Randomised Controlled Trial

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Routine end-ischemic hypothermic machine perfusion in liver transplantation from donors after brain death: results of 2-year follow-up of a randomized controlled trial

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Background: Data on routine hypothermic machine perfusion of livers procured from donors after brain death (DBD) are scarce, and the benefits of the method have only been demonstrated in extended criteria grafts. This study aimed to assess if end-ischemic dual hypothermic oxygenated machine perfusion (dHOPE) is superior to static cold storage (SCS) in preservation of livers procured from DBD donors with respect to long-term outcomes. Existing data on short-term outcomes favours dHOPE in patients receiving high-risk grafts.

Methods: This prospective randomized controlled trial included 104 recipients of DBD livers randomly assigned to SCS arm (78 patients) and the dHOPE arm (26 patients). Endpoints of interest were the occurrence of biliary complications (biliary fistula, anastomotic, and nonanastomotic strictures) and overall patient and graft survival (GS) during the 2-year follow-up.

Results: A total of 36 patients developed biliary complications (at least one event) – six events in dHOPE arm and 30 in SCS arm. There was no significant difference in biliary complications between groups (23.7 vs. 43.4%, $P=0.11$). No differences were found significant with respect to anastomotic (19.9 vs. 33.7%, $P=0.20$) and nonanastomotic strictures (0 vs. 11.1%, $P=0.10$) as well as biliary fistulas (11.7 vs. 12.2%, $P=0.93$). Survival analysis did not show significantly different results in the study population – overall survival: 92.3% in dHOPE and 83.9% in SCS ($P=0.35$), and GS: 92.3 and 81.4% ($P=0.23$), respectively. However, a significant difference in GS was noted in recipients of high-risk grafts – 100% in dHOPE and 73.1% in SCS, respectively ($P=0.038$).

Conclusions: The long-term outcome data suggest that the routine use of dHOPE may be beneficial for recipients of high-risk grafts from DBD donors. The present study does not provide any evidence for the benefits of dHOPE in low-risk grafts.

Keywords: biliary complications, graft survival, ischemia-reperfusion injury, liver transplantation, machine perfusion, organ preservation

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Introduction

The sequelae of ischemia-reperfusion injury (IRI) are not limited to short-term postoperative outcomes and may affect graft performance long after the primary surgery[1]. Restoration of blood flow, although intuitively beneficial to the organ, provides numerous stimuli for hepatocyte and cholangiocyte injury that may affect the long-term status of the graft and biliary tree[2,3]. SCS at 4°C – a staple technique in organ preservation – is responsible for progressive succinate accumulation, ATP depletion, and cell necrosis[4]. These events are exacerbated by a cascade of reactive oxygen species generation and exaggerated activation of the inflammatory response following reperfusion. Organs procured from extended criteria donors (ECD) – grafts with significant macrosteatosis or from donors after cardiac death – are particularly susceptible to the adverse effects of IRI[5].

Reducing IRI is of paramount importance, given the need to safely expand the donor pool. With the growing list of indications for liver transplantation and the increasing discrepancy between supply and demand, the use of ECD grafts seems inevitable, especially in the era of rapid development of liver transplant oncology[6]. Numerous methods have been developed to alleviate IRI, which may involve oxygenated perfusion, including

hypothermic machine perfusion, normothermic organ maintenance allowing assessment of organ viability, or even ischemia-free transplantation[7–9]. These methods appear to be important in safely expanding the donor pool.

Dual hypothermic machine perfusion (dHOPE) allows short-term organ maintenance at 12°C mainly to facilitate the gradual elimination of succinate and to induce mitochondrial reprogramming, leading to ATP replenishment and downstream inhibition of the inflammatory response[4]. Existing data and experimental studies support the notion that hypothermic oxygenation may have a beneficial effect on immediate post-transplant outcomes[5,10,11]. However, this effect has been observed predominantly in the high-risk donor group, so routine use of dHOPE does not seem justified to date[10,12,13]. It has been suggested that the reduction of IRI not only affects the short-term posttransplant period but may also influence the graft and biliary tree status in the longer term[2,11]. Data on long-term outcomes, including patient and graft survival (GS) and biliary tree status, are scarce. Here, 2-year follow-up of patients enrolled in the randomized controlled trial comparing dHOPE and SCS is reported.

HIGHLIGHTS

- This is a randomized controlled trial on the comparison of hypothermic oxygenated machine perfusion with static cold storage (SCS) in liver transplantation from donors after brain death (DBD).
- We report on long-term clinical outcomes with respect to survival analysis and biliary complications.
- The benefits of hypothermic oxygenated perfusion were limited to transplantations from high-risk donors.

Methods

This randomized, parallel controlled trial was designed to compare dHOPE and SCS with respect to the model of early allograft function (MEAF) as the primary endpoint of interest. All patients who underwent liver transplantation from DBD at the Department of General, Transplant, and Liver Surgery between April 2021 and May 2022 were screened for eligibility. Inclusion criteria were age greater than 18 years, deceased donor liver transplantation, and provision of informed consent. Liver transplantation from donors after cardiac death or either reduced or split grafts were excluded. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki of 1975, and the study protocol was approved by the Institutional Review Board (KB/6/2020). All patients gave informed consent prior to enrolment. The work has been reported in line with Consolidated Standards of Reporting Trials (CONSORT) Guidelines[14], Supplemental Digital Content 5, http://links.lww.com/JS9/D95.

The detailed study protocol and power analysis for sample size calculation have been described elsewhere[10]. Briefly, immediately after organ acceptance, the patient was randomly assigned to either the dHOPE or SCS arm by one of the investigators in the department (allocation ratio 1:3). During back table dissection, the livers were flushed with 1 l of cold perfusate (StoreProtect Plus; Carnamedica, Poland). Grafts allocated to the dHOPE group were perfused for at least 2 h at 12°C via both the portal vein (continuous flow; pressure of 3–5 mmHg) and the hepatic artery (pulsatile flow; mean pressure of 25 mmHg). The perfusate was supplemented with 100% oxygen at a flow rate of 500 ml/min to maintain an oxygen partial pressure of at least 450 mmHg. Graft perfusion was performed using the Liver Assist device (Organ Assist, now XVIVO) and PumpProtect solution (Carnamedica, Poland). Perfusion was extended beyond 2 h in the case of ongoing hepatectomy. Grafts in the SCS arm were refrigerated at 4°C in StoreProtect Plus solution (Carnamedica, Poland) until completion of hepatectomy. Patients were unaware of the group allocation, although the surgical team was not blinded due to the nature of the procedure.

Data on both the primary outcome measure, namely MEAF, and short-term secondary outcomes are reported elsewhere[10]. Secondary outcomes reported here included 2-year patient and GS and biliary complications, further subdivided into anastomotic and nonanastomotic strictures and biliary fistulas. Biliary complications were diagnosed on the basis of clinical observations (biliary drainage or leakage found at relaparotomy), the need for endoscopic retrograde cholangiopancreatography, or magnetic resonance cholangiopancreatography findings. High-risk donors were defined as having a donor risk index (DRI) > 1.7[10,15].

Baseline recipient-related, donor-related, and transplant procedure-related factors were compared between the groups. Graft steatosis was assessed by routine wedge biopsies by an experienced pathologist.

Qualitative and quantitative data are presented as *n* (%), median (interquartile range) or mean (± standard error). Fisher's exact test and Mann–Whitney *U* test were used for comparisons where appropriate. Kaplan–Meier estimates were used to estimate the proportions of patients who developed biliary complications and the proportions of surviving patients and grafts over time. Observations were censored at 2 years. The mean time of patient survival and mean time to graft loss were compared using restricted mean survival time analysis. The inverse probability weighting was used to balance the groups with respect to the common confounders. Statistical significance was set at P value <0.05. SAS/STAT, version 15.2 (SAS Institute Inc., 2020, Cary, North Carolina, USA) was used for statistical analysis.

Results

One hundred and four patients were included in the study. Twenty-six liver grafts underwent dHOPE, while 78 organs were allocated to the SCS arm (Supplemental Digital Content 1, http://links.lww.com/JS9/D91). Baseline characteristics of the study group are reported elsewhere[10]. Considering the population of high-risk graft recipients (DRI > 1.7), there were 14 patients in the dHOPE arm and 26 patients in the SCS arm, as well as 12 patients and 52 patients who received low-risk grafts (DRI ≤ 1.7), respectively. Table 1 summarizes the baseline characteristics of the groups. Patients in both groups did not differ significantly in the etiology of liver disease. There were no significant differences in the donor characteristics except for significantly higher donor BMI in the high-risk grafts undergoing dHOPE. The vast majority of procurements in both groups took place outside of the regional area. Cold ischemia times were significantly longer in the

Table 1

Baseline characteristics of patients who received low-risk (donor risk index ≤ 1.7) and high-risk grafts (donor risk index > 1.7) after dual hypothermic oxygenated machine perfusion or static cold storage.

	DRI ≤ 1.7			DRI > 1.7		
Variables	**dHOPE group (*n* = 12)**	**Static cold storage group (*n* = 52)**	***P***	**dHOPE group (*n* = 14)**	**Static cold storage group (*n* = 26)**	***P***
Recipient sex			> 0.99			0.50
Male	8 (66.7%)	35 (67.3%)		10 (71.4%)	15 (57.7%)	
Female	4 (33.3%)	17 (32.7%)		4 (28.6%)	11 (42.3%)	
Recipient age (years)	42.5 (37.5–58)	50.5 (39–61)	0.38	50 (41–67)	50.5 (43–59)	0.94
Model for End-stage Liver Disease	13 (10–22)	13 (9–20)	0.76	11 (7–15)	14.5 (10–21)	0.21
Child–Turcotte–Pugh class			0.44			0.07
A	6 (50.0%)	17 (32.7%)		9 (64.3%)	7 (26.9%)	
B	5 (41.7%)	24 (46.2%)		4 (28.6%)	15 (57.7%)	
C	1 (8.3%)	11 (21.2%)		1 (7.1%)	4 (15.4%)	
Hepatitis C virus infection	2 (16.7%)	5 (9.6%)	0.61	3 (21.4%)	7 (26.9%)	> 0.99
Hepatitis B virus infection	0	9 (17.3%)	0.19	1 (7.1%)	5 (19.23%)	0.40
Alcoholic liver disease	3 (25.0%)	14 (26.9%)	> 0.99	3 (21.4%)	4 (15.4%)	0.68
Autoimmune hepatitis	2 (16.7%)	6 (11.5%)	0.64	1 (7.1%)	5 (19.23%)	0.40
Primary sclerosing cholangitis	2 (16.7%)	9 (17.3%)	> 0.99	4 (28.6%)	4 (15.4%)	0.42
Primary biliary cirrhosis	1 (8.3%)	1 (1.9%)	0.34	0	3 (11.5%)	0.54
Nonalcoholic steatohepatitis	0	2 (3.9%)	> 0.99	1 (7.1%)	1 (3.9%)	> 0.99
Hepatocellular carcinoma	2 (16.7%)	7 (13.5%)	0.67	3 (21.4%)	4 (15.4%)	0.68
Recipient BMI (kg/m^2)	24.2 (22.2–27.1)	25.2 (21.5–27.5)	0.76	26.9 (23.9–28.4)	23.9 (21.2–26.2)	0.05
Liver transplantation technique			> 0.99			> 0.99
Piggyback	8 (66.7%)	35 (67.3%)		8 (57.1%)	16 (61.5%)	
Conventional	4 (33.3%)	17 (32.7%)		6 (42.9%)	10 (38.5%)	
Veno-venous bypass	3 (25.0%)	17 32.7%)	0.29	7 (50%)	10 (38.5%)	0.52
Temporary porto-caval shunt	1 (8.3%)	0	> 0.99	0	1 (3.9%)	> 0.99
Biliary anastomosis			0.45			> 0.99
Duct to duct	8 (66.7%)	41 (78.8%)		11 (78.6%)	19 (73.1%)	
Hepaticojejunostomy	4 (33.3%)	11 (21.2%)		3 (21.4%)	7 (26.9%)	
Intraoperative RBC transfusions (units)	3 (0–7)	4 (2–7)	0.32	4 (2–6)	4.5 (2–8)	0.25
Intraoperative FFP transfusions (units)	3.5 (1–8)	4 (2–6)	0.82	2.5 (1 – 6)	4.5 (2–8)	0.13
Donor age (years)	37.5 (23.5–44.5)	36.5 (30.5–45.5)	0.61	58.5 (55–64)	57 (50–65)	0.54
Donor BMI (kg/m^2)	25 (23–26)	25 (22–27.5)	0.74	29 (26–31)	25 (22–27)	0.001
Donor height (cm)	180 (178.5–186.5)	176 (170–181.5)	0.13	170 (162–178)	170 (163–178)	0.94
Donor risk index	1.41 (1.26–1.58)	1.35 (1.23–1.52)	0.54	1.92 (1.81–2.17)	1.96 (1.79–2.26)	0.87
Extended criteria donor[a]	8 (66.7%)	26 (50.0%)	0.35	9 (64.3%)	13 (50%)	0.51
Donor laboratory tests						
Serum bilirubin (mg/dl)	0.51 (0.39–0.85)	0.50 (0.32–0.80)	0.75	0.43 (0.30–0.64)	0.4 (0.26–0.64)	0.96
Serum aspartate transaminase (U/l)	63 (35.5–102.5)	77.5 (39.5–110)	0.65	68.5 (40–80)	40.5 (30–70)	0.12
Serum alanine transaminase (U/l)	46 (37–87)	55 (30–100)	0.94	64.3 (33–105)	38.5 (23–100)	0.29
Serum sodium (mmol/l)	155 (150.5–167)	151.5 (146–160)	0.14	153 (146–160)	151 (143–160)	0.85
International normalized ratio	1.31 (1.20–1.50)	1.2 (1.11–1.40)	0.15	1.16 (1.07–1.3)	1.22 (1.11–1.36)	0.33
Graft steatosis > 30%	1 (8.3%)	1 (1.9%)	0.34	0	1 (3.6%)	> 0.99
Cold ischemic time (min)	450.0 (352.5–507.5)	561.5 (467.5–630)	0.008	474.0 (420–567)	587.5 (480–675)	0.014
Total hypothermic time (min)	570.0 (532.5–650)	561.5 (467.5–630)	0.43	622.5 (570–690)	587.5 (480–675)	0.16
Donor service area						> 0.99
Local	0	6 (11.5%)	0.58	0	0	
Regional	2 (16.7%)	12 (23.1%)	> 0.99	1 (7.1%)	1 (3.8%)	
National	10 (83.3%)	34 (65.4%)	0.31	13 (92.95)	25 (96.2%)	

Data are presented as *n* (%) and median (interquartile range).

[a]Defined according to Czigany *et al*.[12].

dHOPE, dual hypothermic oxygenated machine perfusion; DRI, donor risk index; FFP, fresh frozen plasma; PRBC, packed red blood cells.

dHOPE groups for both high-risk and low-risk grafts. No other significant differences were found between the groups.

There were 36 overall biliary complications (at least one event) found in the group – six were recorded in the dHOPE arm and 30 in the SCS arm. There were no significant differences in overall biliary complications between the groups (23.7 vs. 43.4%, $P = 0.11$). Differences in the incidence of anastomotic and non-anastomotic strictures were also not significant – 19.9 versus

33.7% ($P=0.20$) and 0 versus 11.1% ($P=0.10$), respectively. Similarly, the difference in the percentages of biliary fistulas was not significant – 11.7 versus 12.2% ($P=0.93$). Subgroup analysis in both high-risk and low-risk donors also showed no significant differences. There were no differences in overall biliary complications between the two arms (dHOPE and SCS) – high-risk grafts: 21.4 versus 34.9% ($P=0.34$) and low-risk grafts: 26.7 versus 46.9% ($P=0.37$). The differences in the proportions of anastomotic and nonanastomotic strictures were as follows – high-risk grafts: 21.4 versus 27.4% ($P=0.61$) and low-risk grafts: 17.5 versus 36.4% ($P=0.34$); high-risk grafts: 0 versus 2.8% and low-risk grafts: 0 versus 13.6% ($P=0.29$). Biliary fistulas were observed in 7.1 versus 12.7% ($P=0.58$) and 17.5 versus 12.0% ($P=0.65$). Structured data on biliary complications with distinction between the groups are presented in Supplemental Digital Content 2, http://links.lww.com/JS9/D92. After excluding biliary fistulas from the analysis, we also found no differences in the incidence of biliary strictures (anastomotic and nonanastomotic) in the general population (19.9 vs. 39%, $P=0.10$), high-risk donors (21.4 vs. 27.4%, $P=0.61$), and low-risk donors (17.5 vs. 43.7%, $P=0.21$).

In the general study population, 2-year overall survival (OS) in the dHOPE and SCS arms were 92.3 and 83.9%, respectively ($P=0.35$). Similarly, the difference in 2-year GS was found not significant, with rates of 92.3% in the dHOPE arm and 81.4% in the SCS arm ($P=0.23$). Considering only high-risk grafts with a DRI > 1.7, the respective survival measures were as follows – OS of 100% (dHOPE) and 76.9% (SCS) ($P=0.06$) and GS of 100% (dHOPE) and 73.1% (SCS) ($P=0.038$) (Fig. 1). In addition, restricted mean survival time analysis showed significant differences in both mean time of patient survival and mean time to graft loss over 2 years for high-risk grafts – 24.0 ± 0.0 months (dHOPE) versus 19.2 ± 1.7 months (SCS) ($P=0.006$) and 24.0 ± 0.0 months (dHOPE) and 18.2 ± 1.9 months (SCS) ($P=0.002$), respectively (Table 2) (Fig. 2). In the low-risk group (DRI ≤ 1.7), no differences were seen between the groups – OS of 83.3 and 87.6% ($P=0.57$) and GS of 83.3 and 85.8% ($P=0.70$). Patient and GS data with distinction between the groups are summarized in Table 3.

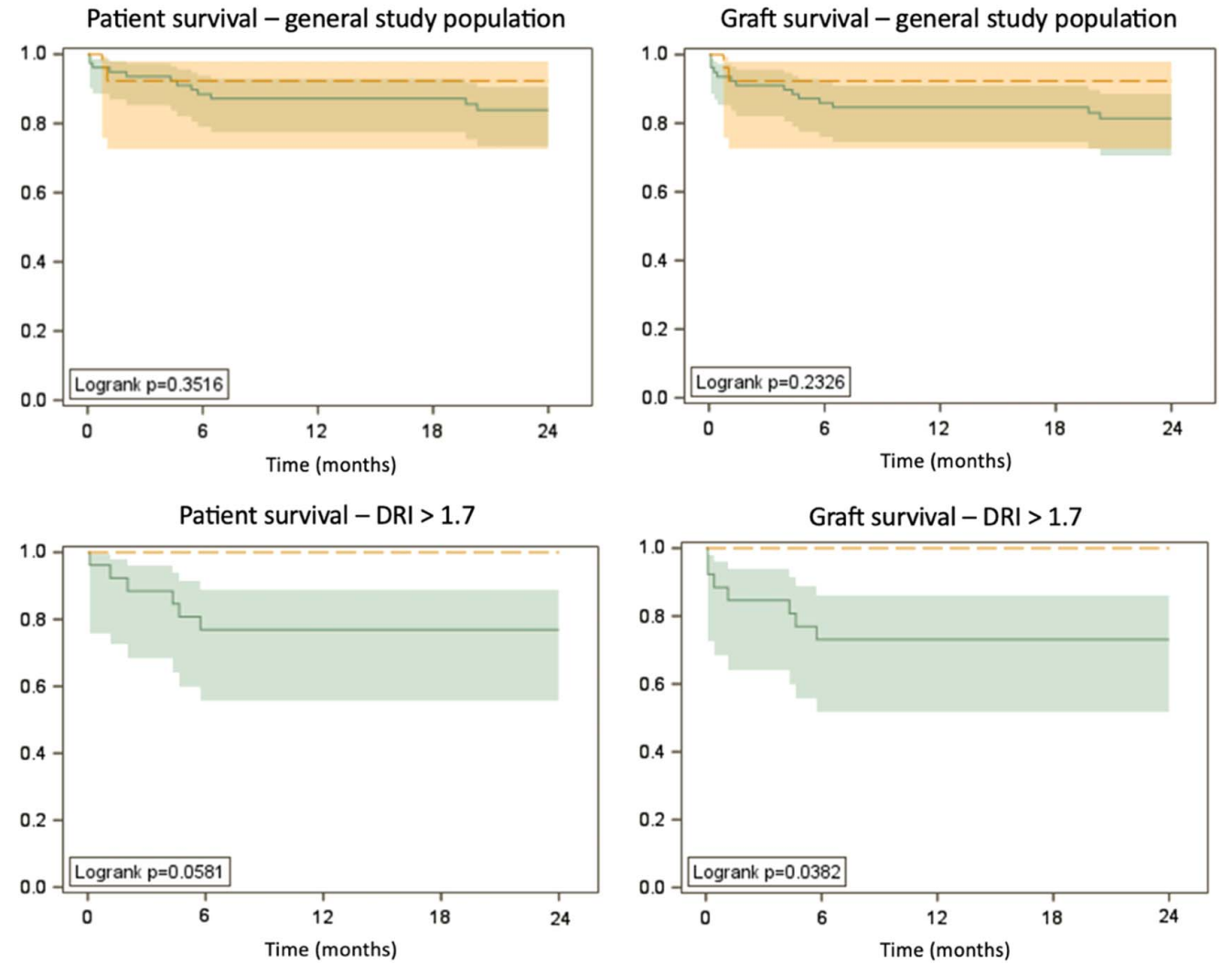

Figure 1. Proportions of patients and grafts surviving across 24 months. The orange line represents patients assigned to the dHOPE group, and the green line represents patients assigned to the SCS group. Colored areas represent a 95% confidence interval. SCS, static cold storage.

Table 2

Mean[a] time to death or graft loss at 24 months in hypothermic oxygenated machine perfusion and static cold storage groups[b].

Variables (months)	HOPE	SCS	*P*
All recipients			
Time to death	22.2 ± 1.2	21.2 ± 0.8	0.47
Time to graft loss	22.2 ± 1.2	20.5 ± 0.9	0.26
DRI > 1.7			
Time to death	24.0 ± 0.0	19.2 ± 1.7	0.006
Time to graft loss	24.0 ± 0.0	18.2 ± 1.9	0.002

[a]The time is presented as a mean value ± SEM.

[b]The mean time to death or graft loss from liver transplantation across 24 months is presented in Figure 1A–D.

DRI, donor risk index; HOPE, hypothermic oxygenated machine perfusion; SCS, static cold storage.

There were 16 cases of both liver-related and recipient-related graft loss. Four recipients underwent retransplantation due to hepatic artery thrombosis (two cases) and primary nonfunction (two cases). Of these, two died in the late postoperative period due to opportunistic infections. All patients requiring retransplantation had been allocated to the SCS group. Among liver-related causes of graft-loss, there were three patients diagnosed with primary nonfunction (SCS group), two patients with hepatic artery thrombosis (SCS group), and three with cholangiosepsis (one in dHOPE group and two in SCS group). Structured data on both liver-related and recipient-related graft loss with distinction between the groups are presented in Supplemental Digital Content 3, http://links.lww.com/JS9/D93.

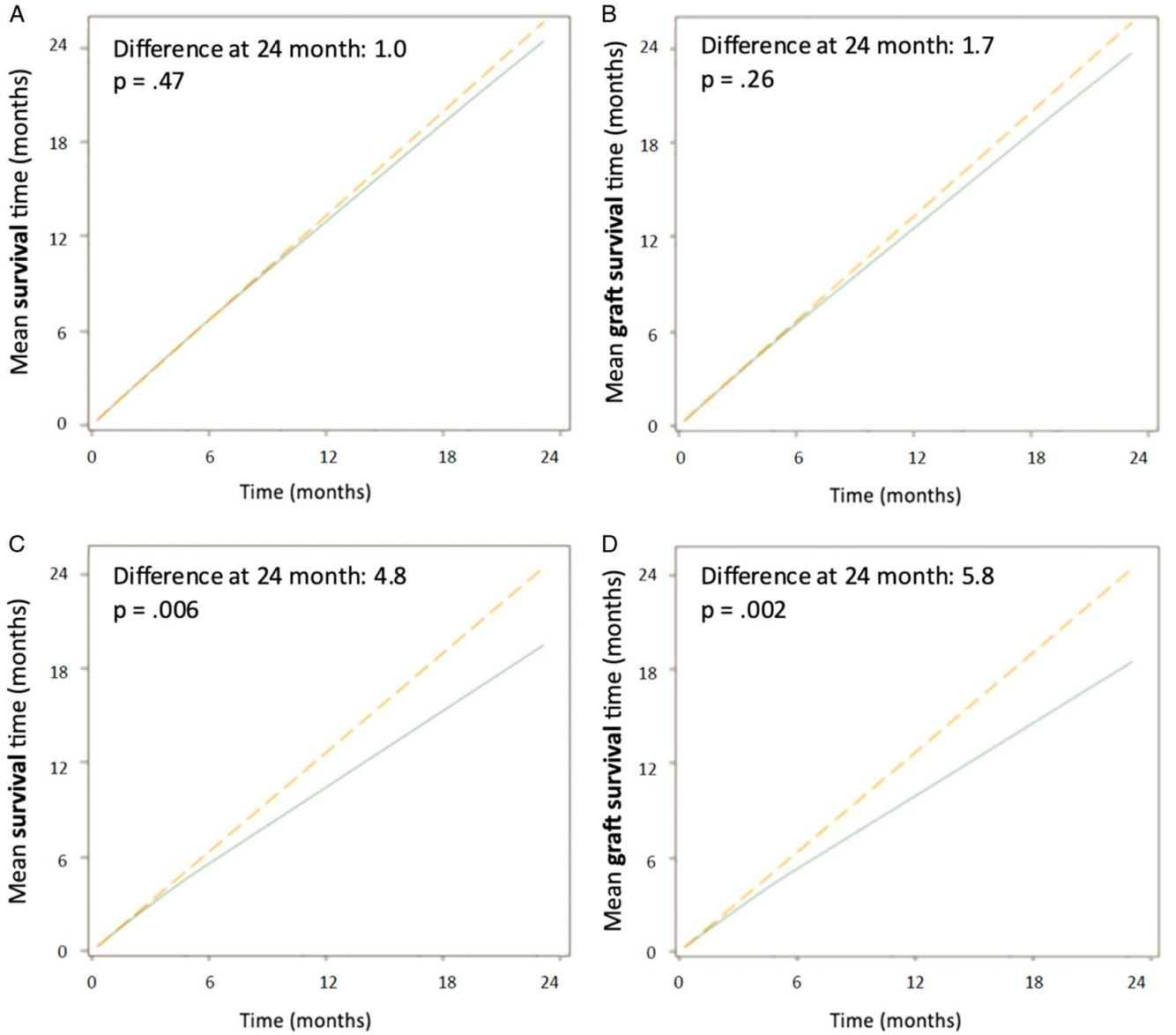

Figure 2. Mean time to death or graft loss across 24 months after liver transplantation. The orange line represents patients assigned to the dHOPE group. The green line represents patients assigned to the SCS group. (A) Mean time to death in the general study population. (B) Mean time to graft loss in the general study population. (C) Mean time to death in high-risk donors. (D) Mean time to graft loss in high-risk donors. SCS, static cold storage.

Table 3

Overall and graft survival[a] across 24 months from liver transplantation both in the group of all recipients and recipients of high-risk and low-risk grafts.

	Time from liver transplantation								
Outcomes	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	***P***
All recipients									
Overall survival									
HOPE	92.3	92.3	92.3	92.3	92.3	92.3	92.3	92.3	0.35
SCS	93.6	88.5	87.2	87.2	87.2	87.2	83.9	83.9	
Graft survival									
HOPE	92.3	92.3	92.3	92.3	92.3	92.3	92.3	92.3	0.23
SCS	91.0	85.9	84.6	84.6	84.6	85.6	81.4	81.4	
High-risk graft recipients									
Overall survival									
HOPE	100	100	100	100	100	100	100	100	0.06
SCS	88.5	76.9	76.9	76.9	76.9	76.9	76.9	76.9	
Graft survival									
HOPE	100	100	100	100	100	100	100	100	0.038
SCS	84.6	73.1	73.1	73.1	73.1	73.1	73.1	73.1	
Low-risk graft recipients									
Overall survival									
HOPE	83.3	83.3	83.3	83.3	83.3	83.3	83.3	83.3	0.57
SCS	96.2	94.2	92.3	92.3	92.3	92.3	87.6	87.6	
Graft survival									
HOPE	83.3	83.3	83.3	83.3	83.3	83.3	83.3	83.3	0.70
SCS	94.2	92.3	90.4	90.4	90.4	90.4	85.8	85.8	

[a]Overall and graft survival are presented as percentages (%) of surviving patients and grafts.
HOPE, hypothermic oxygenated machine perfusion; SCS, static cold storage.

In addition, the inverse probability weighting was used to balance the group of high-risk donors with respect to the common confounders. The data are presented in Supplemental Digital Content 4, http://links.lww.com/JS9/D94.

Discussion

The results of this randomized controlled trial support the notion that the routine use of hypothermic oxygenated perfusion of DBD liver grafts does not affect long-term posttransplant outcomes. Patient mortality and GS, as well as the rates of biliary complications (anastomotic, nonanastomotic strictures, and biliary fistulas), were similar between the two study arms in the general study population.

There are four randomized controlled trials comparing dHOPE with SCS in DBD donor liver transplantation. Three of the trials were designed to detect a difference in short-term outcome measures, namely peak ALT[12], early allograft dysfunction[13], and MEAF score[10]. Studies by Czigany *et al*.[12] and Ravaioli *et al*.[13] showed significant differences in both surrogates for adverse posttransplant outcomes. These analyses were restricted to the group of ECDs and are consistent with our previous findings that pointed towards significant differences in MEAF and Comprehensive Complication Index, but only in post-hoc analysis of high-risk donors (DRI > 1.7)[10]. Similar to our group, Schlegel *et al*.[16] failed to demonstrate a difference with respect to the primary outcome measure (complications graded by Clavien–Dindo of ≥ III within 1 year) in the general study population, whereas in a post-hoc analysis, the difference was detected in the general population for liver-related complications graded by Clavien–Dindo of ≥ IIIb. Our recent findings of significant differences in both mean time of patient survival and mean time to graft loss in high-risk donors support our previous statement and existing data from ECDs. Here, the benefit of approximately 5- and 6-month longer mean patient and GSs in high-risk livers in the dHOPE arm as compared to the SCS arm is shown.

Survival analysis showed no significant differences in patient or GS in either the general study population or in low-risk grafts, which is consistent with published data. In addition, the meta-analysis of randomized clinical trials published by Xie *et al*.[17] showed that both 1-year recipient and GS did not differ significantly between dHOPE and SCS. Based on the presented results, dHOPE may have a positive effect on both patient and GS in high-risk donors. Similar conclusions were drawn by Ravaioli *et al*.[13], who showed significantly higher 1-year GS in their ECD study. Such survival benefits in the general population of DBD livers have not been reported either in our study or in the previously published papers.

Similarly, the data on biliary complications were not found to be significant in any of the study groups. It can be noted that the reported proportions of biliary complications were unanimously in favor of dHOPE over SCS in all groups. However, as the study was underpowered with regard to biliary complications, statistical significance was not reached. Notably, no nonanastomotic biliary strictures were found in any of the grafts that underwent dHOPE. This may confirm the protective effect of the oxygenated perfusion on the biliary tree of the graft. Due to the lack of significance, these observations should not be taken for granted until more data are available. In addition, the patients were not routinely screened for biliary strictures, so some asymptomatic individuals may have been missed. Diagnostic modalities were employed only in symptomatic patients, and thus, the results are aimed at clinically relevant biliary

complications. However, as reported by Xie *et al*.[17], dHOPE significantly reduced the odds of nonanastomotic biliary strictures (OR = 0.28). In addition, the meta-analysis included the study by van Rijn *et al*.[9], who performed the trial only on livers obtained from donors after cardiac death, which are particularly prone to ischemic damage of the biliary tree. Our published observations seem to be important because nonanastomotic biliary strictures are considered to be *par excellence* the sequelae of ischemic biliary tree damage[9,18]. Therefore, there is a need for randomized trials on the routine use of dHOPE in DBD donors, powered with respect to biliary complications as a primary endpoint.

The presented randomized clinical trial is underpowered with respect to the clinical endpoints, which constitutes a major drawback when it comes to inferring long-term data. However, despite the limited number of cases in the high-risk graft group, significant differences in survival outcomes have been detected. A larger number of patients and an adequate power analysis for the long-term clinical outcome would increase the likelihood of reaching significance. As noted elsewhere, despite randomized design, patients in the dHOPE group fell into the lower Child–Pugh–Turcotte class. However, this would improve rather than worsen the effect of the procedure[10].

Conclusion

In conclusion, the long-term outcome data presented here suggest that the routine use of dHOPE may be beneficial for recipients of grafts from high-risk DBD. The present study does not provide any evidence for the benefits of dHOPE in low-risk DBD grafts.

Ethical approval

The study was conducted in accordance with the ethical standards of the Declaration of Helsinki of 1975, and the study protocol was approved by the Institutional Review Board of the Medical University of Warsaw (KB/6/2020).

Consent

All patients gave informed consent prior to enrolment.

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Author contribution

M.M.: conception and design, data acquisition, manuscript preparation, analysis, interpretation, and final approval. A.Z.: data acquisition, manuscript drafting, and final approval. P.R.: data acquisition, manuscript drafting, and final approval. M.K.: data acquisition, manuscript critical revision, and final approval. W.H.: data acquisition, manuscript critical revision, and final approval. Z.L.: data acquisition, analysis and interpretation of data, manuscript critical revision, and final approval. M.M.-P.: data acquisition, manuscript critical revision, and final approval. M.S.: data acquisition, manuscript critical revision, and final approval. B.S.: data acquisition, manuscript critical revision, and final approval. B.G.: data acquisition, manuscript critical revision, and final approval. M.K.: analysis and interpretation of data, manuscript critical revision, and final approval. M.G.: conception and design, interpretation of data, manuscript critical revision, analysis, interpretation, and final approval.

Conflicts of interest disclosure

The authors declare no conflictsof interest.

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Guarantor

Marcin Morawski, Michał Grąt.

Data availability statement

The data will be available upon reasonable request.

Provenance and peer review

The paper was not invited.

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