The escalating impact of hepatocellular carcinoma on UK liver transplantation; an analysis of the United Kingdom Liver Transplant Database

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Introduction:

- The exponential rise in the incidence and mortality of hepatocellular carcinoma (HCC) in the UK is placing a huge demand on liver transplantation services.
- We provide an epidemiological overview of the evolving indications and outcomes of liver transplantation in order to help in the prediction of future demands of UK liver transplantation and the subsequent planning of service provision.

Methods:

- The United Kingdom Liver Transplant (UKLT) database contains information about 13002 orthotopic liver transplants carried out between March 1994 and March 2012.
- Patients who underwent elective transplant were categorised according to primary diagnosis at the time of transplantation.
- Kaplan-Meier methods were used to estimate time-trends in unadjusted 5-year patient and graft survival.
- To assess whether disease aetiology predicted survival cox proportional hazard models were estimated for time to graft loss and time to survival.

Results:

Figure 1: Time trends in proportion of patients transplanted per disease indication group

Key:
Cancer = HCC; HCV = Hepatitis C; PSC = Primary Sclerosing Cholangitis; HBV = Hepatitis B; Primary biliary cirrhosis; ALD = Alcoholic liver disease; AID = Autoimmune disease; Metabolic = Metabolic causes inc NAFLD + NASH

- 25% of all liver transplants are for patients with HCC (figure 1).
- 43% of all patients transplanted for HCC had a concomitant HCV infection.
- The highest proportion (11%) of DCD livers were used in patients with HCC.

Table 1: Time trends in 5-year patient and graft survival

y Diagnosis	Time period of Transplantation					
	Patient Survival			Graft Survival		
	1994-1998	1999-2003	2004-2007	1994-1998	1999-2003	2004-2007
Cancer	47.3 (39.7-54.4)	60.7 (55.2-65.8)	71.7 (66.4-76.4)	44.6 (37.2-51.8)	57.7 (52.1-62.8)	68.7 (63.2-73.5)
HCV	69.7 (63.6-75.0)	70.3 (65.0-75.0)	73.0 (66.5-78.4)	64.4 (58.1-70.0)	63.9 (58.4-68.9)	68.6 (62.0-74.3)
PSC	73.5 (66.8-79.1)	79.0 (73.0-83.8)	78.8 (72.3-83.9)	67.0 (60.0-73.1)	73.7 (67.4-78.9)	68.9 (61.8-74.9)
HBV	70.7 (62.1-77.6)	82.9 (74.8-88.7)	89.1 (78.3-94.7)	64.9 (56.1-72.3)	79.3 (70.6-85.6)	83.8 (72.4-90.8)
PBC	81.1 (77.2-84.5)	82.8 (78.7-86.2)	81.9 (75.7-86.6)	75.0 (70.7-78.8)	78.8 (74.4-82.5)	76.1 (69.6-81.5)
ALD	67.5 (62.5-72.0)	74.5 (70.1-78.4)	78.2 (73.9-81.9)	64.1 (59.0-68.7)	70.3 (65.7-74.4)	74.3 (69.8-78.2)
AID	69.1 (62.7-74.6)	73.4 (67.8-78.1)	82.4 (76.1-87.2)	61.4 (54.8-67.3)	69.9 (64.2-74.9)	76.9 (70.1-82.3)
Metabolic	67.1 (55.2-76.4)	74.1 (63.3-82.1)	79.4 (65.8-88.1)	61.7 (49.7-71.7)	73.0 (62.0-81.1)	72.2 (58.2-82.3)
Others	67.3 (58.8-74.4)	71.9 (63.6-78.6)	80.3 (73.7-85.4)	61.7 (53.1-69.1)	69.0 (60.5-76.0)	74.9 (67.9-80.6)

- Patient and graft survival improved for all disease indications over the successive era (see table 1).
- Despite improvements, HCC has the least successful post transplantation outcomes (see table 2).

Table 2: Cox regression analysis for overall 10-year survival

Adjusted patient and graft survival at 10 years by primary liver disease		
Primary Diagnosis	Patient Survival	Graft Survival
Cancer	I	I
HCV	0.72 (0.63-0.84)	0.79 (0.69-0.91)
PSC	0.48 (0.40-0.57)	0.62 (0.53-0.72)
HBV	0.44 (0.35-0.56)	0.48 (0.39-0.60)
PBC	0.41 (0.35-0.48)	0.47 (0.41-0.55)
ALD	0.62 (0.54-0.71)	0.67 (0.59-0.77)
AID	0.61 (0.52-0.72)	0.68 (0.58-0.79)
Metabolic	0.58 (0.45-0.74)	0.64 (0.51-0.80)
Others	0.57 (0.47-0.69)	0.61 (0.51-0.73)

- HCC still has significantly worse survival after adjustment for recipient and donor characteristics.
- This maybe explained by the use of more marginal grafts being transplanted into HCC patients in an oncologically appropriate time frame.

Figure 2: Utilisation of DCD livers in the UK 1994 – 2012

Conclusion:

- HCC is the fastest growing indication for transplantation in the UK
- In order to meet the demand imposed by HCC the donor pool needs to increase and the demand stabilised.
- To achieve this the use of appropriate DCD livers in patients with HCC must be further explored (see figure 2).