda R, Baker A, Rela M, Heaton N. Successful segmental auxiliary liver transplantation from a non-heart beating donor: implications for split liver transplantation. *Transplantation* 2003; **75**: 1443.
11. Muiesan P, Girlanda R, Jassem W, *et al.* Single-center experience with liver transplantation from controlled non-heartbeating donors: a viable source of grafts. *Ann Surg* 2005; **242**: 732.
12. Strong R, Ong TH, Pillay P, Wall D, Balderson G, Lynch S. A new method of segmental orthotopic liver transplantation in children. *Surgery* 1988; **104**: 104.
13. UK Transplant. http://www.uktransplant.org.uk (accessed 16 October 2008).

14. Abt PL, Desai NM, Crawford MD, *et al.* Survival following liver transplantation from non-heart-beating donors. *Ann Surg* 2004; **239**: 87.
15. Monbaliu D, Crabbé T, Roskams T, Fevery J, Verwaest C, Pirenne J. Livers from non-heart-beating donors tolerate short periods of warm ischemia. *Transplantation* 2005; **79**: 1226.
16. Attia M, Silva MA, Mirza DF. The marginal liver donor – an update. *Transpl Int* 2008; **21**: 713.
17. Casavilla A, Ramirez C, Shapiro R, *et al.* Experience with liver and kidney allografts from non-heart-beating donors. *Transplantation* 1995; **59**: 197.
18. Maheshwari A, Maley W, Li Z, Thuluvath PJ. Biliary complications and outcomes of liver transplantation from donors after cardiac death. *Liver Transpl* 2007; **13**: 1645.
19. Fung JJ, Eghtesad B, Patel-Tom K. Using livers from donation after cardiac death donors – a proposal to protect the true Achilles heel. *Liver Transpl* 2007; **13**: 1633.