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Transplantation of Extended Criteria Donor Livers Following Continuous Normothermic Machine Perfusion Without Recooling

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Background. Traditional liver transplant strategies with cold preservation usually result in ischemia-reperfusion injury (IRI) to the donor liver. Regular normothermic machine perfusion (NMP) donor livers suffer IRI twice. Here, we aimed to introduce a novel technique called continuous NMP without recooling to avoid a second IRI and its application in livers from extended criteria donors. **Methods.** Seven donor livers transplanted following continuous NMP without recooling, 7 donor livers transplanted following standard NMP, and 14 livers under static cold storage (SCS) were included in this study. Perioperative outcomes were recorded and analyzed between groups. **Results.** During the NMP without a recooling procedure, all livers cleared lactate quickly to normal levels in a median time of 100 min (interquartile range, 60–180) and remained stable until the end of perfusion. In the NMP without recooling and standard NMP groups, posttransplant peak aspartate aminotransferase and alanine aminotransferase levels were both significantly lower than those in the SCS group ($P=0.0015$ and 0.016, respectively). The occurrence rate of early allograft dysfunction was significantly lower in the NMP without recooling group than in the SCS group ($P=0.022$), whereas there was no difference in the NMP group with or without recooling ($P=0.462$). **Conclusions**. Our pilot study revealed a novel technique designed to avoid secondary IRI. This novel technique is shown to have at least a comparable effect on the standard NMP, although more data are needed to show its superiority in the future.

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INTRODUCTION

Liver transplantation (LT) is considered the most curative and lifesaving treatment for patients with end-stage liver disease, primary liver cancer, and/or fulminant hepatic failure. With improvements in surgical methods, immunosuppressants, and infection controls, 1-y survival after LT can reach approximately 90%[1]; however, the shortage of donor organs limits the progression of LT and the access

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X.H. participated in conception and design. W.J., M.C., and X.H. provided administrative support. Z.C., C.C., and X.H. participated in provision of study materials or patients. Z.C. and T.W. participated in collection and assembly of data. T.W., Q.Z., C.H., and J.Y. participated in data analysis and interpretation. Z.C., T.W., C.C., and Q.Z. participated in manuscript writing. Z.C., T.W., C.C., Q.Z., X.H., J.Y., Y.M., C.H., X.H., W.J., and M.C. gave final approval of article.

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The authors declare no conflicts of interest.

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

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to transplantation.[2] In China, the number of patients on liver transplant waiting lists is increasing, and the organ shortage crisis is obvious.[3] The current supply of available donor livers is not enough to meet the needs of patients awaiting LT, resulting in thousands of deaths every year.[4] Therefore, expansion of the pool of available liver grafts is of great significance, and this demand has led to the wider use of extended criteria donors (ECDs).[5] ECD livers mainly come from donors with advanced age, steatosis, and medical comorbidities and from donation after circulatory death (DCD)[6]; however, ECD livers are usually associated with a higher risk of early allograft dysfunction (EAD) or even primary nonfunction (PNF).[7-9] Furthermore, the determination of whether a graft can be used for transplantation largely depends on a surgeon's subjective assessment of the graft's appearance. As a result, many potential donor organs remain unused.

Static cold storage (SCS) remains the standard method for organ preservation. It helps to reduce cellular physiological metabolism but fails to slow the destruction of cellular integrity. This issue may become more evident when using ECDs, as they are more vulnerable to ischemia-reperfusion injury (IRI).[10-12] Alternative preservation methods have been developed to reduce the impact of SCS and institute protective measures during preservation. Normothermic machine perfusion (NMP) for organ preservation has progressed significantly and has been proven to be effective in reducing graft injury, prolonging preservation, and increasing utilization in several clinical trials[13-15]; however, the liver is usually flushed with cold solution before implantation, which may cause double IRI to the organs due to the experience of going from cold to warm and then from warm to cold. Innovation is needed to improve the function of transplanted livers. Ischemia-free LT was designed to completely avoid ischemia injury during transplantation.[16] Our previous study demonstrated that ischemia-free LT has obvious advantages for reducing the rate of EAD in LT with steatotic livers[17]; however, its use is limited when the donor and the recipient are not in the same hospital, and for technical reasons, the liver should come from the donor after brain death. Therefore, we proposed a novel method to avoid double-warming ischemic injury by implanting donor livers directly following continuous NMP without recooling.[18] In this pilot study, we aimed to introduce this novel technique and its application in ECDs.

MATERIALS AND METHODS

All the procedures in this pilot study were performed in accordance with the 1964 Declaration of Helsinki and later versions. All the organs used in our study were from organ donation, and none were from executed prisoners. The study was approved by the Institutional Ethics Committee for Clinical Research and Animal Trials of the First Affiliated Hospital of Sun Yat-sen University, and an informed consent waiver was granted by the Institutional Ethics Committee given the minimal-risk nature of the study.

Definition of ECD and Study Participants

Donor livers were evaluated using the criteria reported in a previous review conducted by Vodkin and Kuo[7] with slight modifications (Figure 1A). In general, ECD livers mainly

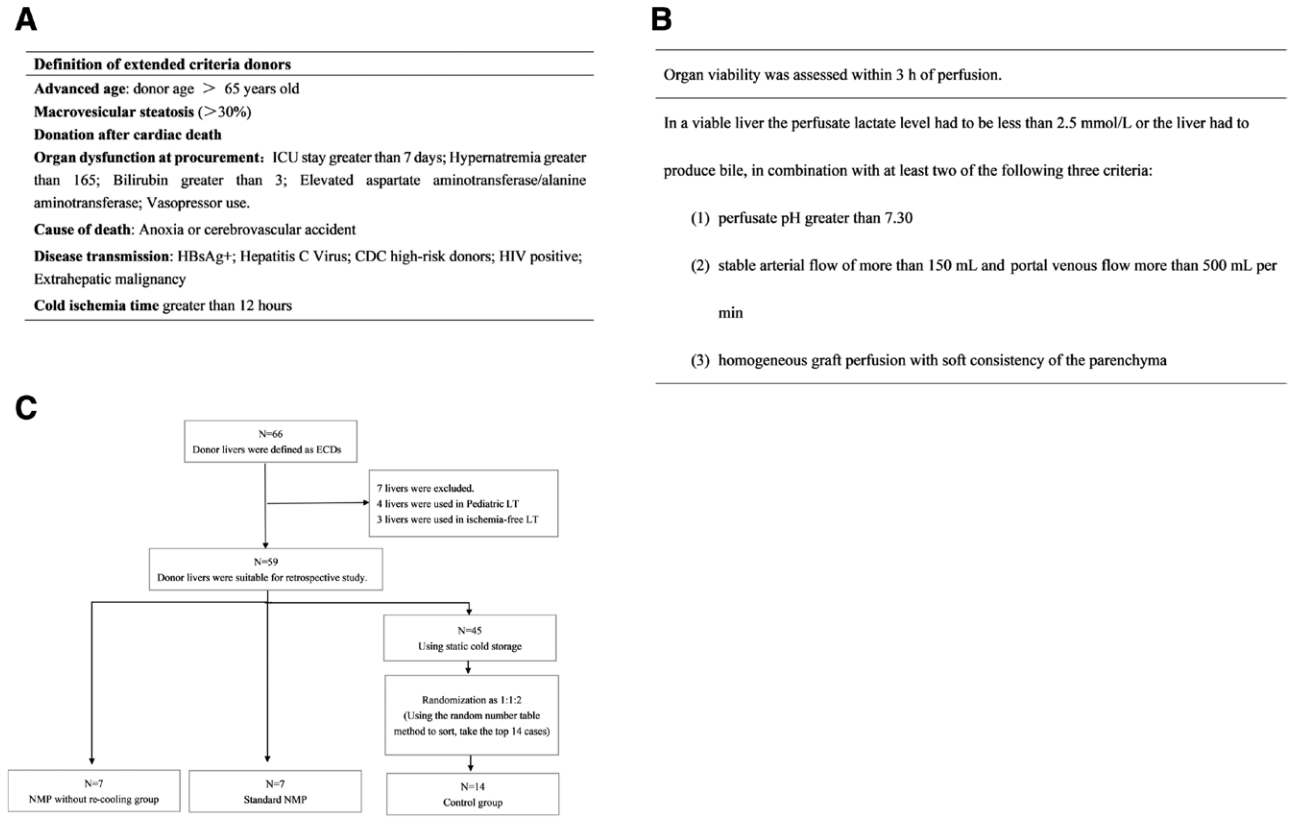


FIGURE 1. Information about ECD livers enrolled in our study. A, Definition of ECDs used in this pilot study. B, Criteria for viability assessment after perfusion. C, Study liver flowchart. DCD, donation after circulatory death; ECD, extended criteria donor; HBsAg, hepatitic B surface antigen; ICU, intensive care unit; LT, liver transplantation; NMP, normothermic machine perfusion.

come from donors with advanced age (>65 y old), steatosis (macrovesicular steatosis >30%), organ dysfunction at procurement, cause of death including anoxia or cerebrovascular accident, disease transmission, and long cold ischemia time (CIT; >12 h) and DCD. In total, from January 2019 to December 2020, 66 donor livers were defined as ECDs and transplanted in our center. The inclusion criteria of recipients were as follows: 18 to 75 y old, active on the waiting list for LT, and able to give informed consent. The exclusion criteria were as follows: multivisceral or combined organ transplantation; living donor LT; and high risk of transmitted infections. Seven donor livers were transplanted following continuous NMP without recooling, 7 donor livers were transplanted following standard NMP, and 14 cases of 45 livers transplanted after SCS were selected into the control group for comparison. The study liver flowchart is presented in Figure 1C. The donor liver index was used as a supplement to the assessment of donor livers.[19]

Description of LT Following Continuous NMP Without Recooling

We described the details of this technique in a previous publication.[18] Briefly, each liver was procured in a standard manner using the University of Wisconsin solution for cold preservation. After back table preparation, the donor liver was reprocessed in NMP to 37 °C following a flush with lactated Ringer's solution. The common bile duct was isolated, and a polyethylene tube was inserted for bile collection. Before perfusion, the suprahepatic inferior vena cava was blocked, and the infrahepatic inferior vena cava (IHIVC) was catheterized with a 32 to 34 Fr caval cannula for outflow to the organ reservoir of Liver Assist (Organ Assist, Groningen, the Netherlands). The portal vein (PV) via an interposition vascular graft (the donor 3 cm long iliac artery vein) and the splenic artery or gastroduodenal artery of the donor liver cannula were catheterized with a straight 24 Fr cannula and an 8 of 12 Fr arterial cannula, respectively, and were then connected to the device for perfusion. All cannulas were of sufficient length for liver transfer from the machine to the recipients' abdominal cavity.

The components of perfusate are presented in **Supplementary Table 1** (**SDC,** http://links.lww.com/TP/C286), and perfusion was adjusted depending on the positioning of the liver to maintain acid-base equilibrium and electrolyte balance. NMP was continuous from the time of preservation until the end of the vessel anastomosis (Figure 2B). An experienced surgeon oversaw the tubing placement and the connections to ensure the success of moving the liver from machine to recipient.

The donor liver was transplanted into recipients undergoing NMP circuiting in situ. The donor suprahepatic inferior vena cava was anastomosed with the counterpart of the recipient with an end-to-end anastomosis. The PV and hepatic artery (HA) were anastomosed with their counterparts in an end-to-end manner. These anastomoses were performed under continuous NMP of the allograft, as both the HA and the PV contain branches (the gastroduodenal artery and the interposition vascular graft, respectively) for perfusion. Afterward, the clamps on the PV and HA were removed, and the blood supply was recovered. Subsequently, NMP was stopped, and the interposition vascular graft and the splenic artery were ligated (Figure 2A). The IHIVC cannula was then removed, and the donor's IHIVC was anastomosed to the recipient's IHIVC or ligated according to the surgical procedure (cava replacement or piggy-back, respectively). The common bile duct was end-to-end anastomosed after removal of the draining tube.

Liver Viability Assessment

Serial perfusate, bile, and tissue samples were taken at regular time intervals. For a liver to be considered, the lactate level of the perfusate needed to be <2.5 mmol/L within 3 h of perfusion, and the acid-base equilibrium and electrolyte balance had to be stably maintained throughout the perfusion process. In addition, maintenance of stable HA and PV flows was achieved before implantation (Figure 1B).[20]

Outcome Measurements

Perioperative outcome measurements, including intraoperative transfusions, blood loss, assessment of liver graft function (PNF and EAD), postoperative transaminases and bilirubin, intensive care unit stay, vascular and biliary complications, acute kidney injury, and 30- and 90-d graft survival, were collected and analyzed.

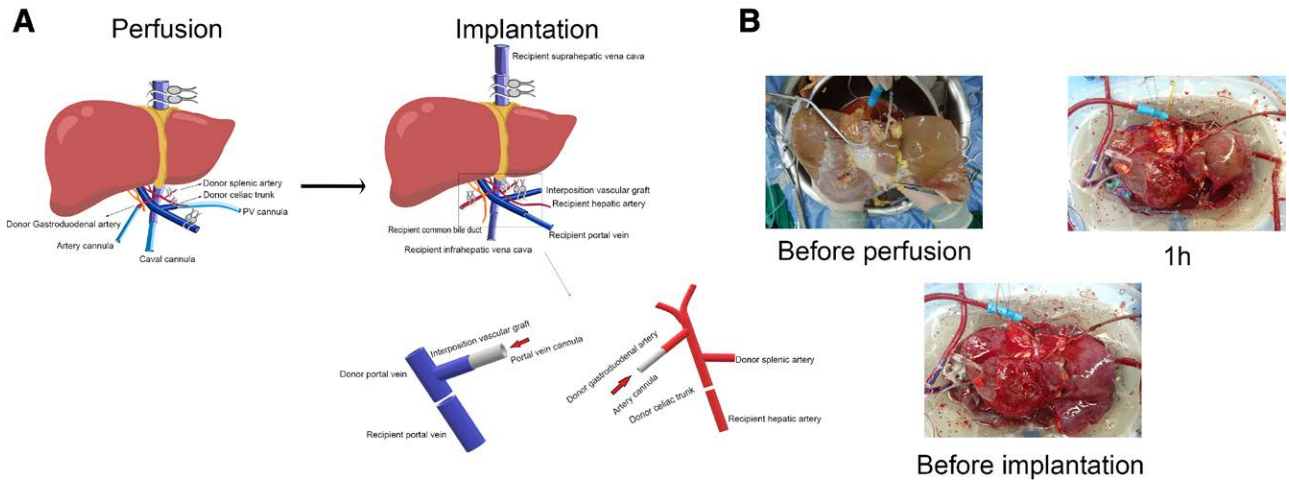


FIGURE 2. Schematic diagram of NMP without recooling and changes in liver appearance during perfusion. A, Diagram of perfusion and implantation. B, The appearance of the liver before perfusion, with 1 h of perfusion, and before implantation. NMP, normothermic machine perfusion; PV, portal vein.

Statistical Analysis

Continuous parameters, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase, CIT, NMP time, donor liver index, model for end-stage liver diseases, international normalized ratio (INR), and lactate dehydrogenase, are presented as the mean ± SE. Continuous parameters were compared with the ANOVA. The chi-square test or Fisher exact test was used to compare categorical parameters. All statistical analyses of the data were performed with SPSS version 26.0. A $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Baseline Characteristics of Donors and Recipients

The baseline characteristics of the donors are presented in Table 1. The livers used in this pilot study consisted of 19 donor after brain death and 9 DCD cases. The mean donor ages were 45.86 ± 3.58, 30.71 ± 5.81, and 40.79 ± 4.29 y in the NMP without recooling group, the standard NMP group, and the SCS group, respectively. In the assessment of donor organ function, the laboratory test results, including the concentrations of sodium, creatine, hemoglobin, AST, ALT, and bilirubin, were similar in all groups ($P > 0.05$). All transplanted livers used in this study are presented in Figure 3. Baseline data of recipients were also compared, as presented in Table 1. The majority (n = 26, 92.9%) of recipients were men, and the mean donor ages of enrolled recipients were 50.43 ± 2.89, 50.14 ± 5.34, and 53.86 ± 3.00 y in the NMP without recooling group, the standard NMP group, and the SCS group, respectively. The comparisons of preoperative conditions, including ALT, INR, bilirubin, model for end-stage liver diseases, CIT, NMP time, and the donor risk index, showed similar results in all groups($P > 0.05$).

Perfusion Parameter Assessment

Dynamic changes in perfusion parameters during the NMP without the recooling procedure in 7 donor livers are presented in Figure 4. The median total preservation time was 320 min (interquartile range [IQR], 270–480). During the NMP procedure, all livers cleared lactate to normal levels quickly[21] in a median time of 100 min (IQR, 60–180) and maintained stable lactate levels until the end of perfusion (Figure 4D). The Pco_2, HCO_3^-, and pH levels also remained stable within the normal range throughout the whole perfusion (Figure 4A–C). In addition, the HA and PV flows were stable (≥150 mL/min and 0.5 L/min, respectively), as presented in **Figure S1** (**SDC,** http://links.lww.com/TP/C286). NMP without recooling can achieve a similar result as standard NMP in alleviating liver injury and reduce the rate of EAD.

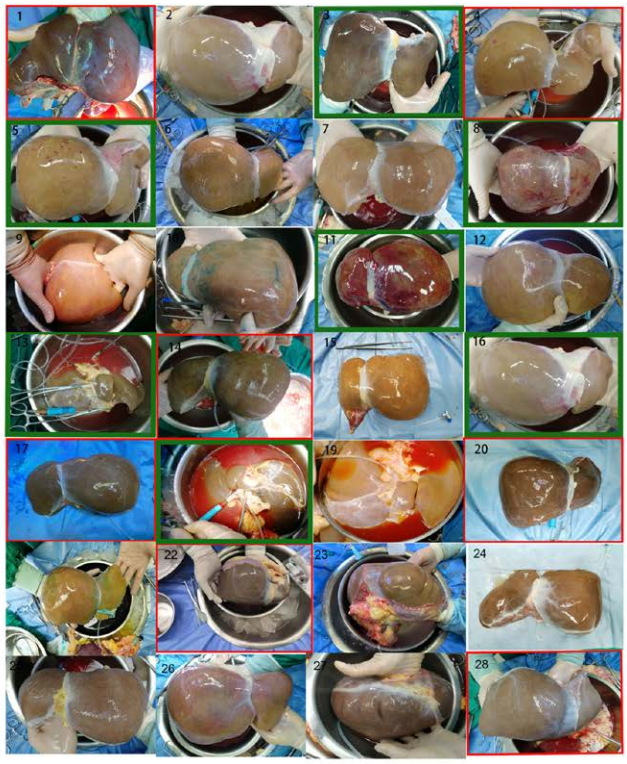
Perioperative data comparisons between the NMP without recooling, standard NMP, and SCS groups are shown in Table 2. Intraoperative transfusion was significantly more frequent in the NMP without recooling group and was similar between the standard NMP and SCS groups ($P = 0.013$). Blood loss was similar among the 3 groups ($P = 0.509$). In comparisons of postoperative liver function recovery, posttransplant peak AST and ALT were both significantly lower in the NMP without recooling and standard NMP groups than in the SCS group ($P = 0.0015$ and 0.016, respectively), whereas no differences were found between the NMP without recooling and standard groups ($P = 0.814$ and 0.815, respectively; Figure 5A). The posttransplant INR, peak bilirubin, γ-glutamyl transpeptidase, creatine, and lactate dehydrogenase levels among the groups were similar ($P = 0.222$, 0.922, 0.152 0.159, and 0.257, respectively; Figure 5B and C). Dynamic changes between groups in the first 14 d posttransplant are presented in Figure 5D through G.

TABLE 1.

Baseline data comparison between NMP without recooling and SCS groups

	NMP without recooling (N = 7)	Standard NMP (N = 7)	SCS (N = 14)	*P*
Donor age, y	45.86 ± 3.58	30.71 ± 5.81	40.79 ± 4.29	0.157
Donor sex, male, n (%)	4 (57.1)	5 (71.4)	8(57.1)	0.799
Donor type DBD, n (%)	4 (57.1)	3(42.8)	12 (85.7)	0.110
Sodium (mmol/L)	153.70 ± 3.98	151.31 ± 5.52	154.09 ± 3.85	0.899
Creatine (μmol/L)	107.43 ± 14.60	113.35 ± 36.19	142.05 ± 22.47	0.568
Hemoglobin (g/L)	8.81 ± 0.69	11.33 ± 0.98	10.22 ± 0.66	0.136
AST (U/L)	166.26 ± 55.21	72.29 ± 29.31	362.85 ± 293.58	0.688
ALT (U/L)	120.17 ± 36.80	30.51 ± 8.94	74.00 ± 25.37	0.144
Bilirubin (mmol/L)	24.49 ± 8.21	37.38 ± 21.11	22.49 ± 5.73	0.606
Recipient age, y	50.43 ± 2.89	50.14 ± 5.34	53.86 ± 3.00	0.707
Recipient sex, male, n (%)	7 (100)	6 (85.7)	13 (92.8)	0.584
Pretransplant ALT (U/L)	23.29 ± 6.28	125.86 ± 83.00	52.64 ± 15.14	0.240
Pretransplant AST (U/L)	39.57 ± 13.69	144.14 ± 56.82	82.79 ± 20.32	0.122
Pretransplant INR	1.77 ± 0.33	2.09 ± 0.36	1.57 ± 0.19	0.393
Pretransplant bilirubin (mmol/L)	143.20 ± 63.69	238.40 ± 106.61	191.44 ± 65.68	0.759
MELD	23.00 ± 5.35	22.71 ± 4.77	19.07 ± 3.02	0.722
CIT, h	7.57 ± 0.95	6.86 ± 0.94	6.79 ± 0.42	0.702
NMP, h	5.60 ± 0.53	5.58 ± 0.60	–	0.659
Donor risk index	2.02 ± 0.21	1.75 ± 0.15	1.73 ± 0.13	0.405

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CIT, cold ischemia time; DBD, donor after brain death; INR, international normalized ratio; MELD, model for end-stage liver disease; NMP, normothermic machine perfusion; SCS, static cold storage.



All donor livers enrolled in this study	
Number	Reasons for ECD
1	Anoxia; Cold ischemia time > 12h; donation after cardiac death
2	Donation after cardiac death.
3	Cerebrovascular accident; cold ischemia time > 12h.
4	Cerebrovascular accident; donation after cardiac death; cold ischemia time > 12h.
5	Hypernatremia (173.7mmol/L); cold ischemia time > 12h.
6	HbsAg (+).
7	HbsAg (+).
8	Donation after cardiac death.
9	Macrovesicular steatosis (40%).
10	Cerebrovascular accident; HbsAg (+).
11	Bilirubin > 3 mg/dL.
12	Hypernatremia (166mmol/L); donation after cardiac death; cold ischemia time > 12h.
13	Cerebrovascular accident; donation after cardiac death;
14	Bilirubin > 3 mg/dL; AST: 239 U/L
15	Macrovesicular steatosis (65%).
16	Donation after cardiac death.
17	Cerebrovascular accident; macrovesicular steatosis (50%); donation after cardiac death.
18	Cerebrovascular accident; hypernatremia (166.7mmol/L).
19	Hypernatremia (165.1mmol/L).
20	Anoxia; ALT: 284 U/L, AST: 145 U/L.
21	Hypernatremia (175mmol/L); HbsAg (+).
22	Cerebrovascular accident; ALT: 204 U/L, AST: 410 U/L.
23	Cerebrovascular accident; macrovesicular steatosis (40%).
24	HbsAg (+).
25	ALT: 284 U/L, AST: 145 U/L; donation after cardiac death.
26	HbsAg (+).
27	Cerebrovascular accident; hypernatremia (167mmol/L);
28	Anoxia; hypernatremia (165.2mmol/L);

FIGURE 3. Study liver photographs. The figure shows all 28 livers used in this study. The red frames designate organs under NMP without recooling, the green frames designate organs under standard NMP, and the rest are under SCS. The table shows the reasons for every donor liver for ECDs. ALT, alanine aminotransferase; AST, aspartate aminotransferase; ECD, extended criteria donor; HBsAg, hepatitic B surface antigen; NMP, normothermic machine perfusion; SCS, static cold storage.

Biopsies of samples taken after reperfusion showed spotty necrosis in the standard NMP group, whereas no signs of necrosis were observed in the other 2 groups ($P = 0.021$). In addition, the occurrence rate of EAD was significantly lower in the NMP without recooling group than in the SCS group (0% versus 50%; $P = 0.022$), whereas it was similar between the NMP without recooling and standard NMP groups (0% versus 28.6%; $P = 0.231$). One patient suffered from PNF in the SCS group (7.14%), but the occurrence rate was not significantly different from those in the other groups ($P = 0.595$). The occurrence rates of posttransplant complications, including biliary leakage, anastomotic biliary stricture, HA complications, and acute kidney injury, were similar in all groups ($P = 0.595$, 0.211, 0.595,

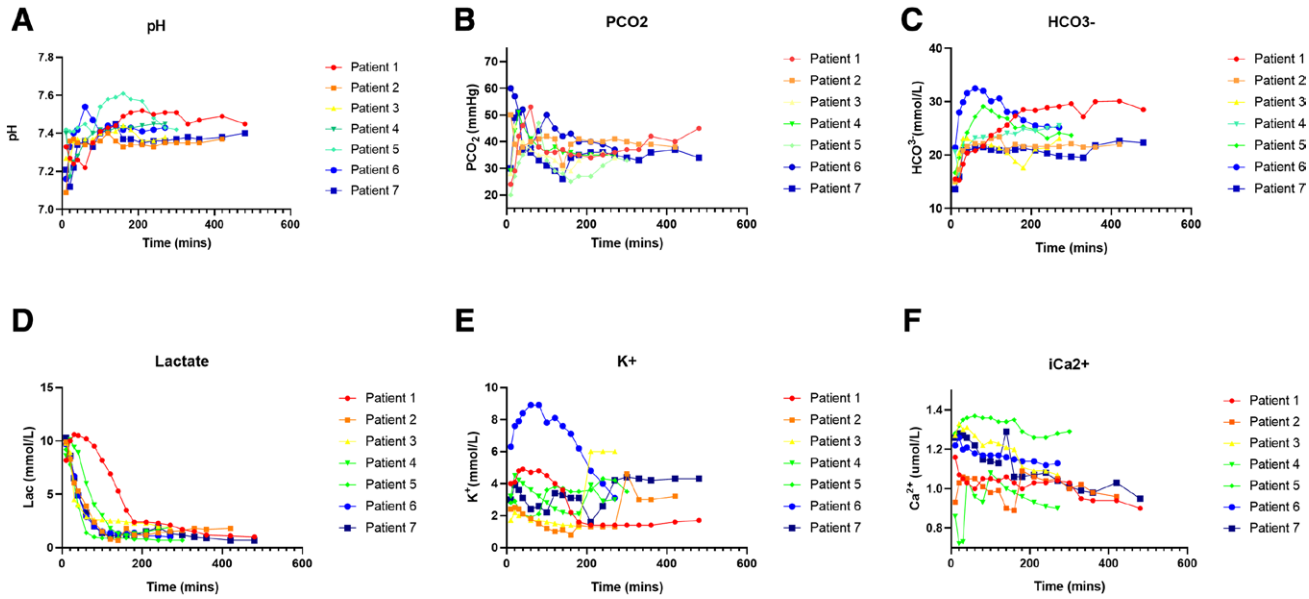


FIGURE 4. Parameter changes during perfusion in NMP without recooling: (A) pH, (B) partial pressure of carbon dioxide, (C) bicarbonate concentration, (D) lactate concentration, (E) potassium concentration, and (F) isolated calcium concentration. Lac, lactate; NMP, normothermic machine perfusion.

TABLE 2.

Perioperative data comparison between NMP without recooling and control groups

	NMP without recooling (N = 7)	Standard NMP (N = 7)	SCS (N = 14)	*P*
Intraoperative transfusions (U)	14.44 ± 2.71	5.65 ± 1.91	5.61 ± 1.71	0.013
Blood loss (mL)	3442.86 ± 496.59	1842.86 ± 461.81	2678.57 ± 883.50	0.509
Peak AST (U/L)	783.86 ± 168.30	980.29 ± 228.74	2949.29 ± 559.51	0.006
Peak ALT(U/L)	269.71 ± 43.22	334.57 ± 62.57	980.64 ± 185.95	0.007
INR	1.29 ± 0.78	1.06 ± 0.04	1.27 ± 0.09	0.222
Peak bilirubin (mmol/L)	110.40 ± 41.58	87.40 ± 17.42	97.52 ± 33.24	0.922
Peak GGT (U/L)	382.57 ± 88.13	231.00 ± 54.28	387.50 ± 42.30	0.152
Peak creatine (μmol/L)	163.83 ± 32.16	99.29 ± 19.85	117.07 ± 15.11	0.159
LDH (U/L)	7253.00 ± 2226.58	3169.86 ± 637.16	6544.14 ± 1465.90	0.257
Spotty necrosis after reperfusion, n (%)	0	3 (42.8)	0	0.021*
EAD, n (%)	0	2 (28.5)	7 (50)	0.089**
PNF, n (%)	0	0	1 (7.1)	0.595
Biliary leakage, n (%)	0	0	1(7.1)	0.595
Anastomotic biliary stricture, n (%)	0	1 (7.1)	0	0.211
Hepatic artery complications, n (%)	0	0	1(3.6)	0.595
Acute kidney injury, n (%)	2 (28.5)	1 (14.2)	2 (14.2)	0.819
30-d mortality, n (%)	1 (14.2)	0	2 (14.2)	0.571
90-d mortality, n (%)	1 (14.2)	0	2 (14.2)	0.571

*$P = 0.051$, comparison between NMP without recooling and standard NMP.
**$P = 0.022$, comparison between NMP without recooling and SCS; $P = 0.462$, comparison between NMP without recooling and standard NMP.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; EAD, early allograft dysfunction; GGT, γ-glutamyl transpeptidase; INR, international normalized ratio; LDH, lactate dehydrogenase; NMP, normothermic machine perfusion; PNF, primary nonfunction; SCS, static cold storage.

and 0.819, respectively). The 30- and 90-d mortality rates were also not significantly different among all groups ($P = 0.571$ and 0.571, respectively).

DISCUSSION

Organ shortage remains the main obstacle to the growth of transplantation and the main cause of waiting list death. In China, >300 000 patients are on the waiting list, whereas only approximately 10 000 transplantations are performed per year.[22] Effective procedures or alternative strategies are urgently needed to solve this crisis.[23] We previously proposed a novel method called continuous NMP without recooling to avoid double IRI to improve the utilization of ECD livers; in this pilot study, we introduced this novel technique and its application in ECDs.

The definition of ECD has been described in previous studies.[24,25] DeLemos and Vagefi[26] summarized the characteristics of various types of ECD liver allografts and suggested that the careful selection of ECD liver donors and appropriate recipient matching should be completed before LT for better survival. The characteristics of these 28 donated livers are presented in Figure 1C. We determined that half (14 of 28, 50%) of the livers in our study were combined for several reasons.

Machine perfusion techniques have been proven to be effective in preserving abdominal organs in clinical trials.[27-29] Studies on whether NMP has the potential to expand the donor pool are ongoing. In St. Vincent's Hospital, Dhital et al reported a case series of heart transplantations using DCD organs and showed that a portable ex vivo organ perfusion platform could be used

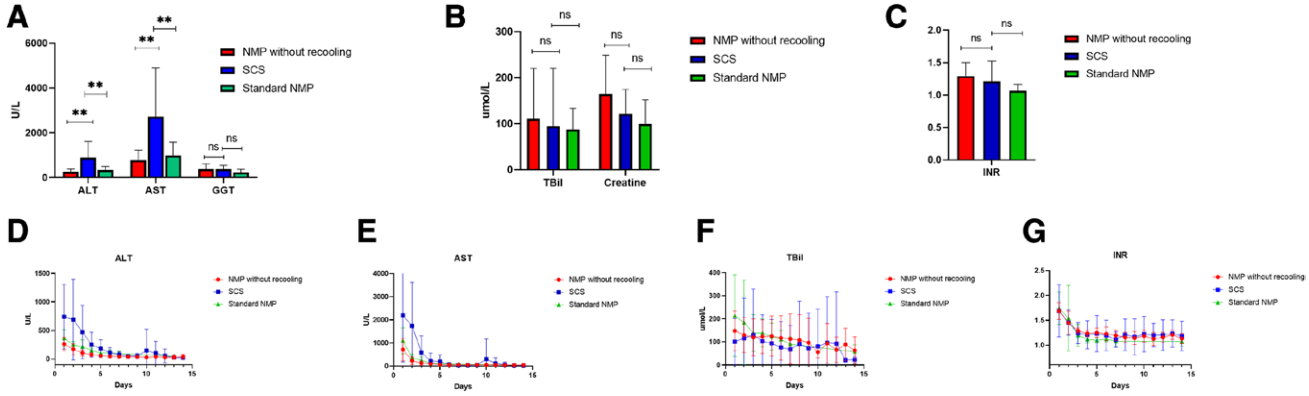


FIGURE 5. Comparison of liver function recovery between groups. Comparison of ALT, AST, and GGT (A); TBil and creatine (B); and INR (C) at 7 d posttransplantation and dynamic changes in ALT (D), AST (E), TBil (F), and INR (G) between groups at 14 d posttransplantation. ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutamyl transpeptidase; INR, international normalized ratio; NMP, normothermic machine perfusion; ns, nonsignificant; SCS, static cold storage; TBil, total bilirubin.

successfully.[30] A pilot study conducted by Mergental et al[20] showed that NMP may increase organ availability for LT. They also demonstrated that NMP had potential in the transplantation of discarded livers in their phase 2 trial.[21] In our study, we observed that the peak levels of ALT and AST were significantly lower in both the standard NMP group and the NMP without recooling group; however, in traditional procedures, cold solution is used to flush liver grafts before implantation to eliminate high potassium concentrations in the perfusate, which may cause another IRI.[31] We observed that 3 of 7 donor livers had spotty necrosis after reperfusion, and 2 of 7 recipients still experienced EAD in the standard NMP group. The reason might be that in standard NMP, the donor liver may experience hepatocellular injury after double IRI[32]; however, because of the small sample size, further investigations are needed. The innovations and highlights of our technology are that this technique is designed to avoid post-NMP cooling of the liver, a continuous blood supply is provided for the donor liver from the beginning of perfusion to the end of implantation, and there is no need for cold perfusion fluid flushing. Observations and improvements in transplant perfusion indexes are the major advantages of NMP.[15,33] Once the liver meets the qualification criteria, transplantation can be performed as soon as possible.[34] The lactate level was a key indicator of concern during perfusion. Kim et al[35] suggested that evaluated lactate concentrations were associated with short-term prognosis after LT. Golse et al demonstrated the predictive value of arterial lactate concentration for primary graft dysfunction.[36] In our study, all perfused organs cleared lactate quickly to normal levels in a median time of 100 min (IQR, 60–180) and remained stable until the end of perfusion. In the NMP without recooling group, no patients developed EADs; this result is consistent with current studies. Perfusion time is another key indicator. A longer perfusion time allows us to select recipients and make adequate preoperative preparations. Based on our experience, 4 to 8 h of perfusion may be enough for functional assessment and nutrient supplementation. Due to the accumulation of metabolic waste during perfusion, high-risk organs probably do not benefit from long-term perfusion. Eshmuminov et al[37] were able to preserve discarded livers under NMP for 1 wk, although not for transplantation. The maximum NMP duration for ECD livers is another ongoing research area.

EAD is a life-threatening complication of LT and mainly results from IRI.[38] This condition has been defined as a delayed decrease in transaminase levels and hyperbilirubinemia in the early posttransplant period and has been associated with graft loss and short-term mortality.[39] ECD livers are more vulnerable to IRI, which has an impact on EAD occurrence.[25] Bellini et al[12] reported in their review that NMP mitigates EAD in ECD livers. In our study, no patients developed EADs in the NMP without recooling group, whereas the incidence of EAD occurrence in the SCS group was 50%. Our results revealed that NMP without recooling has the potential to reduce the occurrence rate of EAD compared with SCS. PNF is the most severe complication and is associated with graft failure requiring emergency retransplantation.[40] Currently, there is no clear definition for PNF. Its characteristics include progressive severely imbalanced liver enzymes, severe coagulopathy, inability of the liver to produce bile, lactic acidosis, hypoglycemia, and multiorgan failure.[41,42] We adopted the definition of PNF that necessitated retransplant within 7 d post-LT.[43] In our study, 1 patient developed PNF in the SCS group. Because of the small sample size and low incidence, it is difficult to draw comparable conclusions in this study. More studies are needed to confirm the potential superiority of NMP without recooling regarding PNF in livers.

Our study has limitations. First, the study is a pilot study from a single center with a small sample size. Therefore, larger samples are needed to confirm the results. Second, to eliminate selection bias, a randomized clinical trial is needed. Third, for future studies, the occurrence rate of late postoperative complications and the 3- and 5-y overall survival rates should be calculated to obtain more robust conclusions.

Conclusion

In conclusion, our pilot study proposed a novel technique designed to avoid secondary IRI, and this novel technique was shown to have a comparable result with the standard NMP. Therefore, this technique is worth promoting. Larger sample data sets in the future will help to draw more accurate conclusions.

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