

## **New guidelines for modification of liver transplantation process**

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At present, hepatic grafts can be preserved in UW solution by the static preservation for less than 12 hours for good outcome of liver transplantation surgery (1). On the basis of research results from isolated animal perfused livers, we suggest that both a safe preservation of hepatic grafts is possible (for up to 18 hours) and that contemporary used liver transplantation process have to be modified according to the following guidelines:

**The first step.** One hour prior to liver procurement, indomethacin should be given to the donor, in order to reduce graft manipulation injury (2). The liver cannot be exposed to ice during graft procurement. Only subnormothermic solutions (e.g., simple physiologic saline at 10°C) can be applied on the surface of the graft in the donor. Rapid cooling by iced water during procurement led to a marked deterioration of microperfusion in peripheral and subcapsular regions during cold reperfusion (3). In line with this finding we found that preservation of rat livers in physiologic saline at the initial temperature of 10 °C was better than preservation at the initial temperature of 4 °C (4). Further, exposure of rat livers to subnormothermia had beneficial effect on liver function upon reperfusion even after 24 hours of cold storage. (5). In addition, subnormothermia is beneficial also for machine-driven perfusion of liver preservation (6-8).

**The second step.** Conventional one is appropriate.

**The third step.** After allocation of the graft to the transplantation center, it can be stored in UW solution for up to 18 hours (9).

**The fourth step.** After the preservation period the liver is extremely sensitized to rewarming injury and the injury can be prevented by short-term oxygenated normothermic reperfusion (9-11). In humans, the duration of ischemic rewarming during graft implantation is associated with the severity of recurrent hepatitis C. (12). Therefore the graft has to be machine perfused. Prior to machine reperfusion, it is needed to washout the liver through the portal vein with 37°C Ringer lactate solution (13). After then, the graft can be implanted to the recipient.

Using the above mentioned guidelines, there should be no primary graft nonfunction and biliary strictures after liver transplantation.

## **REFERENCES**

1. Adam R, Bismuth H, Diamond T, Ducot B, Morino M, Astarcioglu I, Johann M, Azoulay D, Chiche L, Bao YM, et al. Effect of extended cold ischaemia with UW solution on graft function after liver transplantation. *Lancet*. 1992 5;340:1373-1376.
2. Schemmer P, Enomoto N, Bradford BU, Bunzendahl H, Raleigh JA, Lemasters JJ, Thurman RG. Activated Kupffer cells cause a hypermetabolic state after gentle in situ manipulation of liver in rats. *Am J Physiol Gastrointest Liver Physiol*. 2001;280:G1076-1082.
3. Drews G, Deckert F, Witzigmann H, Hauss J, Spiegel HU. Effect of rapid cooling on microperfusion of donor livers. *Zentralbl Chir*. 1998;123:280–284. (in German)
4. Kebis, A., Kukan, M., 2006. Effect of conductive heat transfer on cold ischemia-reperfusion injury of isolated rat liver. *Čes. a Slov. Gastroent. a Hepatol.*, 60(1):36-42 (in Slovak).
5. Kebis A, Kukan M, Grančič P, Jakubovský J. A novel way of liver preservation improves rat liver viability upon reperfusion. *J Zhejiang Univ Sci B*. 2007;8:289-295.
6. Fujita S, Hamamoto I, Nakamura K, Tanaka K, Ozawa K. *Nihon Geka Hokan*. *Nihon Geka Hokan*. 1993 Sep 1;62(5):228-40.
7. Vairetti M, Ferrigno A, Rizzo V, Richelmi P, Boncompagni E, Neri D, Freitas I, Cillo U. Subnormothermic machine perfusion protects against rat liver preservation injury: a comparative evaluation with conventional cold storage. *Transplant Proc*. 2007;39:1765-1767.
8. Vairetti M, Ferrigno A, Carlucci F, Tabucchi A, Rizzo V, Boncompagni E, Neri D, Gringeri E, Freitas I, Cillo U. Subnormothermic machine perfusion protects steatotic livers against preservation injury: a potential for donor pool increase? *Liver Transpl*. 2009;15:20-29.
9. Vajdová K, Smreková R, Mislanová C, Kukan M, Lutterová M. Cold-preservation-induced sensitivity of rat hepatocyte function to rewarming injury and its prevention by short-term reperfusion. *Hepatology*. 2000;32:289-296.
10. Kukan M, Haddad PS. Role of hepatocytes and bile duct cells in preservation-reperfusion injury of liver grafts. *Liver Transpl*. 2001;7:381-400. Review.
11. Kukan M, Vajdová K, Lutterová M, Kristek F, Kebis A, Kuba D, Horecký J. Improvement of rat liver function by energy repletion after the preservation

period: implications for hepatic graft management. *Cryobiology*. 2001;43:303-309.

12. Baron PW, Sindram D, Higdon D, Howell DN, Gottfried MR, Tuttle-Newhall JE, Clavien PA. Prolonged rewarming time during allograft implantation predisposes to recurrent hepatitis C infection after liver transplantation. *Liver Transpl*. 2000;6:407-412.

13. Post S, Rentsch M, Gonzales AP, Palma P, Otto G, Menger MD. Importance of the first minutes of reperfusion in hepatic preservation injury. *Transplant Proc* 1995;27:727-728.