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Research Letter

Long-term outcomes of hypothermic oxygenated machine perfusion in extended criteria donor liver transplantation

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To the Editor,

To address organ shortage, liver transplantation (LT) increasingly relies on extended criteria donation (ECD) grafts, despite their higher risk of post-transplant complications linked to ischaemia–reperfusion injury[1]. Given the rising proportion of ECD, traditional static cold storage (SCS) may not be sufficient. Dynamic preservation with hypothermic oxygenated machine perfusion (HOPE) has shown significant reductions in early allograft dysfunction (EAD) and liver-related and biliary complications[2,3]. However, most studies focus on short-term outcomes, and long-term data are lacking[4]. This single-centre observational study, conducted between January 2018 and November 2021, compared long-term outcomes between HOPE and SCS for patients undergoing LT from brain-dead ECD (DBD-ECD). All HOPE cases were conducted under the PERPHO study[5], a prospective single-arm pilot study assessing short-term benefits in DBD-ECD LT, and implemented prospectively into routine practice with ongoing data collection after conclusion. Study design, endpoints, and statistical analyses are detailed in the Supplementary Methods.

Briefly, to compare HOPE outcomes with SCS, a 1:2 nearest neighbour (calliper restriction: 0.2) propensity-matched (PSM) control group was selected among patients transplanted with DBD-ECD grafts in the same centre and period. All data were collected until 30 November 2024 to ensure maximum follow-up. The primary endpoint was death-censored graft survival, defined as the survival of the liver graft with and without considering death as a competing risk to avoid overestimating graft survival. Secondary endpoints included incidence of EAD according to the Olthoff criteria, primary graft non-function (PNF), and biliary and vascular complications.

During the study period, 1329 patients underwent LT, including 50 HOPE and 1279 SCS. After PSM, 49 HOPE patients were matched with 89 SCS controls (*Fig. S1*). Donors and recipients were men in 56% and 83% of cases with median ages of 71 (i.q.r.: 61.5–79.0) and 62 (i.q.r.: 56.0–64.0) years respectively. Median Model for End-stage Liver Disease (MELD) score of recipients was 18.0 (9.3, 27.0). Cirrhosis was more frequent in the HOPE group (71.4% *versus* 48.3%, $P < 0.001$), whereas overall characteristics, notably ECD-definition characteristics, were similar between groups (*Table S1*). HOPE perfusion lasted 124.0 (i.q.r.: 100.0–151.0) minutes whereas cold ischaemia times were similar between groups (HOPE: 526.0 (i.q.r.: 446.0–632.0) minutes *versus* SCS: 522.0 (i.q.r.: 442.0–657.0) minutes, $P = 0.801$). EAD (34.1%), PNF (4.3%), and retransplantation (9.4%) incidences showed no significant difference between groups. Biliary complications were significantly less frequent with HOPE (8.2% *versus* 24.7%, $P = 0.022$), whereas vascular complications were similar. Severe postoperative complications occurred less often in the HOPE group (30.8% *versus* 52.7%, $P = 0.030$) and median hospital stay was shorter (15.0 (i.q.r.: 12.0–22.0) *versus* 20 (i.q.r.: 13.0–28.0) days, $P = 0.018$) (*Table 1*).

After a median follow-up of 62.5 months (95% c.i.: 35.0, 124.4), death-censored graft survival at 1, 3, and 5 years was significantly higher in the HOPE group (93.8% *versus* 80.8%, $P_{\text{log-rank}} = 0.049$; 91.7% *versus* 78.4%, $P_{\text{log-rank}} = 0.050$; 91.7% *versus* 75.2%, $P_{\text{log-rank}} = 0.035$ respectively) (*Fig. 1a*). In the presence of patient death-competing risks, cumulative incidence of graft loss was less frequent with HOPE (8.1%, 95% c.i.: 4.6, 1.7 *versus* 22.6%, 95% c.i.: 18.1, 27.1; $P_{\text{Gray-test}} = 0.033$) (*Fig. 1b*), whereas death risks were similar (6.1%, 95% c.i.: 3.1, 9.1 *versus* 10.3%, 95% c.i.: 6.8, 13.8; $P_{\text{Gray-test}} = 0.349$). HOPE remained an independent factor for death-censored graft survival in the multivariable Cox (adjusted HR: 0.30; 95% c.i.: 0.10, 0.91; $P = 0.045$) and Fine–Gray models (adjusted sub-HR: 0.38; 95% c.i.: 0.16, 0.58; $P = 0.046$) (*Table S2*).

The findings suggest that HOPE significantly improves long-term graft survival, reducing graft loss incidence, biliary complications, and rates of severe morbidity compared to SCS. These benefits likely stem from reduced ischaemia–reperfusion

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Table 1 Propensity score-matched cohort intraoperative and postoperative outcomes between hypothermic oxygenated machine perfusion and static cold storage for patients with extended criteria donor undergoing orthotopic liver transplantation

Characteristics	Overall, N = 138[1]	Static cold storage n = 89[1]	Hypothermic oxygenated machine perfusion, n = 49[1]	Missing values[2]	P[1]
Intraoperative parameters					
Cold ischaemia time, minutes*	526 (446.0, 632)	522 (441.8, 657)	526 (460.0, 615)	1 (0.7)	0.959†
LT duration, minutes*	347 (273.8, 418)	363 (294.0, 420)	314 (265.0, 363)	0 (0)	**0.049**†
Liver perfusion time, minutes*	0 (0.0, 104)	0 (0.0, 0)	124 (100.0, 151)	0 (0)	**<0.001**†
Red blood cell transfusion, units*	4 (2.0, 7)	4 (2.0, 7)	5 (2.0, 8)	0 (0)	0.682†
Postoperative and long-term outcomes					
Early allograft dysfunction‡	47 (34.1)	30 (33.7)	17 (34.7)	0 (0)	0.999
Primary allograft non function‡	6 (4.3)	4 (4.5)	2 (4.1)	0 (0)	0.999
Retransplantation	13 (9.4)	10 (11.2)	3 (6.1)	0 (0)	0.380
Biliary complications	26 (18.8)	22 (24.7)	4 (8.2)	0 (0)	**0.022**
Arterial complications	34 (24.6)	24 (27.0)	10 (20.4)	0 (0)	0.418
Portal vein/hepatic vein complications	14 (10.1)	10 (11.2)	4 (8.2)	0 (0)	0.770
Postoperative severe complications (Clavien–Dindo ≥ 3)	51 (45.1)	39 (52.7)	12 (30.8)	0 (0)	**0.030**
ICU postoperative stay, days*	5 (3.0, 9)	5 (3.0, 9)	5 (4.0, 8)	0 (0)	0.602
Overall postoperative stay, days*	18 (13.0, 26)	20 (13.0, 28)	15 (12.0, 22)	0 (0)	**0.018**†

[1]Values are expressed with percentages in parentheses unless indicated otherwise; values of P are from McNemar's test for paired data unless indicated otherwise; *values are median (i.q.r.); †Wilcoxon signed-rank test for paired data; [2]missing values in parentheses are percentages; ‡early allograft dysfunction according to the Olthoff criteria and primary allograft non-function defined as liver failure requiring retransplantation or leading to death within 7 days after transplantation. Bold values indicate statistical significance (P < 0.05). ICU, intensive care unit; LT, liver transplantation.

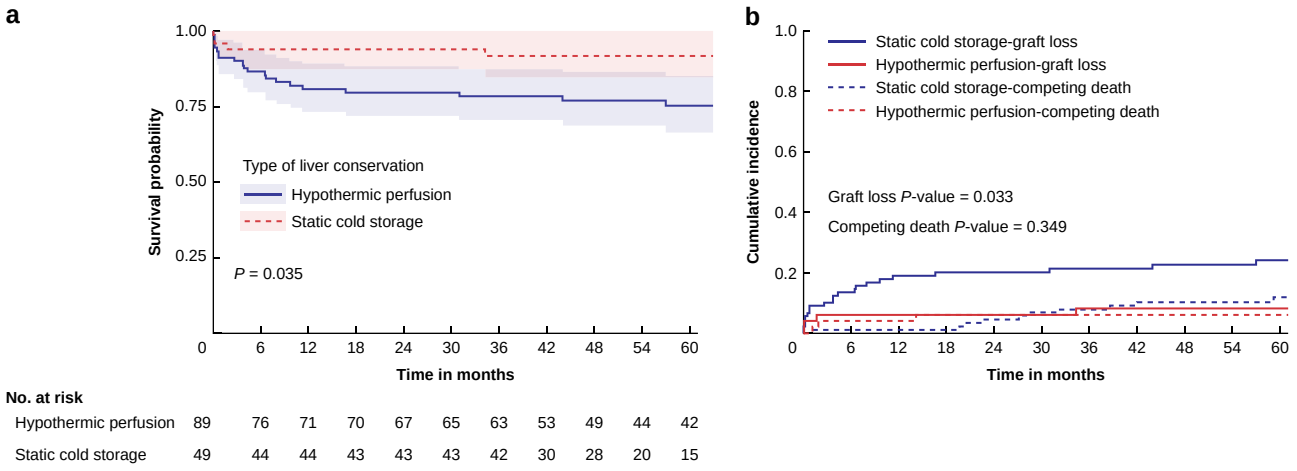

Fig. 1 Kaplan–Meier estimates of overall survival a and Kalbfleisch–Prentice cumulative incidence of graft loss and competing patient death b according to liver conservation for patients with extended criteria donor undergoing orthotopic liver transplantation

injury and biliary damage. Although limited by its single-centre observational design, the results accounting for the competing risk of death offer a more accurate survival and align with previous randomized trials and cohort studies on the short-term benefits of HOPE, reinforcing its role as a valuable preservation strategy for high-risk donor livers.

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Disclosure

The authors have no conflicts of interest to disclose.

Supplementary material

Supplementary material is available at *BJS* online.

Data sharing

The data that support the findings of this study are available on reasonable demand after approval of a proposal by the authors.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Briceño J, Marchal T, Padillo J, Solórzano G, Pera C. Influence of marginal donors on liver preservation injury. *Transplantation* 2002; **74**:522–526
2. Czigany Z, Pratschke J, Froněk J, Guba M, Schöning W, Raptis DA *et al.* Hypothermic oxygenated machine perfusion reduces early allograft injury and improves post-transplant outcomes in extended criteria donation liver transplantation from donation after brain death: results from a multicenter randomized controlled trial (HOPE ECD-DBD). *Ann Surg* 2021;**274**:705–712
3. Jaber F, Abuelazm M, Soliman Y, Madi M, Abusuilik H, Mazen Amin A *et al.* Machine perfusion strategies in liver transplantation: a systematic review, pairwise, and network meta-analysis of randomized controlled trials. *Liver Transpl* 2025;**31**:596–615
4. Xie X, Zheng Q, Li K, Xiang B. Hypothermic oxygenated perfusion in human liver transplantation: meta-analysis of randomized clinical trials. *Br J Surg* 2024;**111**:znad403
5. Rayar M, Beaurepaire JM, Bajeux E, Hamonic S, Renard T, Locher C *et al.* Hypothermic oxygenated perfusion improves extended criteria donor liver graft function and reduces duration of hospitalization without extra cost: the PERPHO study. *Liver Transpl* 2021;**27**:349–362