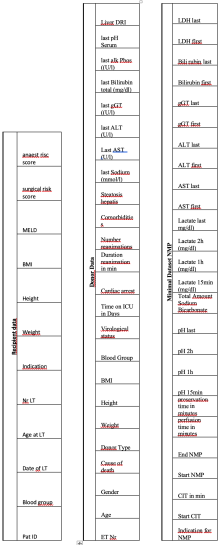
Supplemental material

Table S1: Selection of laboratory parameters assessed in the perfusate during NMP

Glucose
Urea
Creatinine (enzym.-IDMS)
Total protein
Bilirubin total
Sodium
Chloride
Potassium
Magnesium
Calcium
Phosphate inorganic
Aspartate transaminase (AST)
Alanine transaminase (ALT)
Gamma-Glutamyltranferase (gGT)
Alkaline Phosphatase
Cholinesterase
Lactate-Dehydrogenase(LDH)
C-reactive Protein (CRP)
L-Lactate
Osmolality
Colloid osmotic pressure
Activated Partial Thromboplastin time (aPTT)
Quick test (PT)
Fibrinogen
Thrombin time
Antithrombin III (Antigen)
Anti-Factor Xa-Activ direct/indirect
von Willebrand Factor-Antigen
Blood panel with reticulocytes, and differential blood count
Interleukin-6 (IL-6)

ALT, Alanine transaminase; AST, Aspartate transaminase;

Table S2: Minimal data set including recipient data, donor data as well as data regarding NMP course and perfusate analyses



DRI, donor risk index; alk Phos, Alkaline Phosphatase; gGT, Gamma-Glutamyltranferase; ALT Alanine transaminase; AST, Aspartate transaminase; LT, liver transplant, BMI, body mass index; ET, Eurotransplant; alk Phos, Alkaline Phosphatase; ICU, intensive care unit; NMP, normothermic machine perfusion, CIT cold ischemia time; LDH, Lactate-Dehydrogenase; MELD model of End-stageLiver disease.

Section 2

Training of perfusionists and surgical staff

In a next step, we established a center specific step-by-step protocol for setting up the NMP device. Based on guidelines provided by the company, a document was prepared highlighting the crucial steps including pitfalls observed during the hands-on sessions as well as the first cases. The reproducibility of the protocol was evaluated by employing surgical fellows as well as students for setting up the hardware and disposables and priming of the machine under observation.

Perfusionists and surgical staff were considered the user group who would perform the setting up of the NMP device, mounting the disposable set, calibration and conditioning of the system and initiating of NMP. The entire surgical transplant faculty, surgical residents and perfusionists received a 2-day hands on training under guidance of a manufacturing company product specialist and a surgeon experienced with 100+ NMPs (AW). In addition to a repeat training of the device setup, back-table NMP specific preparation and initiation of NMP, relevant pitfalls and other observations form the previous experience with NMP were discussed. Attendance was certified.

Case studies

Case 1: A 34 years old male recipient suffering from secondary sclerosing cirrhosis was referred to our center for recurring massive gastrointestinal bleeding from a varix from a cholecysto-jejunostomy performed in his childhood. Bleeding were neither interventionally nor surgically controllable, and up to 33 packed red-cells/24h were required to maintain hemodynamic stability. The portal vein was completely thrombosed. The patient was granted high urgency status for liver-transplantation. NMP was used to enable the surgical team to safely perform the highest-risk surgical procedure, including the preparation of a varices for portal revascularization. NMP was uneventful during a 7h 35min hepatectomy and vessel preparation. Total duration of the procedure was 12h 17min, total preservation-time was 12h 36min (6h 42min CIT, 5h 52min NMP). The patient was hemodynamically stable over the entire procedure. Initial liver function was good and no further episodes of GI-bleedings occurred. The patient was released on day 22 posttransplant in good clinical condition. The subjective advantage of NMP in this case was the unlimited time allowed for the delicate surgical procedure.

Case 2: In another case, NMP of an extended right liver split was necessary due to a competing surgically highly demanding pediatric left lateral split liver transplantation. After the back-table ex situ liver split was performed, the remaining right extended lobe was placed on NMP, while the left lateral split graft was successfully transplanted into a 4-month old boy with multiple anatomical variations. Since the extended right liver grafts had been allocated to an equally surgically complex 50 years old recipient for retransplantation, simultaneous surgery was deemed impossible with respect to resources

and qualified staff. Perfusion parameters were within normal limits over the entire observation period. Lactate levels decreased from 105mg/dl to 8mg/dl over 11hours and 43min, pH-value remained within physiological range after attribution of 10ml sodium bicarbonate substitution. After 713 min of NMP time and a total preservation time of 1250 min (537min CIT) the graft was reperfused. Immediate graft function was optimal (AST from 163 U/L on day 1 to 57 U/L on day 7, Bilirubin from 4.43 U/L on day 1 to 3.32 U/L on day 7 and an INR of 1.2 on day 7). No postoperative complications related to the liver occurred while other complications delayed rehabilitation in this critically ill patient. The patient eventually recovered and was transferred to a rehabilitation center on day 49 after retransplantation. He continues to do well.

Troubleshooting

We herein present the most frequently encountered problems as well as the specific management;

Alarm “Low Inferior vena cava flow” (number 380): A) early after perfusion start: A low flow rate was observed when a significant bleeding either from a biopsy or a vascular leak occurred. Hereby, the problem was solved by sutures or vascular clips on the bleeding side. Furthermore, a kinking of a cannula or an insufficient moistening of the sensor may trigger this. Correct repositioning of the cannula was sufficient with good final result. B) at the ICU: A kinking of the IVC-tube leading from the IVC cannula. In order to prevent a re-kinking in this case, a notched syringe was placed.

Alarm “Low arterial flow rate” (number 390): This was encountered early after perfusion start with the liver on board due to a kinking of the artery. Correct positioning was sufficient to ensure correct perfusion.

Alarm “Permanent operation of the ascites pump” (number 300): This was encountered in 2 cases. Sufficient wetting of the ascites sensor solved the problem. However, the liver “on board” was inspected for any blood leaks.

Switch to “Liver-on board mode” during priming of the system: Initially we encountered a switch into operating mode while priming of the system and before connection of the organ. We realized that elevated pressure on the reservoir simulated enhanced arterial pressure and let to the switch into operational mode. At our hospital, 1 unit of red packed cells amounts to a volume of 280ml. This is a higher volume/unit compared to other centers and may cause this error. Stop of perfusion during priming solved this issue.